endo bridge®
2019
Bridging the World of Endocrinology
24-27 October 2019
Regnum Carya Convention Center, Antalya - Turkey

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## SCIENTIFIC PROGRAM

### Friday, 25 October 2019

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<td>Modern ways to visualise pituitary tumors - Mark Gurnell</td>
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<td>What is new in the diagnosis and management of acromegaly - Sebastian Neggers</td>
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<td>Autoimmune thyroid disease - mechanistic update - Monica Marazuela</td>
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<td>Immune check - point inhibitors and endocrine dysfunction</td>
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<td>Central mechanisms in control of body weight and their implications for obesity treatment - Uberto Pagotto</td>
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<td>How low should LDL be according to guidelines? - Connie Newman</td>
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<td>Pituitary Diseases and Bone - Andrea Giustina</td>
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<td>Osteoporosis in relation to pregnancy and lactation - Barbara Obermayer - Pietsch</td>
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<td>New modalities in osteoporosis - Joy Wu</td>
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<td>Closing comments and adjourn</td>
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Accredited by the European Accreditation Council for Continuing Medical Education (EACCME).
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<td>Setting a path for success in type 2 diabetes management</td>
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<td>Clinical Experience with SOLIQUA: Innovative Fixed Dose Combination Basal Insulin and GLP1-RA</td>
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<td>0 - 20 / An unusual case of Familial Hypocalciuric Hypercalcemia Treated with cinacalcet</td>
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<td>0 - 35 / Effectiveness of plasmapheresis in severe hypertriglyceridemia induced pancreatitis</td>
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ORAL PRESENTATIONS
MISLEADING INSULIN-LIKE GROWTH FACTOR 1 (IGF-1) LEVELS IN AN ACROMEGALIC PATIENT WITH LIVER CIRRHOSIS

NURDAN GÜL, ÖZLEM SOYLUK SELÇUKBİRİCİK, AYŞE KUBAT ÜZÜM, REFİK TANAKOL, FERİHAN ARAL

DEPARTMENT OF INTERNAL MEDICINE, DIVISION OF ENDOCRINOLOGY AND METABOLISM, ISTANBUL FACULTY OF MEDICINE, ISTANBUL UNIVERSITY, ISTANBUL, TURKEY

INTRODUCTION: Acromegaly is a rare disease characterized by growth hormone (GH) hypersecretion typically from a somatotroph pituitary adenoma. Growth hormone excess in acromegaly leads to subsequent hypersecretion of insulin-like growth factor 1 (IGF-1) which contributes to the clinical findings and is a recommended biomarker for diagnosis, monitoring, and screening of acromegaly. GH/IGF-1 axis is impaired in patients with chronic liver diseases. Coexistence of acromegaly and chronic liver disease is very rare. We herein report a case of acromegaly with accompanying liver cirrhosis that presents with inappropriately normal IGF-1 levels and shows increased IGF-1 levels after liver transplantation (LTX).

CLINICAL CASE: A 48-year-old man with a history of acromegaly was admitted to our outpatient clinic for further evaluation. His symptoms started 23 years ago with progressive enlargement of hands and feet, polyuria and polydipsia. After laboratory investigations he was diagnosed with acromegaly and diabetes mellitus. Pituitary MRI showed a macroadenoma with minimal suprasellar extension. After surgical intervention his symptoms resolved, and he lost to follow-up.

Three years ago he was investigated for abdominal distention and edema and was diagnosed with liver cirrhosis. Liver transplantation was planned, and as he had a history of acromegaly, he was referred to our endocrinology outpatient clinic for evaluation. On physical examination, his height was 1.84 m and his weight was 104 kg. His shoe size was stable. He had coarse facial features and was normotensive.

Laboratory investigations revealed the following RESULTS: glucose 87 mg/dl, prolactin 33.9 ng/ml, testosterone 6 ng/ml, FT4 14.5pmol/L, TSH 2.08 mIU/L, Albumin 3.96 g/dl, 8 a.m. cortisol 8 μg/dl, peak serum cortisol after an i.v. injection of 250 μg of synthetic ACTH was 14 μg/dl. GH 7.3 ng/ml, IGF-1 87.1 ng/ml (94-252).

Upon repeated measurement GH was 5.6 ng/ml and IGF-1 was 114 ng/ml.

Pituitary MRI revealed postoperative changes with no residual tumor. On June 2017 he received liver transplant from a living donor. After the operation he developed diabetes and was started basal-bolus insulin therapy. He complained of tightness of his shoes and deepening of his voice. Laboratory investigations revealed the following results: glucose 160 mg/dl, HbA1c 8.4%, Prolactin 22.3 ng/ml, testosterone 5.4 ng/ml, GH 2.17ng/ml, IGF-1 321ng/ml (53.3-215).

Pituitary MRI showed a previously unnoticed suspicious milimetric residual tumor. He started to use cabergoline. IGF-1 levels were still elevated under 2mg/week of cabergoline and lanreotide 60 mg/28 days was started. On the last visit he was on lanreotide 60 mg every 5 weeks and his GH was 0.18 ng/ml and IGF-1 was 166 ng/ml.

CONCLUSION: Inappropriately normal or low IGF-1 levels may be misleading during the monitoring of acromegalic patients with severe liver disease, and deregulated GH/IGF-1 axis can be restored by LTX in these patients.

KEYWORDS: Acromegaly, liver cirrhosis, IGF-1, Growth hormone
INTRODUCTION: Cyclic Cushing’s syndrome (CS) is a rare disorder and is characterized by normal cortisol secretion period followed by hypercortisolism period. These cycles can be repeated regularly or irregularly with intercyclic phases ranging from days to years. Mostly, clinical signs of CS may be fluctuating or persistent in these cases.

CASE: A 25 year-old woman admitted to another center on May 2015 with acne, hirsutism, amenorrhea and weight gain. She was diagnosed as polycystic ovary syndrome and was given cyproterone acetate, but withdrew the treatment because of hair loss. One year later, spironolactone and combined oral contraceptive were started for the same symptoms. After using these drugs for a year, her symptoms resolved and had no symptoms for 2 years. On May 2018, because of the recurrence of acne, hirsutism, weight gain, menstrual irregularity the patient admitted our endocrinology department. Labarotory findings were compatible with Cushing’s syndrome at that time (morning cortisol: 52 mcg/dl. DHEA-S: 842 mcg/dl, overnight dexametasone suppression test: 5.2 mcg/dl. 24 hour urinary free cortisol (UFC): 2907 mcg (21-85), salivary cortisol: 474 ng/dl, ACTH:26 and 52 pg/ml. Also she had neutrophilic leucocytosis and dyslipidemia. Pituitary MRI was normal and inferior petrosal sinus sampling was planned. When the patient admitted for IPSS four months later, it was remarkable that all findings regressed and she had no symptoms of CS. Low dose dexamethasone supression test was supressed (1.4 mcg/dl) The laboratory investigations showed normal hypothalamo-pituitary-adrenal axis. Repeated episodes of cortisol excess followed by periods of normal cortisol secretion led us to diagnose the patient as cyclic CS and we decided to follow the patient with no further test. Six months later she admitted to our department with diffuse acne on her neck, face, chest and back. She had hirsutism and gained weight around 6 kg. Waist circumference increased to 70 cm from 62 cm in last two months. Also she had fatigue and mood lability. Morning serum cortisol was 29 mcg/dl and salivary cortisol showed 7 fold increase. Low dose dexamethasone suppression test was 25.8 mcg/dl, ACTH: 54 pg/ml. After high dose dexamethasone test, serum cortisol was suppressed by less than 50 percent compared to baseline. On repeated pituitary MRI, a 3 mm adenoma on the right side of pituitary was detected. Inferior petrosal sinus sampling indicated an hypophyseal Cushing disease with no lateralization. After a successful transsphenoidal surgery, an ACTH-secreting pituitary adenoma was removed. Basal morning cortisol level was 0.9 mcg/dl on early postoperative evaluation. The symptoms resolved in a few days. At postoperative first month, she was still on glucocorticoid replacement treatment and had no other hormon deficiency.

CONCLUSION: Fluctuating clinical presentation and inconsistent biochemical findings should alert the physician for cyclic CS.

KEYWORDS: Cyclic cushing syndrome, Inferior petrosal sinus sampling, Fluctuating hypercortisolism
Patients who undergo pituitary surgery are prone to develop Central Diabetes Insipidus (CDI) post-operatively on top of other hormonal deficiencies. CDI is characterized by decrease in release of antidiuretic hormone (ADH) and present clinically with polyuria, nocturia and polydipsia. In patients with End Stage Renal Disease (ESRD) and on maintenance dialysis, CDI may be masked and then unmasked after transplantation. To the best of our knowledge, there have only been 4 published studies with regards unmasking of CDI post-kidney transplantation.

We report a case of a 62 year old male with history of resection of a pituitary macroadenoma and ESRD secondary to Diabetic Nephropathy on maintenance dialysis, admitted for living non-related kidney transplantation. Pre-transplantation, he was on desmopressin for CDI but when he developed ESRD, CDI was masked and desmopressin was discontinued. His kidney transplant went uneventful.

Post-transplantation, he developed polyuria, increasing serum sodium levels, borderline high serum osmolality and low urine osmolality. In lieu of measuring plasma ADH levels, fluid restriction was done which resulted to increase sodium levels. A diagnosis of CDI was made. He was started on oral desmopressin with noted improvement of symptoms. He was eventually discharged improved.

On succeeding outpatient consults, patient’s daily urine output exceeded to 4L/day and his dose of desmopressin was increased to 100mcg twice daily. Thereafter, he remained clinically stable with average daily urine output of 3L/day, normal sodium levels and good renal allograft function.

Successful kidney transplantation leads to unmasking of pre-existing CDI, which when missed may lead to rapid dehydration and hypernatremia. Frequent monitoring is necessary for early detection and management of CDI. Furthermore, CDI is not a contraindication for transplant as long as patient is closely monitored for adequate titration of fluids and prompt management with desmopressin.

**Keywords:** Central Diabetes Insipidus, Panhypopituitarism, Kidney Transplant

**Figure 1. Clinical Timeline From Day of Transplant until Postop Day 8**
BACKGROUND: Adrenocortical carcinomas (ACCs) are rare tumors that effect women more than men and could be seen in women who are in their child-bearing age. Limited usage of radiological imaging and hormonal changes in pregnancy complicates the diagnostic process. Since reliable information on this topic is scarce in the literature management usually depends on clinical experience and expertise derived from non-pregnant patients. Here we report a case of an ACC presented in the third-trimester of pregnancy.

CLINICAL CASE: A 28 year-old woman formerly treated for papillary thyroid carcinoma was admitted to the hospital for elevated liver enzymes during the third trimester of pregnancy. Abdominal ultrasound revealed a 8.6x7.6cm mass originating from the right adrenal gland and reaching to the liver. The patient’s physical exam was unremarkable, and she had no signs or symptoms of Cushing’s Syndrome. Laboratory studies were normal except a 3-fold elevation in liver aminotransferases. Viral and autoimmune hepatitis markers were negative and ceruloplasmin level was normal. She denied using any kind of toxic agent or drug. Abdominal MRI revealed a 9.4 cm right adrenal mass with solid and cystic components. There was no infiltration or pathological lymph node and the mass was reported as adrenal myelolipoma. The patient’s basal ACTH and cortisol levels were 21.8 pg/mL and 18.6 µg/dL respectively. Plasma cortisol levels after an overnight 1 mg and a 2-day low dose dexamethasone suppression test were 8.5 and 8.7µg/dL respectively. The lack of supression in these tests was attributed to pregnancy in the absence of supporting findings.

The patient had a healthy Cesarean delivery in 37 weeks of pregnancy. A postpartum abdominal CT scan demonstrated a 9x6x9.3x7 cm heterogeneous mass arising from the right adrenal and indenting the right kidney to inferior and reported as angiomyolipoma. Because of the massive size of the tumor malignancy could not be excluded even though imaging studies suggested otherwise. Resection of the tumor took place at 3 weeks after delivery. Histological examination revealed 11x1139 cm tumor according to Weiss criteria and it was diagnosed as ACC accompanying myelolipoma. Immediately after resection mitotane and prednisone treatment was started and chemotherapy was planned.

CONCLUSION: Our case report is a fine example regarding diagnostic challenges and evaluation obstacles in pregnant patients with adrenal masses. MRI is known to be a safe study in pregnancy. However it is important to remember that relying solely on imaging can be misleading as in our case. Masses >6 cm should raise high suspicion for ACC even when radiology indicates otherwise. Physiological changes in pregnancy can interfere with functional evaluation and results can be ambiguous. Best treatment option is resection and delivery if possible. Adjuvant mitotane treatment should be offered to post-partum patients especially the ones at high risk of recurrence.

KEYWORDS: adrenocortical carcinoma, pregnancy, Cushing’s syndrome, adrenal mass

Figure 1. Abdominal MRI showing large mass in the right adrenal

Mass in abdominal MRI
CONCLUSION

- Normal blood pressure does not exclude PCC.
- Paroxysmal headache could be a presenting feature of pheochromocytoma.
- Adrenal mass could be co-secretor of more than one hormone, so should check all hormones according to clinical guidelines.

KEYWORDS: Adrenal incidentaloma, Pheochromocytoma, Subclinical cushing syndrom, Mild autonomous cortisol excess.

INTRODUCTION: Adrenal incidentaloma (AI) is an adrenal lesion ≥ 1 cm which is discovered accidentally during an imaging technique not aimed to assess the adrenal gland(1). Most AIs are benign and non-functioning, but in about 20% of cases it is hyperfunctioning: hypercortisolism, hyperaldosteronism, sex steroid or pheochromocytoma(2). It is uncommonly to find AI with dual secretion. Here we report a case of co-secretting pheochromocytoma and MACE.

CASE REPORT: A 15 years old an adolescent male patient presented with paroxysmal headache for two months with progressive decline of vision. The patient consulted an ophthalmologist, who referred him to neurosurgeon. The neurosurgeon advised him to do urgent surgery in form of shunt due to raised ICP which caused papilloedema. After surgery, there was continuous deterioration in vision and more headache. Fortunately the patient developed abdominal pain and palpitation; consulted physician who advised him to do an ECG and abdominal u/s which showed an adrenal mass while ECG showed LVH strain pattern. The physician referred him to endocrine center, where full endocrine and radiological assessment had been done. Triphasic CT scan of abdomen showed left adrenal mass 39x34 mm, heterogenous texture with 30 HU and features suggestive of PCC. Endocrine assessment showed no cushinoid features, body mass index was 18 kg/m2; his hormonal assessment showed elevated normetanephrine (1967.9 pg/mL) and cortisol (26.1 μg/dL), non-suppressible serum cortisol (2.1 μg/dL) after 1-mg overnight dexamethasone suppression test (ONDST), low DHEA-S (35 μg/dL), and ACTH was 19 pg/mL (within lower normal range). Aldosterone, renin, aldosterone/renin ratio (ARR),metanephrine, K+ and all other biochemical assessment was normal.

Left adrenalectomy was performed after good preoperative preparation, removed mass send for histopathological assessment which revealed 6X6 cm soft tissue mass with histopathological features suggestive of PCC, completely resected surrounded by adrenocortical tissue which require immunohistochemical (IHC) staining to exclude adrenocortical tumor.

After surgery there was good clinical & hormonal improvement (Plasma normetanephrine 165 pg/mL, Cortisol= 5.2 μg/dL, ACTH= 37 pg/mL, DHEA-S =64 μg/dL and 1-mg ONDST = 0.8 μg/dL)
Adrenal lymphoma is rare and adrenal insufficiency is infrequently reported in patients with adrenal metastases. Adrenal insufficiency may be the presenting symptom in bilateral involvement of adrenal glands due to lymphoma. Here, we present a patient with adrenal insufficiency who was diagnosed to have bilateral adrenal involvement of nasal type extranodal NK/T cell lymphoma (NKTCL).

**CASE:** A 40 year old man presented with a four months history of fatigue, weight loss, night sweats, abdominal pain and ptosis in left eye. He had hypertension and was taking amlodipine 10 mg which was stopped one week before admission because of hypotension.

Initial investigations revealed a normal CBC and ESR. Na was 136 meq/l (135–145) and K was 5.3 meq/l (3.5–5.5). His serum albumin, LDH and beta-2-microglobulin were 3.2 g/dl (3.5-5), 384 U/l (<240) and 3.2 mg/dl (1.3-2.9 mg/dl), respectively. Short synacthen test was performed since a serum cortisol of 9.1 mcg/dl and an ACTH of 300.4 pg/ml (0-46) were detected. Cortisol response was insufficient (maximum cortisol level was 13.9 mcg/dl) and GC replacement treatment was started.

In CT of the abdomen, there was a 122x99 mm necrotic lesion in the right and a 112x74 mm necrotic lesion in the left adrenal gland. These lesions contained vascular structure and the limits of them were lobulated. CT scan of the chest and pelvis, upper endoscopy and colonoscopy were normal. No pathological lymphadenopathy was detected in neck, axillary and inguinal regions. Rheumatologic, autoimmune and infectious causes of bilateral adrenal mass were excluded.

**CONCLUSION:** Nasal type extranodal NKTCL is an aggressive extranodal NHL accounting for 5% to 10% of all NHLs. The incidence of secondary adrenal involvement in NHL detectable on CT scan is about 5% and increases to 25% when autopsy cases are included. Histopathologically, the most common type of primary adrenal lymphoma or lymphoma involving adrenal gland is diffuse large B-cell. However, other rare types of lymphoma should also be considered as a cause of adrenal insufficiency in patients with bilateral enlarged adrenal glands and negative imaging of the thorax and abdomen.

**KEYWORDS:** Nasal type extranodal NK/T-cell lymphoma, bilateral adrenal lesion, adrenal insufficiency
The patient developed recurrent, severe hypoglycemia. On readmission her laboratory results were blood glucose 40 mg/dL, insulin 22.4 μIU/mL, C-peptide 2.82 ng/mL after 4 hours of fasting. For the investigation of the tumor localization abdominal CT, endoscopic ultrasonography and Gallium-68-DOTATATE PET-CT performed, but no recurrent lesion was found. Dynamic abdominal MRI showed a total of 4 hypointense lesions with 7-8 mm diameter in the subcapsular areas of liver. No pancreatic mass was detected. This suggested that hypoglycemia due to excessive insulin secretion by the liver metastases. Diagnostic imaging confirmed multiple metastatic insulinoma of the liver. With these findings, surgery was performed for the resection of liver masses. Totally 5 masses were resected and tumor pathology was grade 2 neuroendocrine tumor. Postoperatively the patient continued to have symptomatic hypoglycemic episodes. Abdominal dynamic MRI showed multiple tumor foci remained in the liver. Oral temozolomide and capecitabine therapy was started on.

**Conclusion:** Insulinomas are usually slow-growing tumors but have malignant and metastatic potential. Although malignant insulinoma is seen rare in patients with insulinoma, in patients who diagnosed with insulinoma recurrence of the disease should be considered.

**Keywords:** insulinoma, metastatic, malign
Male reproductive endocrinology

AN ISOLATED FSH DEFICIENCY CASE DUE TO FSH\(\beta\) SUBUNIT PROMOTER POLYMORPHISM C.-211G>T

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BACKGROUND: FSH is a dimeric glycoprotein which is secreted by anterior pituitary gland and contributes to Sertoli cell proliferation and sperm maturation. Deficiency of FSH may cause sperm abnormalities with azospermia, testicular atrophy and subfertility/infertility without virilization defects or low testosterone levels in men. Isolated FSH deficiency is a rare disease that only 16 cases have been reported in the literature so far. Herein, we report a case of isolated FSH deficiency with a c.-211G>T polymorphism at the FSH\(\beta\) subunit promoter.

CONCLUSION: The c.-211G>T polymorphism of the FSH\(\beta\) subunit promoter may cause low FSH levels and subfertility/infertility. Isolated FSH deficiency is a rare cause of subfertility/infertility in men. Patients may be presented with normal sexual development, normal androgen levels and normal spermiogram.

KEYWORDS: Isolated FSH deficiency, subfertility, infertility, FSH\(\beta\) c.-211G>T, polymorphism

Table 1. Results of the LHRH stimulation test

<table>
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<tr>
<th>Time</th>
<th>FSH (mIU/mL)</th>
<th>LH (mIU/mL)</th>
<th>Testosterone (ng/dL)</th>
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<tr>
<td>0 min</td>
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<td>600</td>
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<td>25th min</td>
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Table 2. Family’s hormone profile

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<th>FSH (mIU/mL)</th>
<th>LH (mIU/mL)</th>
<th>E2/Testosterone (pg/mL, ng/dL)</th>
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<td>24.8</td>
<td>23.6</td>
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<tr>
<td>Father</td>
<td>63</td>
<td>4.5</td>
<td>3.6</td>
<td>438</td>
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<tr>
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<td>561</td>
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<tr>
<td>Third brother</td>
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<td>27</td>
<td>0.87</td>
<td>1.81</td>
<td>666</td>
</tr>
</tbody>
</table>
A 49-year-old woman with a history of panic disorder and insomnia presented to our endocrinology clinic because of central hyperthyroidism. Previously she had daily symptoms of insomnia, fatigue, tremor, and palpitation, weakness of legs, hot flushes and depression during previous 6 months. She used escitalopram 20 mg x 1 for depression. In laboratory tests Thyrotropin (TSH) was 3.97 mU/l (0.3-4.2), free Thyroxine (T4) was 33.8 pmol/l (11-22) and free triiodothyronine (T3) 12.3 [pmol/l] (3.1-6.8). Free T4 and T3 by dialysis method were also elevated. Other anterior pituitary hormones were in normal range. TSH-receptor-antibodies were negative. THRA and THRB -gene sequencing analyses were negative which excluded thyroid hormone resistance. Thyroid ultrasound showed a thyroid gland of normal size. TSH response to TRH [3.64-4.22-4.22 mU/l] was consistent with TSH- secreting pituitary adenoma. Sex hormone- binding globulin (SHBG) was elevated (166 nmol/l) and N-telopeptide of type I collagen (U-NTX) was in normal range.

On MRI pituitary was normal. There was a soft mass right sinus cavernosus, of size 10 x 13 x 13 mm. It was in contact with the carotis interna and protruding into the sinus sphenoidalis. According the radiologist opinion this finding was primarily meningioma. In Gallium- 68 DOTANOC –PET-CT sinus cavernous tumour expressed somatostatin receptors. This is typical also for meningioma.

A somatostatin test was done with long acting octreotide. During somatostatin analogy thyroid hormone levels were normalized and her symptoms resolved. Long acting octreotide continued 20 mg i.m. once a month until surgery. This test confirmed TSH secretion from the pituitary. She is now a waiting surgery.

**DISCUSSION:** Diagnosis of TSH- secreting pituitary adenomas are challenging because of the rareness of the disease and the variety of symptoms. Because of that the time to diagnosis may be long. In this clinical case biochemistry was suitable for TSH- secreting pituitary adenoma, but the atypical site of adenoma caused diagnostic challenge.

The author has not received any financial assistance from any organization.

**KEYWORDS:** pituitary, adenoma, thyreotropin, TSH-oma

**FIGURE 1.** MRI showed a tumour mass in right sinus cavernosus.
CUSHING’S DISEASE DUE TO A PITUITARY ADENOMA AS A COMPONENT OF COLLISION TUMOR: CASE REPORT

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INTRODUCTION: Meningiomas are generally slow-growing and benign tumors of adults and accounting for approximately 25% of all intracranial tumors. They typically occur intraparanymal, however, they can also be in sella turcica, representing about 1% of all sellar masses. The coexistence of two morphologically different tumors attached to each other is called collision tumor and collision sellar tumors are very rare. Collision tumors with pituitary adenoma-sellar meningioma have been discovered in only 4 cases to date. As the fifth one, we will be presenting a case of coexistent suprasellar/sellar mass, including a pituitary Corticotroph adenoma and a sellar meningioma in the same anatomic position.

CASE REPORT: A 34-year-old female presented to our clinic with complaints of menstrual irregularity, severe proximal muscles weakness and 10-15 kg weight gain within a year. She had truncal obesity, moon face with plethora, thin skin, hirsutism on both the chest and abdomen. 24-h urine free cortisol was elevated. Basal plasma ACTH level was 58 pg/mL. Diurnal rhythm of plasma cortisol was impaired and after a 48-hour, 2-mg dexamethasone suppression test, plasma cortisol level was 13.6 mg/dL. Overnight 16-mg dexamethasone suppression test showed the insufficient suppression of cortisol which was not greater than 50% (21.4 to 12.5). The pituitary magnetic resonance imaging (MRI) revealed a solid mass suggested as tuberculum sellae meningioma arising from the sellar region (Figure I). High resolution computed tomography of the lungs, 18F-FDG PET/CT, 68Ga-DOTATATE PET/CT and upper endoscopy/colonoscopy were performed and there were no pathological finding reported indicating any ectopic ACTH secreting lesion. The meningioma was decided to be operated on by the neurosurgeons due to its size and localization. The extended endoscopic endonasal approach to sellar/suprasellar region was performed and meningioma was resected successfully together with an adenoma, which was noticed intraoperatively. The patient had complaints of nausea and vomiting postoperatively. Plasma cortisol was 2.6 mg/dL and oral hydrocortisone treatment was initiated immediately. Histopathological examination was reported as a collision tumor composed of pituitary Corticotroph adenoma according to the 2017 World Health Organization classification of pituitary adenoma and meningioma.

DISCUSSION: Our case report appears to be the first one with Cushing’s disease due to a pituitary Corticotroph adenoma surrounding suprasellar/sellar meningioma which are the components of a collision tumor. Even if high dose dexamethasone suppression test fails to suppress cortisol level, considering a suprasellar/sellar meningioma as a possible component of a collision tumor presenting as an ACTH dependent Cushing’s syndrome is highlighted here. There is still no proven pathogenetic mechanism explaining the relationship between a pituitary adenoma and a suprasellar/sellar meningioma as a collision tumor.

KEYWORDS: Cushing’s Disease, adenoma, meningioma, collision tumor

Figure 1. Gadolinium-enhanced magnetic resonance images of the sellar region. (A, B, C) Before transsphenoidal surgery, T1-weightened with contrast sagittal, T1-weightened without contrast coronal, T2-weighted without contrast coronal views, respectively. Suprasellar/sellar lesion, in close relation to optic chiasm. (D, E, F) After transsphenoidal surgery, T1-weighted with contrast sagittal, T1-weighted without contrast coronal, T2-weighted without contrast coronal views, respectively, tumor resection.
INTRODUCTION: Pituitary adenomas are the most common type of sellar masses. Craniopharyngioma, Rathke cleft cyst, dermoid, epidermoid germinoma, metastasis, meningioma, arachnoid cyst, sarcoidosis, tuberculosis, histiocytosis, lymphocytic hypophysitis, schwannoma, infundibular glioma, cavernous carotid artery aneurysm and pituitary involvement of lymphoma or leukemia are included in the differential diagnosis of sellar and parasellar masses. Sellar involvement of lymphoma is rare and is asymptomatic in most cases. Diabetes insipidus (DI) is the most common clinical presentation as blood supply of posterior pituitary is directly from systemic circulation. Besides diabetes insipidus, patients can present with headaches, ophthalmoplegia or visual field defects. It is essential to differentiate pituitary involvement of lymphoma from benign lesions for avoiding unnecessary surgical interventions. Here, we report a case of lymphoma with massive invasion of the pituitary region and panhypopituitarism. He exhibited any sign of diabetes insipidus both on admission and following glucocorticoid replacement, in spite of massive stalk thickening.

CLINICAL CASE: A 73-year-old man was referred to our emergency department with severe headache, cough and fever. He was immediately hospitalized with the diagnosis of pneumonia, as his medical condition was poor. His medical history revealed a diagnosis of pituitary adenoma and panhypopituitarism that was performed recently and he was advised to have pituitary surgery. On admission he was on glucocorticoid and thyroxine replacement therapy. He had no history of polyurea and/or polydipsia and his serum sodium levels were low normal even though his magnetic resonance imaging (MRI) of the sella exhibited a pituitary mass with massive stalk thickening. The patient’s fever persisted in spite of antibiotic therapy and his blood cultures were negative. Multiple pathological lymph nodes were visualized at abdominal and thoracic imaging that was performed for detecting origin of fever. Pathologic examination of lymph nodes was reported as malignant large B cell lymphoma. He received mini-CHOP chemotherapy regimen for six courses and the lesion at pituitary MRI resolved significantly. He remained in remission for over 12 months following chemotherapy. During follow-up, sudden onset-headache and visual disturbances occurred. Pituitary MRI showed recurrent lesion in sella consistent with lymphoma involvement. Radiotherapy was planned.

CONCLUSION: We find this case worth reporting as he exhibited any sign or symptom of diabetes insipidus, even though he had massive pituitary stalk thickening at sellar MRI. Lymphoma involvement should be kept in mind in the differential diagnosis of pituitary lesions with stalk thickening.

KEYWORDS: Pituitary, lymphoma, diabetes insipidus, macroadenoma
Erdheim-Chester disease is a rare, non-Langerhans histiocytosis. In recent years, as a result of increasing awareness, it is more frequently diagnosed and the number of cases in the literature is rapidly increasing.

A 23-year-old man was admitted to the hospital with headache, polydipsia and polyuria six years ago. The patient underwent a transcranial surgery because of a 10x18x20 mm pituitary lesion. Pathologic examination was consistent with xanthomatous hypophysitis. At the sixth postoperative month, he presented to our clinic with same complaints and was followed at the outpatient clinic. During the period that he was receiving replacement therapy for panhipopituitarism. At the end of second year of the operation, a pituitary enlarged lesion was detected. One hundred-twenty milligrams methylprednisolone was started and gradually reduced to the replacement dose. Radiotherapy was applied for the pituitary lesion. He was also hospitalizated for several times due to pneumonia, urinary tract infection and sinusitis in the last three years.

The last hospitalization was due to blurred vision and ptosis. On imaging, a 18x35x35 mm residual lesion was detected with extending to both cavernous sinuses and expanding the base of the sella. PET/CT (positron emission tomography) was performed with suspicion of secondary hypophysitis. A compression of mesencephalon and pons lesion was also detected (Figure 1). On the other and, a dural involvement in the third ventricle and posterior interhemispheric area was observed (Figure 1). A new biopsy was performed from the pituitary lesion for dura-based tumors. Tumor tissue wasn’t detected on pathologic examination. Increased connective tissue and fibrosis were also observed.

During hospitalizations due to infection, no microorganism was detected in blood and urine cultures and procalcitonin was always negative. In our patient; diabetes insipidus, gonadotropin deficiency, hyperprolactinemina, brain lesions and increased osteoblastic activity in long bones (Figure 2) were observed. In the control PET/CT, we found that bone lesions became more prominent, brain lesions persisted and paranasal involvement was added. Moreover, he was diagnosed as Erdheim-Chester (EC) due to the fact that CD68, CD163 positive, CD1a and CD207 were negative in immunohistochemical examination of the first biopsy specimen. Interferon was started because there was no response to steroid and radiotherapy.

In the literature, EC is usually recognized with bone lesions. Different clinical presentation of our patient might be the cause of delay in diagnosis. Even if EC cases are diagnosed earlier, there is no consensus on treatment yet. The fact that most of the treatment options are only involved in clinical trials makes treatment difficult.
RARE TWO CAUSES OF CUSHING’S SYNDROME: PIGMENTED ADRENAL CORTICAL ADENOMA AND ADRENOCORTICOTROPIC HORMON SECRETING PHEOCHROMOCYTOMA

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INTRODUCTION: Cushing syndrome (CH) secondary to ectopic ACTH secretion is mostly associated with lung small cell cancer and lung neuroendocrine tumor, and there are very few reports about ectopic ACTH secretion secondary to pheochromocytoma. Pigmented adrenal cortical adenoma is one of the rare causes of CH, and after dexamethasone suppression test (DST) an increase in cortisol level compared to basal cortisol value should lead the clinician to primary pigmented adrenal adenoma in differential diagnosis.

In this report, a rare case of pheochromocytoma secreting ACTH and another case with pigmented adrenal cortical adenoma were discussed.

CASE 1: A 52-year-old female patient was diagnosed with T2DM for 1 year and HT for 10 years. She underwent surgery for spontaneous vertebral fracture 1 year ago. In post-operative follow-up delayed wound healing and abdominal abscess developed. MRI imaging for abscess revealed adrenal adenoma of 2 cm on the left and 4 cm on the right side. The patient’s cushingoid phenotype was remarkable. ACTH independent CH was diagnosed and the decision was made to operate of the larger adenoma at the right side. The operation pathology was consistent with pigmented adrenal cortical adenoma. The patient is being followed up with the diagnosis of postoperative adrenal insufficiency for 1 year.

CASE 2: A 51-year-old female patient with HT was diagnosed with bipolar disorder for the last 3 months. She admitted to psychiatry clinic because of increased manic episodes and consulted to endocrinology for impaired glucose tolerance. She had cushingoid phenotype. Pituitary MRI revealed normal findings, there was no pituitary adenoma. Ectopic CH was detected as a result of inferior petrosal sinus sampling. Whole body CT revealed a mass lesion in the right adrenal gland with longest diameter was 4 cm, the lesion was containing high and low density areas which was consistent with solid and cystic areas and contrast washout was detected 60%.

Gallium 68 PET CT showed no involvement of the adrenal lesion and there was no other focus was detected. 24-hour urine metanephrine and normetanephrine was detected in normal range. Unilateral surrenalectomy was performed as salvage therapy for the patient whose psychiatric condition worsened, and post operative right surrenalectomy pathology was consistent with pheochromocytoma positively stained with ACTH, chromogranin and 5HT. The patient is being followed up with the diagnosis of postoperative adrenal insufficiency for 1 year.

DISCUSSION: We presented two cases that a only lucky endocrinologist could face them because of their rarity. Unilateral surrenalectomy was an approach that was used as a salvage therapy for pituitary and ectopic CH two decades ago. By this approach it has been shown that cortisol secretion can be reduced by 16% and can provide remission up to 2 years in pituitary Cushing patients. In our second case, as lucky endocrinologists, we achieved both diagnosis and remission with salvage therapy.

KEYWORDS: Ectopic Cushing’s syndrome, pheochromocytoma, pigmented adrenal cortical adenoma
Autoimmune Polyendocrine Syndromes (APS) were initially defined as a multiple endocrine gland insufficiency associated to a variety of autoimmune disease in a patient. Neufeld & Blizzard (1980) suggested a classification of APS, based on clinical criteria only, describing four main types. APS-1 is characterized by presence of chronic candidiasis, chronic hypoparathyroidism, Addison’s disease. It is a very rare syndrome interesting young subjects correlating to different mutations of AIRE [AutoImmuneRegulator] gene on chromosome 21. We are presenting this rare case in a 15 year old boy presented with carpopedal spasm and seizures. He has history of Addison’s disease diagnosed few months back. He has history of hyponatremia, hyperkalemia and hypotension few months back. He is on maintenance dose of steroids. His blood tests showed Na 112, calcium 5.6, PTH not detected. He had oral candidiasis. He was started on IV hydrocortisone, IV hypertonic saline, IV calcium supplementation. He had Tanner stage II. His FSH, LH and testosterone were very low. He was diagnosed with polyglandular Autoimmune Endocrinopathy Type 1 as he had Addison’s Disease, Primary Hypoparathyroidism, chronic candidiasis and hypogonadotropic hypogonadism. He is put on steroids, fludrocortisone, low dose testosterone, calcium supplementation and antifungal treatment. Currently, his condition is stable on above medications.

**KEYWORDS:** Autoimmune polyglandular syndromes, autoimmune diseases, Addison’s disease, hypogonadism, hypoparathyroidism.
INTRODUCTION: Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder caused by loss or severe decrease of activity in various enzymatic steps necessary for cortisol biosynthesis in adrenal cortex. The most common form is caused by mutations in the gene; CYP21A2 which encodes 21α-hydroxylase enzyme that converts progesterone to deoxycorticosterone (DOC) and 17-Hydroxyprogesterone (17-OHP) to 11-deoxycorticisol. 21α-hydroxylase enzyme deficiency results in decreased cortisol and aldosterone synthesis and bilateral adrenal hyperplasia due to unopposed ACTH action. Progesterone and 17-OHP accumulate before the blockage and divert to androgen synthesis pathways. The clinical presentation is subclassified as; the salt-losing type, simple classical type and the non-classical type (NCAH). Phenotype is determined by the less severe CYP21A2 mutation with the highest residual 21OH enzymatic activity. Herein, we will discuss about the therapeutic approach to an infertile woman with 21α-hydroxylase deficiency whose phenotype is in classic/non-classical boundary.

CLINICAL CASE: A 36-year-old woman was admitted with the complaint of infertility. She had the story of menarche at 15 years-old and had irregularity since then. She has never experienced progesterone withdrawal bleeding. A labial fusion surgery was performed at the age of 26y. She was the offspring of a consanguineous marriage.

At physical examination; her weight was 63.2 kg, height was 151 cm and blood pressure was 120/70 mmHg. Her external genitalia appeared as normal. Her laboratory results were: FSH: 3.96 mIU/ml (1.37-9.9), LH: 1.43 mIU/ml (1.68-15), Estradiol (E2):110 pg/ml (30-119), Progesterone: 32.6 ng/mL (0.15-0.3), 17 OH-P: 55.6 ng/mL (0.11-1.08), details in Table 1. Her high serum 17 OH-P accompanied with high progesterone, total testosterone, DHEA-S and low serum cortisol levels were consistent with 21 hydroxylase deficiency CAH [21 OHD CAH]. Genetic analysis showed that she was homozygous for CYP21A2-518T->A(pI173) (p.Ile73Asn) mutation. The glucocorticoid; methyl prednisolone 4mg/day was started to enable normal cycling. Her serum plasma renin activity was also high, so fludrocortisone 50 mcg/day was added to therapy. Her progesterone levels were found to be suppressed; 9.0ng/ml (0.15-0.3) following three months of therapy and spontaneous menstruation began. Her husband was found to be genetically normal, the couple was encouraged for pregnancy.

CONCLUSION: Women with 21 OHD CAH frequently experience menstrual disorders, infertility and miscarriages. Glucocorticoid treatment is suggested for patients who have infertility or have a history of previous miscarriage. Glucocorticoids enable conceiving, prevent early pregnancy losses and improve pregnancy outcomes. Hydrocortisone 20-25 mg/day or prednisone 2.5-5 mg/day is the recommended doses. Fludrocortisone may given if plasma renin activity is high.

KEYWORDS: Congenital adrenal hyperplasia, Infertility, CYP21A2 gene mutation

<table>
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<tr>
<th>Table 1. Laboratory findings of the patient</th>
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<tr>
<td>Serum creatinine: 0.71 mg/dL (0.7-1.3)</td>
</tr>
<tr>
<td>Na: 137 mmol/L (136-145)</td>
</tr>
<tr>
<td>K: 4.6 mmol/L (3.5-5.1)</td>
</tr>
<tr>
<td>ωCortisol: 2.7 mcg/dL (4.3-22.4)</td>
</tr>
<tr>
<td>PRA: 4.1 ng/mL/hour (0.2-1.6)</td>
</tr>
<tr>
<td>Total testosterone: 2.7 ng/ml (0.14-0.53)</td>
</tr>
<tr>
<td>Progesterone: 32.6 ng/mL (0.15-0.3)</td>
</tr>
<tr>
<td>17 OH-P: 55.6 ng/mL (0.11-1.08)</td>
</tr>
<tr>
<td>DHEA-S: 535 mcg/dL (35-430)</td>
</tr>
<tr>
<td>Androstenedione: 2.87 mcg/L (0.9-3)</td>
</tr>
<tr>
<td>TSH: 2.1 uIU/mL (0.4-4.67)</td>
</tr>
<tr>
<td>free T4: 15.2 pmol/L (11.5-22.7)</td>
</tr>
<tr>
<td>Prolactin: 8.5 ng/mL (2.8-29.2)</td>
</tr>
</tbody>
</table>

PRA: Plasma renin activity 17-OHP: 17-Hydroxyprogesterone ωEarly morning cortisol
INTRODUCTION: The most common causes of hypoglycemia in non-diabetic patients are insulinoma, extra pancreatic tumors and rarely autoimmune hypoglycemia. We reported a case of insulin autoimmune syndrome, which is very rare in the differential diagnosis of hypoglycemia, also known as Hirata disease, characterized by spontaneous hypoglycemia, high insulin levels and insulin antibody positivity.

CASE: A 75-year-old woman who was diagnosed with hypertension (HT) and atrial fibrillation (AF) for 20 years was referred to our clinic on the occasion of nausea, sweating and palpitations, which started about two months ago, and a low blood glucose level was detected in another clinic. It was learned that the patient applied to the emergency department 3 times with these complaints in the last 2 months, his complaints improved with dextrose infusion, his blood sugar was measured 39 mg/dL at the last admission and confusion was accompanied. The patient described the symptoms are mostly seen after breakfast, 2-3 hours after excessive amounts of foods, sometimes at any time of day irrespective of meals, and she often feels the need for a snack during the day. He denied using oral antidiabetic drugs, insulin or herbal substances but admitted using propafenone and rivaroxaban for AF and lisinopril+hydrochlorothiazide for HT. She was hospitalized and followed up for the signs of hypoglycemia. Renal function, liver function, thyroid function tests, cortisol level, HbA1c and routine biochemical parameters were normal (Table 1). Symptomatic hypoglycemia occurred 3-4 times a day and tests during the hypoglycemic period showed that glucose level was 48 mg/dL insulin 7389 mU/L and c-peptide 10.12 µg/L. Laboratory tests repeated at the time of another hypoglycemic event showed glucose level was 28 mg/dL insulin 4942 mU/L and c-peptide 10.94 µg/L so endogenous hyperinsulinemia was considered. Abdomen ultrasound, endoscopic ultrasonography and MRI performed with a preliminary diagnosis of insulinoma showed normal homogeneous appearance in the pancreas. Ga-68 DOTATATE PET/CT examination showed that there was focal and mild to moderate involvement of the pancreatic corpus but it was not significant for insulinoma. Selective arterial calcium stimulation test was performed. The results obtained were not conclusive in terms of localizing the presence of an insulin secreting tumor or nesidioblastosis. The insulin autoantibody test was positive so insulin autoimmune syndrome was diagnosed. The patient was negative for thyroid autoantibody, ANA, RF and celiac antibody values. The dietary arrangement was made, steroid treatment was started and hypoglycemia improved with current therapy during follow-up.

CONCLUSION: In patients with hypoglycemia showing high levels of insulin and no other diagnosis could be made with imaging methods, Hirata disease should be considered for further differential diagnosis as a rare cause of endogenous hyperinsulinemia.

KEYWORDS: Hypoglycemia, insulin autoimmune syndrome, Hirata
Paragangliomas (PGs) are usually benign, slow-growing tumors, arising from paraganglia cells. PGs are associated either with the sympathetic tissue in extraadrenal locations like sympathetic PGs of the abdomen or parasympathetic tissue the parasympathetic PGs of the head and neck.

**CASE PRESENTATION:** An 81-year-old woman was presented with nodular goiter and a mass lesion that had been incidentally discovered on neck ultrasonography and followed as parathyroid adenoma (PA)/lymphadenopathy (LAP) without an increase in size and symptoms like pain, dysphonia and sweating for 2 years. Serum biochemistry weren’t compatible with primary hyperparathyroidism. The mass lesion was detected on neck MRI which was reported as PA or metastatic LAP. Total thyroidectomy and mass excision was performed after 2 years from initial diagnosis. She had hypertensive attack with manipulation of the tumor and intravenous antihypertensive treatment was needed. She was admitted to our department because of an intraoperative hypertensive attack and to be evaluated for secondary hypertension (HT). She had HT for 10 years, stable on medical treatment. Family history was unremarkable for thyroid disorders, pheochromocytoma or PG. Physical examination was unremarkable. Ambulatory BP revealed a mean BP of 138/76 mmHg and maximum BP of 159/90 mmHg. 24-hour urinary catecholamine sampling was negative. She was euthyroid. There was no significant renal arterial stenosis in doppler. There was no adenoma on adrenal CT. At histopathological examination, a 2 mm of medullary thyroid carcinoma (MTC) with C-cell hyperplasia located on the left lobe of thyroid was detected. The aforementioned mass lesion was also reported as MTC but immunohistochemistry study showed calcitonin negativity. Pathological reevaluation of the mass lesion was compatible with typical of PG. Immunostaining for SDHA, SDHB were positive, highlighting the presence of a nonmutated gene. Ret mutation was sent because of concomitant MTC with c-cell hyperplasia and PG.

**DISCUSSION:** Head and neck PG usually present with no catecholamine synthesis, resulting in a clinically symptoms from the mass effect or incidentally. The differential diagnosis for head and neck PGs include metastatic neuroendocrine tumor, MTC or PA. Differentiating PG from MTC metastasis is important because of the difference in prognosis, treatment and follow up. Although neck and head PGs are thought as nonfunctional, in literature, vagal PG and infratemporal fossa PG are associated with catecholamine synthesis and hypertensive attacks likewise our patient. Carotid body tumor resection can result in a reduction of systolic BP at essential hypertensive patients. Also, the antihypertensive treatment of our patient was stopped. Herein we present a case that had been followed with a PA or metastatic LAP and was finally diagnosed with functioning neck PG after an intraoperative hypertensive crisis. We suggest that head and neck PGs can be sometimes functional and associated with secondary HT.

**KEYWORDS:** Head and neck paraganglioma, hypertensive attack, atypic neck mass

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**Figure 1.** The mass lesion which was reported as parathyroid adenoma or metastatic lymphadenopathy is approximately 3 cm in size with a hypointense appearance on T1 images with contrast involvement in contrast-enhanced images, located at the paratracheal region and inferior right lobe of thyroid lobe.
CONCLUSION: Mauriac syndrome is a rare, almost forgotten complication of T1D. However, optimal glycemic control may improve hepatic dysfunction and developmental delay. To recognize this rare syndrome and advise adherence to insulin therapy is important.

KEYWORDS: Type 1 diabetes, Mauriac syndrome, hepatomegaly

INTRODUCTION: Mauriac syndrome is a rare syndrome characterized by growth retardation, delayed puberty, hepatomegaly, elevated liver enzymes and cushingoid appearance in patients with type 1 diabetes (T1D). Although it is associated with poor glycemic control, its etiology is not fully understood. After widespread use of insulin therapy, this syndrome is less common. Here we present a case of T1D with mauriac syndrome who presented with poor blood glucose control and elevated liver enzymes.

CLINICAL CASE: A 21-year-old female patient with T1D was admitted to the hospital for poor glycemic control. She was diagnosed T1D at the age of 3. Although she had administered insulin injections regularly in early childhood, after teenage she had applied insulin treatment irregularly, often skipped doses and rarely went to doctor visit. The patient’s history revealed that she did not enter puberty spontaneously and started using transdermal estradiol therapy at the age of 15. After 2 year of estradiol treatment, combined estrogen-progestin oral contraceptives (COC) was started and she was still using it. Patient had a hemoglobin a1c of 13.4, ALT: 35 u/l (5 - 33), AST: 75 u/l (5 - 32), GGT: 57 u/l (8-61). Physical examination revealed short stature and cushingoid appearance with moon face, buffalo hump, abdominal obesity, and thin skin of the arms and legs. In the abdominal examination, the liver was palpated 6 cm below the rib and there was no splenomegaly. Four days later, check of liver tests were demonstrated some significant elevations: ALT: 502 u/l, AST: 1523 u/l, GGT:117 u/l with normal bilirubin. Abdominal ultrasonography showed hepatomegaly with riedel lobe variation and a mild granular pattern secondary to fatty parenchyma (grade 1 hepatosteatosis). Abdominal computed tomography showed hepatomegaly [230 mm] with no other pathological finding [Figure-1]. Viral hepatitis markers, ANA, ASMA, AMA, alpha-1-antitrypsin antibody, celiac autoantibodies were negative and serum ceruloplasmin, transferrin saturation were normal. The patient had no complaints during the elevation of liver enzymes, but her enzyme levels gradually decreased within one week and regressed near to baseline values [Table-1]. Cushing syndrome screening tests were performed: 1 mg overnight dexamethason supression test (DST) was 2.28 μg/dL, two day 2 mg DST was 1 μg/dL, late-night salivary cortisol and 24-hour urinary cortisol excretion was normal.

The patient was thought to have mauriac syndrome due to her current findings. During follow-up, blood glucose levels could be controlled with insulin therapy, and COC was stopped. It was planned to control liver function tests and menstruation by providing glycemic control.

Table 1. Laboratory results of the case

<table>
<thead>
<tr>
<th>Test</th>
<th>Day of admission</th>
<th>After 2 Days</th>
<th>After 4 Days</th>
<th>After 7 Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT, u/l (5 - 33)</td>
<td>35</td>
<td>502</td>
<td>376</td>
<td>226</td>
</tr>
<tr>
<td>AST, u/l (5 - 32)</td>
<td>75</td>
<td>1523</td>
<td>1053</td>
<td>116</td>
</tr>
<tr>
<td>GGT, u/l (8-61)</td>
<td>57</td>
<td>117</td>
<td>166</td>
<td>156</td>
</tr>
<tr>
<td>Total bilirubin, mg/dl (0 - 1.2)</td>
<td>0.17</td>
<td>0.33</td>
<td>0.34</td>
<td>0.27</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>13.4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
INTRODUCTION: Parathyroid carcinoma (PC) is a very rare endocrinological malignancy. It accounts for less than 1% of all hyperparathyroidism cases. It is notoriously resistant to radiotherapy and chemotherapy. Radical surgery remains the only viable initial treatment option; however, relapses are frequent, and metastatic disease is not unexpected. Patients with disseminated disease most likely succumb to complications related to uncontrolled hypercalcemia. Hemodialysis (HD) is frequently required. There are few medical treatment options for such cases, namely bisphosphonates, calcimimetics, and denosumab. Here we present a case of metastatic PC induced extreme hypercalcemia of 24 mg/dL who failed bisphosphonates, could not tolerate calcimimetics and in the end controlled with denosumab.

THE CASE: A forty-two years old male patient was diagnosed with PC in 2009 while being evaluated for nephrolithiasis. He was treated with recurrent surgeries for local recurrences and intravenous zoledronic acid (ZA) between years 2009-2013. He received HD intermittently when ZA failed. He did not seek medical follow-up between years 2013-2016. In the year 2016, he developed mediastinal, lung and, bone metastasis, presenting with a calcium level of 16.4 mg/dL. He received radiotherapy to mediastinum, ZA and eight sessions of HD. He did not seek medical follow-up until January 2019 when he was admitted with a calcium level of 24 with underlying new and widespread lung metastasis plus an inoperable mass in the neck. He received ZA, HD and could not tolerate cinacalcet due to nausea. He was started on denosumab on February 2019 with an induction dose of 120 mcg once two weeks. Maintenance dose was 120 mcg once a month. In these six months of follow up; no HD session was needed. His nadir calcium was 8.4 mg/dL in the third month of treatment. Afterward, calcium levels elevated and stabilized between 10-12 mg/dL without associated symptoms or electrocardiography changes. Patient’s last dose in July had to be postponed 20 days due to difficulty in obtaining the drug. His calcium rose to 16.1 mg/dL but, when the drug was re-administered, it fell to 11.3 mg/dL. He did not exhibit any symptoms of hypercalcemia and was allowed home. The patient’s timeline of PTH, calcium, and phosphorus are presented in Table 1.

CONCLUSION: PC is a rare disease with a few treatment options available for management. There are a few case reports of such extreme hypercalcemia exceeding 20 mg/dL in the literature. Denosumab proved its value in this case as a last resort. We believe it might also be used beforehand in PC cases with uncontrolled hypercalcemia.

KEYWORDS: Parathyroid carcinoma, hypercalcemia, denosumab

Table 1. Patient’s calcium, PTH and phosphorus levels before and denosumab treatment

<table>
<thead>
<tr>
<th>Date</th>
<th>Calcium</th>
<th>Phosphorus</th>
<th>PTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/2016</td>
<td>12.6</td>
<td>1.6</td>
<td>537</td>
</tr>
<tr>
<td>09/2017</td>
<td>12.9</td>
<td>1.6</td>
<td>546</td>
</tr>
<tr>
<td>25/02/2019 first dose (concomitant with hemodialysis and zoledronic acid)</td>
<td>24.4</td>
<td>3.2</td>
<td>&gt;2000</td>
</tr>
<tr>
<td>17/03/2019</td>
<td>10.2</td>
<td>2.2</td>
<td>N/A</td>
</tr>
<tr>
<td>27/03/2019</td>
<td>11</td>
<td>1.1</td>
<td>&gt;2000</td>
</tr>
<tr>
<td>09/04/2019</td>
<td>8.55</td>
<td>1.5</td>
<td>4012</td>
</tr>
<tr>
<td>29/04/2019</td>
<td>10.3</td>
<td>1.5</td>
<td>4404</td>
</tr>
<tr>
<td>28/05/2019</td>
<td>8.5</td>
<td>1.5</td>
<td>N/A</td>
</tr>
<tr>
<td>27/06/2019 fourth dose</td>
<td>11.8</td>
<td>1.5</td>
<td>N/A</td>
</tr>
<tr>
<td>16/07/2019</td>
<td>10.3</td>
<td>1.8</td>
<td>5235</td>
</tr>
<tr>
<td>31/07/2019 missed dose</td>
<td>13.1</td>
<td>2.7</td>
<td>2947</td>
</tr>
<tr>
<td>04/08/2019 fifth dose</td>
<td>19.3</td>
<td>2.4</td>
<td>N/A</td>
</tr>
<tr>
<td>21/08/2019 current</td>
<td>11.3</td>
<td>2</td>
<td>&gt;2000</td>
</tr>
</tbody>
</table>
AN UNUSUAL CASE OF FAMILIAL HYPOCALCIURIC HYPERCALCEMIA TREATED WITH CINACALCET

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INTRODUCTION: Familial hypocalciuric hypercalcemia (FHH) is a rare and autosomal dominant disease which is usually caused by inactivating mutations in the calcium-sensing receptor (CASR) gene. It is generally a benign condition with mild hypercalcemia and absence of hypercalcaemic symptoms. However, we herein report a family with FHH and moderate to severe hypercalcemia.

CASE DISCUSSION: An 19-year-old woman was admitted to our out-patient clinic with the complaint of fatigue. Physical examination revealed no physical abnormality. Laboratory investigations showed a calcium level of 13 mg/dl on admission. Further investigations revealed high serum parathyroid hormone levels 112 (15-65 ng/dl) besides with low Vitamin D, normal magnesium and phosphorus levels and low 24 hour-urinary calcium. The calcium/creatinine clearance ratio was calculated to be 0.002 and 0.004 on different occasions. Her mother and 14 years-old brother revealed the similar laboratory features. Neck ultrasonography, neck three-dimensional CT, sestamibi scintigraphy, SPECT/CT and Cholin-PET CT which were done for the diagnosis of primary hyperparathyroidism detected no parathyroid lesions. She did not have history of renal stones or fracture, and abdominal ultrasonography and bone mineral density did not reveal nephrolithiasis or osteoporosis. In genetic examination, both the patient, her mother and brother were heterozygote for CASR mutation of R185Q. Her calcium levels were between 11.8-12.6 mg/dl under hydration therapy and could not tolerate oral furosemide therapy. Because of high levels of calcium despite hydration therapy; cinacalcet was given for six months. She could tolerate 60 mg/day cinacalcet and her calcium levels decreased to 10.5-11 mg/dl under this therapy.

CONCLUSION: FHH syndromes are related to inactivating mutations of the CASR gene with heterozygous and homozygous mutations. In FHH, typical presentation is mild and asymptomatic hypercalcemia is seen, however it may be marked and clinically evident in 10% of cases. Calcimimetics are not indicated except in case of symptomatic forms. Heterozygote mutations of CASR R185Q is generally associated with severe neonatal hyperparathyroidism which is a severe life-threatening disorder with marked hypercalcemia and beginning in the neonatal period of life. The treatment is based on cinacalcet for this type. Our case is interesting because of its clinical course, age of onset and mutation for CASR.

KEYWORDS: familial hypocalciuric hypercalcemia, CaSR, cinacalcet
CASE 1: A 45-year-old woman was referred to division of Endocrinology and Metabolic Diseases due to hypercalcemia in routine evaluations. She was asymptomatic other than constipation. Laboratory workup showed serum calcium (Ca) of 12.2 mg/dL (reference range (RR): 8.6-10.2) with serum parathyroid hormone (PTH) of 122 pg/mL (RR: 15-65). Neck USG revealed a hypoechoic nodule with a maximum diameter of 16 mm located posteriorly in the right thyroid lower pole. The USG-guided FNA of this nodule was non-diagnostic. 99mTc sestamibi parathyroid scintigraphy and the following 4-dimensional neck computerized tomography was negative for parathyroid adenoma. Suspecting an IPA, a second FNA of the nodule followed by PTH measurement from the needle washing (FNA-PTH) was performed. FNA-PTH level was 1020 pg/mL. The patient underwent right hemithyroidectomy and histopathological examination confirmed the nodule to be a parathyroid adenoma. Postoperatively, serum Ca and PTH levels of the patient returned to normal values.

CONCLUSION: Ectopic parathyroid adenoma within the thyroid gland can be difficult to recognize. The sensitivities of neck USG and scintigraphy are <50% for these cases. FNA-PTH measurement has been suggested to be useful in localizing IPA by providing biochemical evidence, especially in the setting of inconclusive neck USG and 99mTc sestamibi imaging.

KEYWORDS: parathyroid adenoma, intrathyroidal, parathyroid hormone, fine needle aspiration

CASE 2: A 39-year-old women was admitted to our clinic for annual control of asymptomatic PHPT. She was diagnosed 7 years ago. At the time of the diagnosis, she had normocalcemic PHPT. Neck USG was normal other than a nodule, 9x7x11 mm in size, located in the lower left thyroid lobe. There was no tracer uptake on 99mTc sestamibi parathyroid scintigraphy. FNA biopsy of the nodule was reported to be a benign thyroid nodule. She didn’t have parathyroid surgery and was managed conservatively. In this year’s routine control, laboratory workup showed a serum Ca level of 11.1 mg/dL and a PTH level of 80 pg/mL. 24-hour urinary Ca level was 408 mg/day. We repeated the imaging studies. The findings of neck USG were the same as those of 7 years ago, but 99mTc sestamibi scintigraphy, unlike previous, revealed a low level of focal tracer uptake at the left thyroid lower pole. We performed FNA-PTH measurement. FNA-PTH was 603 pg/mL, which was suggestive of an IPA. Based on these results, left hemithyroidectomy is scheduled for the patient.

CONCLUSION: Ectopic parathyroid adenoma within the thyroid gland can be difficult to recognize. The sensitivities of neck USG and scintigraphy are <50% for these cases. FNA-PTH measurement has been suggested to be useful in localizing IPA by providing biochemical evidence, especially in the setting of inconclusive neck USG and 99mTc sestamibi imaging.

KEYWORDS: parathyroid adenoma, intrathyroidal, parathyroid hormone, fine needle aspiration
Severe hypothyroidism is often associated with hyponatremia. The mechanism of hyponatremia in hypothyroidism is not fully understood. It is suggested that hypothyroidism induces hyponatremia either by inappropriate release of ADH or by decrease in GFR. Regardless of the mechanism, the net effect is impairment of water excretion. On the other hand, hypothyroidism can manifest with myopathies. Hypothyroid myopathy is most often limited to myalgia, muscle stiffness and cramps, with sometimes moderately elevated levels of muscle enzymes. However, rhabdomyolysis due to hypothyroidism is very rare.

We present a case of a young male patient, aged 36, with medical history of rhabdomyolysis resulting in acute renal failure (hypothyroid myopathy in retrospect), initially treated at the Clinic of nephrology, then transferred to the Clinic of neurology due to persistent myalgia, where he was diagnosed as generalized demyelinating senso-motory polyneuropathy and treated with parenteral corticosteroid therapy. Due to repeated episodes of general weakness, myalgia and general prostration the patient was hospitalized at the intensive care unit at the Clinic of endocrinology. Initially, his laboratory findings showed severe hypothyroidism, with thyroid stimulating hormone above 75mU/L and free thyroxine levels below 4,5pmol/L, followed by severe hyponatremia (105mmol/L) and hyperkalemia (6mmol/L). The patient was drowsy, but alert. Substitution therapy with levothyroxine was immediately started, per protocol. His sodium levels were constantly lowering (115...111...112...106...104...98mmol/L), despite the administration of hypertonic sodium chloride and fluid restriction. In addition to this therapy, parenteral glucocorticoid therapy in high doses was introduced, as hyperkalemia, (unusual in the setting of hypothyroidism, but often seen in adrenal insufficiency) and previous corticosteroid treatment at the Clinic of neurology, lead us to diagnose iatrogenic adrenal insufficiency. In the midst of the patient’s lowest sodium levels, he had an episode of headache, nausea, vomiting (elevated intracranial pressure), and hypothermia. The patient’s serum osmolality was low (196,38mOsm/kg), but his urine osmolality (412.88mOsm/kg) and urine electrolytes were all within the normal ranges (euvolemic hypotonic hyponatremia). As his fT4 levels started to improve, his overall clinical condition improved significantly.

Severe hyponatremia is a life threatening problem if not carefully managed. Severe hyponatremia in the setting of severe hypothyroidism was a challenge for an entire team of experienced endocrinologists. Although hypothyroidism is a rare cause of rhabdomyolysis, it should be suspected in patients presenting with muscle aches and high CK concentrations in the absence of other, causes of rhabdomyolysis, even in the absence of its clinical features. As soon as the diagnosis is made, thyroid hormone replacement should be promptly instigated.

**KEYWORDS:** severe hypothyroidism, hyponatremia, rhabdomyolysis
INTRODUCTION: Resistance to thyroid hormone is a syndrome that is characterized by decreased responsiveness of target tissues to thyroid hormones. The most common cause is mutations in the beta isoform of the thyroid hormone receptors. Thyroid hormones play an important role in vertebrate embryogenesis, fetal development, and maturation. Thyroid hormone resistance in mother may cause fetal hyperthyroidism in pregnancy. Here, we report a case that has been diagnosed with thyroid hormone resistance in early pregnancy and gave birth to a healthy baby.

CASE DISCUSSION: A 20-year-old woman at the 5th week of pregnancy has been consulted from gynecology clinic for abnormal thyroid function tests. Physical examination revealed no physical abnormality and the patient was clinically euthyroid. She had a history of previous pregnancy that ended with miscarriage at the 28th week. Laboratory investigations showed a serum thyrotrophin of 6.59 mU/mL (0.27-4.2 mU/mL), free thyroxine of 2.31 ng/dL (0.87-1.7 ng/dL) and free triiodothyronine of 7.03 pg/mL (2.4-4.4 pg/mL). Repeated tests also revealed similar results. When we searched previous thyroid functions, we noticed that her thyroid function tests had also similar abnormality in 2012. Unreliable results due to heterophile antibody, thyroid hormone resistance and thyroid hormone secreting pituitary adenoma (TSHoma) were considered in the differential diagnosis. We checked the tests using methods that didn’t interfere with heterophile antibody and had the same results. Thyroid function tests of her mother and father was normal. We consulted patient to the genetic clinic for genetic test and decided to perform pituitary magnetic resonance imaging (MRI) without gadolinium. Her pitutary MRI showed no mass associated with TSHoma. Genetic test revealed heterozygous c.1378G>A mutation in first exon of THRB gene. The patient and fetus were followed regularly during pregnancy, there was no evidence of thyrotoxicosis in the fetus, so we didn’t give anti thyroid drug treatment to mother. At the end of 39th week, she gave birth to a 2900 gram healthy baby. There was no abnormality in newborn’s thyroid function tests.

CONCLUSION: Thyroid hormone resistance may cause increased rate of miscarriages, premature labor, and low birth weight in pregnancy. Wild type infants of mothers with thyroid hormone resistance have lower birth weight and suppressed postnatal TSH compared with infants harboring the THRB gene mutation. So prenatal diagnosis is usually offered to establish genetics of fetus. Instead of this we followed fetal growth and development with periodic ultrasonography examinations.

KEYWORDS: THRB, pregnancy, thyroid hormone resistance
A THYROTOXICOSIS CASE RELATED TO CEMIPLIMAB TREATMENT

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BACKGROUND: Use of immune check-point inhibitors (ICPI) and targeted therapeutic agents initiated a new era in medical oncology. On the other hand, various endocrinopathies are increasingly seen as side effects of these treatments. It is important that oncologists and endocrinologists know how to diagnose and manage this type of adverse effects. Here, we present a thyrotoxicosis case associated with use of a new PD-1 monoclonal antibody. To the best of our knowledge, this is the first report showing thyroid dysfunction related to cemiplimab.

CLINICAL CASE: Fifty-two-year-old female patient with a history of lung adenocarcinoma treated with new PD-1 inhibitor cemiplimab for one month, was referred to endocrinology clinic due to recent onset thyroid dysfunction. She had irritability, increased sweating and palpitations but did not have hot intolerance, diarrhea, weight loss or any symptoms suggestive of thyroid ophthalmopathy. She had a pulse of 104 beats/min and a nontender thyroid. The remainder of the physical exam was unremarkable. Thyroid function tests (TFT) were as follows; TSH:0.02 uIU/mL (N: 0.38-5.33 uIU/mL), fT4: 26.8 pmol/L (N: 7.86-14.41 pmol/L), fT3: 8.01 pmol/L (N: 3.8-6 pmol/L). Serum anti-thyroglobulin antibody was negative and anti-thyroid peroxidase (TPO) antibody level was 105.3 IU/mL (N< 9 IU/mL). Previous TFT were in normal limits before cemiplimab therapy. Thyroid ultrasonography revealed decreased parenchymal echogenicity and multiple nodules in the slightly enlarged gland. Color doppler study showed normal flow pattern. Thyroid scintigraphy showed diffusely decreased activity of the gland (Figure-1). Iodine uptake was reduced (1.5% and 3% at 4th and 15th hours, respectively). Cemiplimab induced thyroiditis was considered and propranolol was started. The patient is at the second month of cemiplimab treatment for lung adenocarcinoma and she does not have any symptoms related to thyrotoxicosis. The latest thyroid function tests are as follows; TSH:0.05 uIU/mL, fT4: 16.05 pmol/L, fT3: 6.49 pmol/L.

CONCLUSION: ICPIs have many side effects on the endocrine system among which thyroid abnormalities are the most common. Because the cancer-related symptoms of patients are more severe, drug-induced endocrinopathies are often overlooked. Physicians should be vigilant for potential endocrine dysfunction in patients under ICPI treatment in accordance with guidelines.

KEYWORDS: thyrotoxicosis, immunotherapy, cemiplimab
The postoperative pathology report revealed multifocal >1cm PTC and multiple LCH involvement in the thyroid gland. Later on she was consulted with the Department of Hematology and Nuclear Medicine, it has been decided that, due to the apparent LCH or - gan involvement and relatively high risk PTC, she should be started on oral cladribine therapy first then followed by radioactive iodine therapy. The patient is still continuing her follow ups in our center.

CONCLUSION: LCH, is a proliferative disease and that has a wide range of clinical appearance; local and/or systematic. It is mostly seen in children, however it can also be seen among adults, especially smokers. Throughout literature, its involvement of the endocrine glands such as, hypothalamus, hypophysis and thyroid has previously been reported. Even though LCH and PTC (mostly papillary microcarcinoma) were also previously reported occasionally, the coexistence of aggressive (>1 cm, multifocal) PTC and LCH is extremely rare. Finally, it is very important to consider thyroid malignancy in patients with overt and autoimmune hyperthyroidism especially the ones that were accompanied with thyroid nodules and thyroid gland involvement in young smoking LCH patients.

KEYWORDS: Papillary Thyroid Carcinoma, Langerhans Cell Histiocytosis, Graves’ Disease.
OBJECTIVE: It is not known about the effectiveness of bariatric surgery on glycemic regulation in the patients with maturity-onset diabetes of the young (MODY). We present two cases with MODY undergoing bariatric surgery.

CLINICAL CASES: Case 1: Nineteen-year-old female was referred with obesity. She had type 1 diabetes mellitus (T1D) and PCOS for 6 years. Metformin was used for the first year. She had been taking insulin aspart 3x22 units, detemir 1x40 units for 5 years, and oral contraceptive drug for the last year. Her mother had type 2 diabetes mellitus (T2D).

Height was 164 cm, weight: 105 kg, body mass index (BMI): 39.17 kg/m², and vital signs and examination of organ systems were unremarkable. Ferriman-Gallwey score was 21.

The patient knew that she had T1D. Fasting blood glucose (FBG) was 199 mg/dL, postprandial blood glucose (PPBG): 239 mg/dL, HbA1c: 11.1%, basal fasting C-peptide (Cp): 1.53 ng/mL. The other laboratory tests were in normal limits. Anti-GAD and ICA were negative. Diagnosis at a younger age, positive family history, adequate Cp, and negative autoantibodies increased the possibility of MODY. Genetic analysis revealed heterozygous mutation in HNF1A at c.942C>T. MODY 3 was diagnosed.

The patient was willing to undergo bariatric surgery to lose weight. Based on age, diabetes duration, Cp level, and BMI, we approved and laparoscopic Roux-n-Y gastric bypass (RYGB) surgery was performed. The patient lost 20 kg postoperatively in two months and left off insulin. Metformin 1000 mg 2x1 and gliclazide 30 mg 1x1 were given postoperatively.

CASE 2: Thirty-three-year-old female having T2D for 7 years was referred with obesity. Metformin and glimepiride was given for the first month of diagnosis of T2D, then intensive insulin regimen was initiated (insulin aspart 3x12 units and detemir 1x24 units). Her mother had a history of T2D.

Height was 158 cm, weight: 110.9 kg, BMI: 44.4 kg/m²; and vital signs and examination of organ systems were unremarkable. FBG was 195 mg/dL, PPBG: 269 mg/dL, HbA1c: 9.4%, and Cp: 1.89 ng/mL; and the other laboratory tests were in normal limits. ICA and AntiGAD were negative. Negative autoantibodies, diagnosis at a younger age, response to sulfonylurea, adequate Cp levels, positive family history increased the possibility of MODY. Genetic analysis revealed heterozygous missense mutation in KCNJ11 (c.527G>A), and diagnosis was MODY 13.

The patient was willing to undergo surgery. Laparoscopic RYGB was performed. The patient left insulin at first; however, 2 months later, insulin was re-initiated.

CONCLUSION: To our knowledge, our cases are the first that RYGB was performed in MODY. Our patients were left off insulin postoperatively. However, insulin was given 2 months later for one patient. Beta cell secretion defect may persist or even deteriorate after RYGB in MODY in compliance with the natural course of disease. As a result, when deciding RYGB, the purpose of glycemic regulation should not be the only indication for the patients with MODY.

KEYWORDS: MODY, bariatric surgery, gastric bypass, maturity-onset diabetes, diabetes, metabolic surgery.
INTRODUCTION: Maturity onset diabetes of the young (MODY) is usually presented in adolescence or young adulthood (typically age <25 years) with autosomal dominant transmission and absence of pancreatic islet autoantibodies. There are many different genetic abnormalities of MODY. Most common mutations are hepatocyte nuclear factor-1-alpha (HNF1A) and the glucokinase (GCK) gene, which causes MODY type 3 and type 2, respectively. Mutations in carboxyl ester lipase (CEL), ATP-binding cassette, subfamily C, member 8 (ABCC8), B-lymphocyte kinase (blk) are rare and associated with the different MODY phenotypes. In this unique case, we presented a 22-year man who have 3 different mutations including Cel, ABCC8 and blk gene mutations.

CASE: Two years ago a 22 year old gentleman was admitted to the cardiology department complaining of dyspnea and palpitation and diagnosed with rheumatic heart valve involvement with ascending aortic aneurysm. He consulted with the clinical genetic department for a possible diagnosis of Marfan Syndrome. However surprisingly, the genetic evaluation revealed CEL, ABCC8, blk mutation which is related to MODY tip 8,11,12, respectively. He was then referred to the endocrinology department. His detailed past medical history revealed that he was previously diagnosed as insulin resistance and given metformin therapy for 2 years. On physical examination, he was normal except being obese with BMI 38.9 kg/m². His laboratory test was; fasting blood glucose: 81 mg/dl, post-prandial blood glucose:102 mg/dl, HbA1C:%5.1, c-peptid:2.6 ng/ml, insulin:12.7 uIU/ml. His mother was 51 years old and had a 9 year history of diabetes and using metformin [2*1000 mg]. Her genetic screening showed CEL and ABCC8 mutations. Her laboratory tests showed fasting blood glucose:122 mg/dl, post-prandial blood glucose:226 mg/dl, HbA1C: %6.7, c-peptit: 5.01 ng/ml, insulin:31 uIU/ml. He also had 6 siblings. Since they have been living in different cities, we didn’t have an opportunity to examine them.

DISCUSSION: Our patient had 3 different MODY mutations together, all 3 mutations may lead to diabetes; but our patient’s glucose profile was normal and he has not developed diabetes. We further analysed mutations; blk gene mutation may associated with obesity related diabetes, our patient had obesity and insulin resistance. CEL mutations may have an effect on pancreas exocrine function and may increase pancreatitis risk. Thus the patient and his mother were checked for amylase and lipase level and underwent MR Imaging of the pancreas; they were both normal. ABCC8 mutation primarily causes neonatal diabetes, but recent evidences showed that it may also effect adults.

IN CONCLUSION: We presented a case 22 years old who had three MODY mutations together and had not developed diabetes but was obese. Further studies are needed to clarify the clinical importance and other possible consequences of these 3 mutations being found together.

KEYWORDS: CEL, blk, ABCC8, MODY
CONCLUSION: Primary hyperparathyroidism (PHPT) is one of the most frequent endocrine diseases. It may cause osteoporosis, nephrolithiasis and hypertension. NPHPT may be the initial period of PHPT where calcium (Ca) levels are in normal range. Early diagnosis of PHPT is important in order to prevent its complications. IH may appear to be NPHPT, therefore clinical evaluation and laboratory tests such as urinary calcium levels should be combined to prevent misdiagnosing IH patients as NPHPT and referring them for potential parathyroid surgery.

KEYWORDS: hypercalciuria, normocalcemia, hyperparathyroidism, renal stones, differential diagnosis

Table 1. Laboratory results of the patient

<table>
<thead>
<tr>
<th>Test</th>
<th>Before thiazide diuretic (initial)</th>
<th>After thiazide treatment</th>
<th>Normal ranges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total calcium (mg/dl)</td>
<td>9.8</td>
<td>9.9</td>
<td>8.4-10.2</td>
</tr>
<tr>
<td>Phosphorus (mg/dl)</td>
<td>3.6</td>
<td>3.1</td>
<td>2.3-4.7</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>4.3</td>
<td>4.3</td>
<td>3.5-5.2</td>
</tr>
<tr>
<td>Urea (mg/dl)</td>
<td>32</td>
<td>24</td>
<td>19-44</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.7</td>
<td>0.69</td>
<td>0.72-1.25</td>
</tr>
<tr>
<td>Magnesium (mg/dl)</td>
<td>2.31</td>
<td>2.05</td>
<td>1.6-2.6</td>
</tr>
<tr>
<td>PTH (pg/ml)</td>
<td>400.7</td>
<td>261 - 135</td>
<td>18.5-88</td>
</tr>
<tr>
<td>25 OH D3 vit (ng/ml)</td>
<td>17</td>
<td>24</td>
<td>30-100</td>
</tr>
<tr>
<td>Alkaline phosphatase (IU/L)</td>
<td>85</td>
<td>66</td>
<td>&lt;135</td>
</tr>
<tr>
<td>TSH (μIU/ml)</td>
<td>2.17</td>
<td>1.87</td>
<td>0.35-4.94</td>
</tr>
<tr>
<td>FT4 (ng/dl)</td>
<td>0.72</td>
<td>0.87</td>
<td>0.7-1.48</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>2</td>
<td>17</td>
<td>0-20</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>16</td>
<td>13</td>
<td>&lt;31</td>
</tr>
<tr>
<td>Ca level/spot urinary sample (mg/dl)</td>
<td>13.3</td>
<td>8.6</td>
<td></td>
</tr>
<tr>
<td>24-hr urinary phosphorus (mg/day)</td>
<td>754</td>
<td>990</td>
<td>400-1300</td>
</tr>
<tr>
<td>24-hr urinary calcium (mg/day)</td>
<td>460</td>
<td>147</td>
<td>100-300</td>
</tr>
</tbody>
</table>

INTRODUCTION: Idiopathic hypercalciuria (IH) is the most common risk factor for calcium renal stones. It is characterized by normocalcemia, elevated calcium excretion and altered PTH levels. The cause of increased renal calcium reabsorption is not clear but it appears to be a complex polygenic state. Since PTH levels can be elevated, IH is in the differential diagnosis of normocalcemic primary hyperparathyroidism (NPHPT). Here, we report a case of IH misdiagnosed as NPHPT and referred to surgery.

CASE: A 44-year-old female presented to the internal medicine outpatient clinic with complaints of fatigue. The patient had a history of left acetabular mass lesion operation in 2003 (pathology: benign giant cell tumor) and a thyroid lobectomy in 2004 (pathology: lymphocytic thyroiditis). After the surgery in orthopedics, serum PTH level was 791 pg/ml (N: 9-55), calcium level was 9.6 mg/dl, and P level was 3.5 mg/dl (year 2003). The patient was then referred to the endocrinology outpatient clinic, but she was lost to follow-up. In 2017, the patient was again admitted to the hospital with fatigue. Her PTH level was found to be 380 pg/ml and she was referred to the endocrinology department.

The patient’s laboratory results at the time of admission to the endocrinology department are shown in the table below. Her bone mineral density was normal. She had a medical history of urolithiasis but the new urinary ultrasound (US) was normal. Neck US revealed several isoechoic nodules of 12x10 mm in the inferior left thyroid lobe. Parathyroid MIBI scintigraphy showed mild activity involvement in the lateral aspect of the left lobe. The suspect parathyroid lesion was presumed to be parathyroid adenoma. PTH washout was found to be negative. Neck MRI revealed no lesions and the patient was thought to have NPHPT. Parathyroidectomy with neck exploration was recommended. She was admitted to the general surgery board. The urinary calcium was 683 mg/day at the time of preoperative endocrine and surgical council. The patient was diagnosed with idiopathic hypercalciuria (IH), therefore the operation was canceled, and indapamide 1.5 mg/day treatment was started. After 3 months, the patient’s urine Ca level decreased to 147 mg/day. After 6 months, her PTH level decreased to 135 pg/ml, and she remained normocalcemic (table 1).
Hypercalcemia in hyperthyroidism is usually asymptomatic, and related to a concurrent primary hyperparathyroidism. In this report, we describe a case of symptomatic hypercalcemia secondary to Graves’ disease alone. Case Report. A 24-year-old Filipino female presented to the emergency department with generalized weakness, vomiting and abdominal pain. No other symptoms were noted. She was otherwise previously healthy. Family history was unremarkable. During physical exam, she was noted to have a non tender palpable thyroid gland without bruit. Her ECG showed sinus tachycardia. The complete blood count and electrolytes were normal however, ionized calcium was high at 1.6mmol/L (NV 1-1.3). Renal function was normal. Hydration with saline and Furosemide 20mg once daily was started though calcium levels remained elevated. Other causes of hypercalcemia were excluded as PTH was appropriate suppressed (8.8ng/L; NV 14-72), vitamin D was also suppressed (15.29 nmol/LNV: >30). CT scan of chest and abdomen and bone scan did not point to any underlying malignancy nor metabolic bone disease. Medication history was also unremarkable. She was hyperthyroid with a suppressed thyroid stimulating hormone level of 0.004pmol/L (NV:0.55-4.78), free T3 of >20pmol/L (NV:2.3-4.2), free T4 of 8.4pmol/L (NV:0.89-1.76). Thyroid receptor antibody levels were raised at 41.07 (NV:<1 kU/L) supporting the diagnosis of Graves’ disease. She was started on propylthiouracil 50mg four times daily, along with propranolol 40mg three times daily. She was subsequently seen after two weeks with normal repeat calcium level and thyroid function test. Conclusion. This report aims to highlight that thyroid disease should always be considered as a cause of hypercalcemia. A concomitant primary hyperparathyroidism should also be evaluated. The definitive treatment for the hypercalcemia is correction of thyroid function.

**KEYWORDS:** hypercalcemia, hyperthyroidism, Philippines

Hypercalcemia in hyperthyroidism is usually asymptomatic, and related to a concurrent primary hyperparathyroidism. In this report, we describe a case of symptomatic hypercalcemia secondary to Graves’ disease alone. Case Report. A 24-year-old Filipino female presented to the emergency department with generalized weakness, vomiting and abdominal pain. No other symptoms were noted. She was otherwise previously healthy. Family history was unremarkable. During physical exam, she was noted to have a non tender palpable thyroid gland without bruit. Her ECG showed sinus tachycardia. The complete blood count and electrolytes were normal however, ionized calcium was high at 1.6mmol/L (NV 1-1.3). Renal function was normal. Hydration with saline and Furosemide 20mg once daily was started though calcium levels remained elevated. Other causes of hypercalcemia were excluded as PTH was appropriate suppressed (8.8ng/L; NV 14-72), vitamin D was also suppressed (15.29 nmol/LNV: >30). CT scan of chest and abdomen and bone scan did not point to any underlying malignancy nor metabolic bone disease. Medication history was also unremarkable. She was hyperthyroid with a suppressed thyroid stimulating hormone level of 0.004pmol/L (NV:0.55-4.78), free T3 of >20pmol/L (NV:2.3-4.2), free T4 of 8.4pmol/L (NV:0.89-1.76). Thyroid receptor antibody levels were raised at 41.07 (NV:<1 kU/L) supporting the diagnosis of Graves’ disease. She was started on propylthiouracil 50mg four times daily, along with propranolol 40mg three times daily. She was subsequently seen after two weeks with normal repeat calcium level and thyroid function test. Conclusion. This report aims to highlight that thyroid disease should always be considered as a cause of hypercalcemia. A concomitant primary hyperparathyroidism should also be evaluated. The definitive treatment for the hypercalcemia is correction of thyroid function.

**KEYWORDS:** hypercalcemia, hyperthyroidism, Philippines
INTRODUCTION: Metastatic papillary thyroid carcinoma (PTC) without an identifiable primary tumor despite extensive microscopic examination of the thyroid gland is rare but true phenomenon. We present a case who has papillary thyroid carcinoma without primary focus in thyroid gland.

CASE REPORT: A 66-year-old male patient was referred to our department after T2-vertebral biopsy was reported as papillary thyroid carcinoma metastasis. He had a history of prostate cancer which diagnosed 5 years ago and cured after 2 years follow-up. After recovery, while screening with PET, lymphadenopathy was detected and biopsy was taken. Pathology was reported as non-Hodgkin lymphoma. The patient who had treated with chemotherapy and cured, was referred to biopsy again because of increased vertebral activity had been shown at screening PET. And this biopsy was the biopsy with papillary thyroid carcinoma metastasis.

Thyroidectomy was planned for him who had diffuse bone and lung metastasis including hip, vertebra and femur. There was no primary focus in thyroid tissue pathology. Thyroglobulin value after thyroidectomy was >5000 ng/ml. Since the right iliac bone metastasis had a risk of fracture after iodine, it was requested to be evaluated by orthopedics. As the patient did not accept the operation, radiotherapy was planned as the second choice for stabilization.

200 mci of radioactive iodine treatment was planned by nuclear medicine after radiotherapy. Whole body scan was performed on the 7th day. Focal iodine uptake was observed in the left parotid gland, 2 focus in thyroid region, right hip joint, right iliac bone and left femur. In addition, increased activity uptake was observed at low intensity in both hemithorax. PET was planned due to no regression in thyroglobulin values. According to the previous findings, there was no change in the number of bone metastases in PET, but there was a decrease in metabolic activities. The patient was followed up with TSH suppression and 200 mci of radioactive iodine was given twice more since thyroglobulin levels remained constant.

On physical examination of the patient, lipoma-like swelling on the skull was enlarged. There was no activity increase in PET in the area where this lesion is present.

The patient was consulted with neurosurgery and brain tomography was planned. Tomography showed metastatic lesion in the skull and the operation was planned by neurosurgery. Postoperative pathology was reported as papillary thyroid cancer metastasis. Radioactive iodine treatment was planned again by nuclear medicine. Since the patient had a history of non-Hodgkin’s lymphoma, it was planned that hematology would consult for radioactive iodine treatment.

CONCLUSION: Metastatic papillary thyroid cancer without primary focus is rare. It is possible to be seen with different malignancies as in our patient. Although the surveillance of the disease is considered to be good, such complex cases can also be seen.

KEYWORDS: metastatic papillary cancer, radioactive iodine, skull metastasis
INTRODUCTION: Medullary thyroid carcinoma (MTC) accounts for 2%–4% of thyroid cancers. Lymph node involvement can be seen in 50%–75% of patients at initial diagnosis. Lymph nodes in the central compartment are most often involved, followed by levels II and V. Rarely, upper mediastinal and supraclavicular lymph node involvement can be seen. Here we present a medullary thyroid carcinoma case diagnosed with supraclavicular lymph node biopsy.

CLINICAL CASE: A 49-year-old woman with newly diagnosed essential thrombocytosis applied for neck discomfort. Physical examination revealed a supraclavicular lymph node. A homogenous solid, internal vascularised, with a smooth border of 21 * 25 * 33 millimeters (mm) hypoechoic mass on the left side of the neck lateral to the common carotid artery and jugular vein were observed by ultrasonography. Fine-needle aspiration biopsy (FNA) showed medullary thyroid carcinoma (ki 67 %), calcitonin, chromogranin, TTF 1, PANCK diffuse positive metastasis. Ultrasound examination of the thyroid gland was normal. Calcitonin level was 1476 pg/mL, CEA was 102 ng/mL. Other laboratory findings were shown in Table 1. Urinary fractionated metanephrines, parathormone level was normal. PET-CT detected left supraclavicular 23*23 mm mass (SUV max=3.7), and left cervical level 1B, 2B and bilateral level 2A millimetric lymph node (SUV max=1.9). DOTA Ga-68 scintigraphy also showed left supraclavicular 23*23 mm lymph node involvement. Total thyroidectomy and left neck dissection performed. The pathology report revealed 0.8 * 0.6 * 0.4 centimeters medullary microcarcinoma in the left lobe of the thyroid and also lymphatic invasion was positive. In total twelve left side level 4 and pretracheal lymph nodes were found negative, and in 1 of 10 lymph node excision in left side level 3 was detected as metastatic and diameter was 4 cm. Pathologic staging was pT1a (s), pN1b, cM0, stage IV A.

CONCLUSION: Basal serum calcitonin levels were associated with lymph node metastasis. Central compartment skip was detected in approximately 25% of cases. It is unsafe to use the lymph node status of the central compartment of the neck to define the pN status because of the lateral neck skip metastasis risk. A significant inverse correlation between the skip metastasis and the total number of involved lymph node was detected.

KEYWORDS: Medullary carcinoma, skip metastasis, calcitonin

Table 1. Laboratory results

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mg/dL)</td>
<td>93</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0.52</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>42</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>15</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td>9.4</td>
</tr>
<tr>
<td>Parathormone (pg/mL)</td>
<td>42</td>
</tr>
<tr>
<td>TSH (µU/mL)</td>
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</tr>
<tr>
<td>Free T4 (ng/dL)</td>
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</tr>
<tr>
<td>Hgb (g/dL)</td>
<td>15.4</td>
</tr>
<tr>
<td>HCT (%)</td>
<td>45.5</td>
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<tr>
<td>WBC (/µL)</td>
<td>11.2</td>
</tr>
<tr>
<td>PLT (/µL)</td>
<td>984</td>
</tr>
<tr>
<td>Sedimentation (mm/h)</td>
<td>15</td>
</tr>
</tbody>
</table>
POORLY DIFFERENTIATED THYROID CANCER PRESENTING WITH THYROTOXICOSIS AND DISSEMINATED BONE METASTASIS

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2DEPARTMENT OF ENDOCRINOLOGY AND METABOLISM, KARADENIZ TECHNICAL UNIVERSITY, TRABZON, TURKEY
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INTRODUCTION: Poorly differentiated thyroid carcinomas (PDTC) are a rare subtype of thyroid carcinomas that are biologically situated between well-differentiated thyroid carcinomas (WDTC) and anaplastic thyroid carcinomas. Even a minor poorly differentiated component of only 10% of a given carcinoma significantly affects patient prognosis. Here we present a 63-year-old female patient who presented with diffuse bone pain and thyrotoxicosis, and diagnosed with PDTC and diffuse bone metastasis.

CLINICAL COURSE: A 63 years old female patient with nodular goitre was suggested thyroidectomy 20 years ago, but she has declined the operation. She presented with back and hip pain which intensified in the last two months and could not be relieved with nonsteroidal anti-inflammatory drugs. In laboratory examination she had thyrotoxicosis and methimazole was started. Technetium-99m scintigraphy revealed a hypoactive nodule in the right thyroid lobe. The sacroiliac magnetic resonance imaging showed a 45x36 mm lesion in the right half of the sacrum. In 18F-FDG PET scan, a 65x60 mm lesion with calcifications and necrotic areas filling the right thyroid lobe and isthmus of the neck, extending into the upper mediastinum at the inferior, narrowing the trachea at this level, with borders that cannot be clearly distinguished from neighbouring anatomical structures was observed. Additionally, there were mediastinal lymph nodes and metastatic foci in the right lung, left scapula, T5 vertebrae, right sacrum, left ischium and right femur. Bone biopsy from the left scapula resulted in WDTC metastasis. Since her thyroid functions were not normalized despite 60 mg/day methimazole treatment, total thyroidectomy and lymph node dissection were performed after 3 days of plasmapheresis. Histopathologically, a 60 mm tumoral tissue in the right thyroid lobe was detected. Approximately 20% of the tumor was composed of poorly differentiated cancer cells including trabecular, solid and insular pattern. The remaining areas were morphologically WDTC. There were also capsular and lymphovascular invasion. An additional follicular variant papillary carcinoma of 3 mm was observed in the same lobe. Four central lymph nodes were excised and all were reactive. At the 6th day of surgery, her serum TSH was <0.008 uIU/ml (0.55-4.78), free thyroxine was 0.60 ng/dl (0.89-1.76) and free triiodothyronine was 2.47 pg/ml (2.3-4.2) and methimazole treatment was stopped. The patient was discharged with radioactive iodine treatment planned.

CONCLUSION: PDTC patients have worse outcomes than patients with WDTC. There is no difference in the outcomes of PDTC and WDTC with poorly differentiated component. In our case; approximately 20% of the tumor was composed of poorly differentiated cancer cells and at the time of diagnose patient had bone metastasis without cervical LAP metastasis.

KEYWORDS: thyrotoxicosis, bone metastasis, thyroid carcinoma
INTRODUCTION: Thyrotoxicosis during pregnancy is often caused by Graves disease and gestational transient thyrotoxicosis. Subacute thyroiditis (SAT) in pregnancy is very rare and there are only a few case reports in the literature. Thyroid dysfunction in pregnancy can cause fetal and maternal complications. Treatment with nonsteroidal antiinflammatory drugs (NSAIDs) and glucocorticoids (GC) may be a problem during gestation. In this case report, we aimed to describe a case of SAT diagnosed and followed up during pregnancy.

CLINICAL CASE: A 36-year-old woman at 4 weeks of gestation was referred to our hospital because of thyrotoxicosis. The patient had the symptoms of fatigue, irritability, palpitation, and anterior neck pain. She didn’t have a previously known thyroid disease and her thyroid function tests were found to be normal 5 months ago. She had a miscarriage last year. The patient’s physical examination showed that; blood pressure of 145/80 mmHg and a heart rate of 105 beat/min and a temperature of 37.3°C. The right lobe of thyroid gland was tender to palpation. Ultrasound revealed bilateral hypoechoic patchy areas especially in the right lobe (figure 1). Laboratory results obtained at the initial visit were as follows: normal white blood cell (WBC) count, TSH=0.01 mU/L (0.2-4.2), free T4=4.74 ng/dL (0.93-1.97), free T3=12.5 pg/mL (2-4.4), erythrocyte sedimentation rate (ESR)=48 mm/h, C-reactive protein (CRP)=43.2 mg/L (0-5) and all thyroid antibody tests were negative. Her clinical and laboratory findings were compatible with SAT. Paracetamol 3x500 mg was started to control pain. We planned close follow-up and control to patient and she was informed about the advantages and disadvantages of GC therapy if paracetamol fails to control the symptoms. Laboratory, USG (figure 1) and clinical status of the patient was normalized during follow-up and treatment was terminated. 40 days after diagnosis free T4 was 0.68 ng/dL (0.93-1.97) and levothyroxine was started.

CONCLUSION: SAT is a transient and self limited disease triggered by viral agents. There are very rare cases reported in the literature during pregnancy. The diagnosis and treatment may yield difficulties during gestation. NSAIDs are used as first-line treatment but should not be preferred primarily during pregnancy. Paracetamol is the safest in symptomatic treatment although it has no anti-inflammatory effect. In nonresponsive cases GC are needed. However, GC therapy should be discussed for its benefit/hazard ratio. There is no consensus on dose and duration of GC treatment. Experiences in this issue are based on case-based studies.

KEYWORDS: Subacute thyroiditis, pregnancy, glucocorticoid treatment
INTRODUCTION: Mandibular hypoplasia, deafness, progeroid features and lipodystrophy (MDPL) syndrome is an autosomal dominant disorder characterized by mandibular hypoplasia, sensorineural deafness, progressive lipodystrophy, skin scleroderma, ligament contractures as well as hypogonadism and undescended testes in males. We would like to present a case of MDPL with a mutation in the POLD1 (polymerase delta 1) gene.

CASE: Twenty-three years old male patient was consulted by rheumatologist in our hospital. In his past medical history, he was diagnosed with scleroderma. Because, he had contractures in his elbow and ankle joints, he admitted to the Rheumatology Clinic for further treatment modalities. He was born at full term by vaginal delivery. His parents had consanguineous marriage. His mother stated that there was a problem with his physical appearance since 6 year old. He was in good weight and physical appearance for four to five years. Later on, his legs and arms and his nose began to get thinner. Finally, he was followed-up with the diagnosis of scleroderma. It is not known what medications were prescribed during this period of time. It was stated that there was a problem with his physical appearance since 6 year old. He was in good weight and physical appearance for four to five years. Later on, his legs and arms and his nose began to get thinner. Finally, he was followed-up with the diagnosis of scleroderma. It is not known what medications were prescribed during this period of time. It was stated that there was the most prominent sign was the progressive thinning of the arms and the legs. Moreover, subcutaneous fat loss was noted predominantly on his facial cheeks. He had six siblings whom don’t possess any of those signs. According to rheumatology doctor, his progress was not compatible with the diagnosis of scleroderma. It was expected that scleroderma clinic would been progressive with multisystemic involvement without any special treatment. But this was not the case for our patient. Besides, he had sensorineural hearing loss. His weight was 50 kg, and his height was 185 cm. He had prominent eyes, beaked nose, small mouth. There was generalized loss of subcutaneous fat. His laboratory examination were as follows: fasting glucose 73 mg/dL, creatinine 0.49 mg/dL, fasting insulin 16.6 mU/L, ALT 65 U/L, AST 36 U/L, total cholesterol 195 mg/dL, triglyceride 467 mg/dL, HDL 41 mg/dL, LDL 107 mg/dL. His leptin level was 1.75 n/mL (0.5-3.2). Fatty liver was observed with ultrasonography. Pituitary hormones was as follows: basal cortisol 17.2 mcg/dL, IGF-1 124 ng/mL (116-358), total testosterone 19 ng/dL (280-800), FSH 25.2 mIU/mL (1.5-12.4), LH 9.17 mIU/mL (1.7-8.6). He had hypergonadotropic hypogonadism. He had prepubertal ambiguous genital appearance. He had no scrotum and testes were not observed in inguinal canal. His total body MRI revealed that there was generalized loss of subcutaneous fat and hepatosteatosis. Testosterone replacement was given. There was no mutation in LMNA and ZMPSTE24 genes. He had p.S605del heterozygous mutation in the POLD1 gene.

CONCLUSION: This is the first case of MDPL syndrome described in Turkey. We emphasize the lipodystrophy with the features of MDP syndrome which can mimic scleroderma.

KEYWORDS: lipodystrophy, mandibular hypoplasia, deafness, hypogonadism
dl. Blood was centrifuged and chylomicronemia was determined. Insulin infusion, pancreatic rest and intravenous hydration therapies were applied to the patient. The abdominal pain and vomiting of the patient was not relieved with initial treatment. Lipid apheresis was applied for hypertriglyceridemia. Lipid parameters just before plasmapheresis was TG:1508 mg/dl, and after plasmapheresis was 372 mg/dl. Clinical symptoms of pancreatitis relieved without complication with these treatments and patient was discharged with basal-bolus insulin treatment and gemfibrozil treatment.

**CONCLUSION:** Plasmapheresis may be an effective treatment option for hypertriglyceridemia induced pancreatitis. There are case series about lipid apheresis and it is not a routine treatment modality for hypertriglyceridemia induced pancreatitis recently. More clinical experience and data are needed to support the effectiveness and safety of plasmapheresis in hypertriglyceridemia induced pancreatitis.

**KEYWORDS:** pancreatitis, hypertriglyceridemia, plasmapheresis
POSTER PRESENTATIONS
SUCCESSFUL TREATMENT OF PHEOCHROMOCYTOMA CRISIS WITH EMERGENCY SURGERY: A CASE REPORT

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A 48-year-old woman was admitted to hospital due to sudden, severe, tearing chest pain, tingling, and headache. Laboratory results showed elevated troponin (34.4 ng/L) and lactate (18.6 mmol/L). ECG changes were not specific. Intubation and mechanical ventilation were required due to pulmonary edema. Pulmonary embolism and aortic dissection were ruled out. Echocardiography showed characteristic basal and midventricular segmental akinetic pattern typical of inverted Takotsubo cardiomyopathy. Significantly decreased left ventricular ejection fraction (LVEF = 20%) was consistent with clinical presentation of cardiogenic shock. Shortly before transfer to the intensive care unit an episode of pulseless electrical activity ensued, which recurred later at the catheter laboratory. Short-term resuscitation was successful. Coronarography was normal. Veno-Arterial extracorporeal membrane oxygenation (ECMO) and intra-aortic balloon pump were inserted due to cardiogenic shock. Pheochromocytoma crisis was suspected because of blood pressure rising up to 250 mmHg and a typical echocardiographic pattern. Abdominal CT showed a heterogeneous left adrenal mass 7 cm in diameter with central hemorrhage. Catecholamines and their metabolites were not determined due to continuous vasoactive support. Because of hemodynamic instability and worsening of the patient’s general condition we decided to perform urgent left-sided adrenalectomy on the fourth day of hospitalization without the usual preoperative pharmacological preparation. During surgery the tumor was completely removed. Histopathological report was consistent with malignant pheochromocytoma (Pheochromocytoma of the Adrenal gland Scaled Score, PASS 8/20). Follow-up echocardiography showed improved myocardial contractility. Some hours after the surgery it was possible to remove ECMO cannulas, while intra-aortic balloon pump was removed the next day. Femoral venous thrombosis was identified on the venous side of ECMO cannula. Transient hemodialysis was performed due to acute kidney failure. The patient was extubated five days after the surgery, vasoactive support was discontinued. Catecholamines and their metabolites were normal. No distant metastases were discovered upon additional imaging. Discharge from hospital was possible 35 days after admission. Careful surveillance was recommended by the oncology team.

Pheochromocytoma crisis is a rare emergency caused by catecholamine-induced hemodynamic instability with consequent multiple organ failure and high mortality and should be considered in patients with unexplained cardiogenic shock. The basic diagnostic procedure is abdominal CT. Veno-Arterial ECMO can improve survival in the most difficult cases, where urgent, early surgery without usual preoperative medical preparation may be necessary.

KEYWORDS: pheochromocytoma, pheochromocytoma, crisis, cardiogenic shock, emergency adrenalectomy
Cushing’s syndrome (CS) during pregnancy is a rare phenomenon with fewer than 150 cases documented in the literature. Adrenal adenomas were reported to be the commonest cause, followed by Cushing’s disease. The pregnancy excessively affects the maternal hypothalamic-pituitary-adrenal axis, resulting in increased hepatic production of corticosteroid-binding globulin (CBG), increased levels of free cortisol, and placental production of CRH and ACTH. The diagnosis of CS during pregnancy is challenging while misdiagnosis of CS is also common, as the syndrome may be easily confused with preeclampsia or gestational diabetes. Because CS during pregnancy is usually associated with severe maternal and fetal complications, its early diagnosis and treatment are critical.

Case 1: A 24 year old patient arrived our clinic with symptom of swelling especially in face and through whole body which started at her 6th month of pregnancy and still durated 12 months after giving birth. She had no history of previous known disease or medication usage. She had moon face, buffalo hump, obesity, purple abdominal striae and facial plethora (figure 1, figure 2). Her weight was 83 kg and height was 158 cm. In her blood tests, creatinine: 0.71 mg/dl, fasting plasma glucose: 79 mg/dl, alanine aminotransferase(ALT):26 U/L, Thyrotropin(TSH): 1.67 µIU/ml, calcium: 9.2 mg/dl were found. Overnight 2mg dexamethasone suppression test (DST) revealed result of 17.1 mcg/dl cortisol level. 2 day DST’s result was 18.8 mcg/dl while nighttime cortisol was 13.7 and morning cortisol was 16.2 mcg/dl. ACTH level was 10.7 pg/ml. In pituitary MRI there were two lesions: one 5 mm in right lateral, the other 3 mm in left lateral. Since ACTH level was not above 20 pg/ml we intended to perform abdominal computed tomography and high dose DST either to discriminate if the main tumor is pituitary or non-pituitary.

CONCLUSION: It is likely that earlier recognition and treatment would improve outcome in CS patients. There is a need for development of criteria for interpretation of diagnostic tests and increased consideration of CS in pregnancy. In patients as such like our case, the diagnosis would be delayed until after birth and in whom the ACTH level is mildly high and there are lesions on both side of the pituitary gland, although the birth has evolved months before; the diagnosis is challenging either. Invasive diagnostic procedures would be necessary in those patients.

KEYWORDS: cushing’s syndrome, pregnancy, onset
INTRODUCTION: Pheochromocytomas are rare tumors originating from sympathetic and parasympathetic ganglia causing a wide variety of symptoms. Sustained or paroxysmal hypertension is the most common sign of pheochromocytoma. However orthostatic hypotension and syncope can occur rarely.

CASE REPORT: A 55 year old male patient was referred to the emergency department with syncope. The supine blood pressure (BP) was 190/100 mm/Hg. Physical examination was nonsignificant. But when he stood up, he had dizziness and his BP was 70/40 mm/Hg. He was hospitalised in cardiology clinic. During follow up, visual loss occurred after he stood up. His medical history revealed a prior history of adrenal adenoma and hypertension lasting 5 years. He had also been hospitalised in neurology clinic after a hypertensive attack and diagnosed as encephalopathy with unknown etiology 2 months priorly. At the current assessment no pathology was detected in brain diffusion MR. After 24 hours his vision was improved. Pheochromocytoma was suspected due to supine hypertension, severe orthostatic hypotension. Measurement of Catecholamine levels in 24-hour urine and adrenal CT was planned. Metanephrin level was 3200 ug/24h, normetanephrine was 1889 ug/24h, noradrenaline was 339 ug/24h, and adrenaline was 193 ug/24h, respectively. An enhanced CT scan of adrenal gland revealed a lesion occupying a space in the right adrenal (3.6x2.5cm). Doxazosin treatment was started. A week after, propranolol was added to the current treatment. During hospitalization period there was no hypo-hypertension attack. He underwent operation and the pathological evaluation yielded pheochromocytoma. The patient survived without any antihypertensive drug after the surgery.

CONCLUSION: Pheochromocytoma is a rare tumor and paroxysmal hypertension is a common finding in patients. But different clinical features can be found as it occurred in our patient. Of all the abnormalities of BP, the coexistence of supine hypertension and severe orthostatic hypotension in the same patient may pose a therapeutic dilemma. Because treatment of one aspect of this condition may worsen the other. Excess norepinephrine secretion impairs endothelium dependent as well as smooth muscle dependent vasodilatation, possibly leading to coronary spasm mimicking acute myocardial infarction or retinal artery spasm leading to temporary vision loss. It has also been postulated that tumour cell death may lead to cell lysis and subsequent massive release of catecholamines and severe hypertension. In contrast, excess epinephrine secretion causes severe hypotension. Or, tumour necrosis may cause overwhelming tumour cell death and an abrupt cessation of catecholamine secretion, thereby leading to severe hypotension. It is obvious that patients with pheochromocytoma can face various clinical problems. As a result, we think that our patient is worth to be presented as an unique case of pheochromocytoma with uncommon clinical entity.

KEYWORDS: hypotension, syncope, pheochromocytoma, vision loss
INTRODUCTION: Pheochromocytoma is a rare catecholamine secreting tumor affecting 0.1-0.6% of hypertensive patients. The classical triad of pheochromocytoma includes headache, palpitations, and diaphoresis. Cardiac complications as arrhythmias, cardiomyopathy, and myocardial infarction may be seen. We presented a patient with a giant pheochromocytoma, who manifests cardiac symptoms mimicking acute coronary syndrome before the diagnosis.

CLINICAL CASE: A 28-year old male admitted with uncontrolled hypertension, palpitations and irritability with one year of symptom history. One year ago, he admitted to the emergency department with chest pain and palpitation. Electrocardiogram (ECG) demonstrated ST depression in anterior derivations. Troponin I level was normal. Urgent cardiac catheterization showed slow coronary flow in the left anterior descending artery. Any intervention for revascularization was not needed. Nevertheless, the symptoms of the patient resumed and he admitted to the hospital a few times more with similar cardiac symptoms mimicking acute coronary syndrome. When the patient referred to our department, his blood pressure was 140/90 mmHg. Heart rate was 120 beats/minute and ECG showed sinus rhythm. The physical examination was normal. The patient was evaluated for a possible catecholamine-secreting tumor. We determined increased 24 hours urinary catecholamine metabolites; metanephrine, 5587 μg/24 hours, normetanephrine, 9233 μg/24 hours, and dopamine, 728 μg/24 hours. Urinary adrenaline and noradrenaline levels were normal. Magnetic resonance imaging demonstrated a 167x70 mm sized heterogeneous mass including cystic components in right adrenal gland, which pushes the right kidney to inferior (Figure 1). MIBG scan showed increased uptake in the right adrenal localized mass.

4-mg/day doxazosin treatment was initiated before surgery. 40 mg/day propranolol was added to achieve a much better tachycardia control. After ensuring the efficiency and tolerability of the therapy, the patient underwent to right adrenalectomy by open surgery. A 990-g weighted mass excised totally with its capsule. The histopathological evaluation confirmed pheochromocytoma. Capsule invasion was not seen and the Ki67 index was <5. The patient had an uneventful recovery period. Catecholamine levels measured 2 weeks after surgery decreased to normal. We continue to follow the patient as asymptomatic.

CONCLUSION: Pheochromocytomas are uncommon tumors. The circulating high catecholamine metabolites can lead to various cardiac problems. ECG has seen normal in many of the cases, however, clinical presentation and ECG findings can mimic acute coronary syndrome. In conclusion, when physicians confront patients who have uncontrolled hypertension or unexplained heart diseases, especially in younger patients, pheochromocytoma diagnosis should be kept in mind.

KEYWORDS: pheochromocytoma, acute coronary syndrome, giant adrenal mass

Figure 1. 167x70 mm sized heterogeneous mass including cystic components in the right adrenal gland
BACKGROUND: Hypercortisolemia associated with Cushing’s disease is one of the rare causes for secondary hypertension.

CASE: A case of 48-year-old male patient with hypertension, central obesity, insomnia and impotence is presented. Patient presented with rounded and plethoric facial appearance. Initial overnight 1 mg Dexamethasone Suppression Test demonstrated no cortisol suppression (Cortisol 547 nmol/L) and he was referred to University Clinic of Endocrinology, Diabetes and Metabolic Disorders for further investigation. Baseline laboratory results were ACTH = 101.3 pg/ml, Triglycerides = 1.9 mmol/L, Total Cholesterol = 6.4 mmol/L, HDL = 1.2 mmol/L, LDL = 4.9 mmol/L, Na = 140 mmol/L, K = 4.3 mmol/L, Ca++ = 1.19 mmol/L, VMA = 28.9 µmol/dU, Metanephrines = 1.0 µmol/dU. Daily cortisol rhythm was impaired (1200/808 nmol/L, 1600/704.6 nmol/L, 2000/680.0 nmol/L, 2400/730.4 nmol/L, 0600/901.0 nmol/L), while High Dose Dexamethasone 8 mg Suppression Test showed cortisol suppression (906 nmol/L..255.1 nmol/L). Additional tests included OGTT, DXA and chest X-ray with normal findings, abdominal CT with normal findings of adrenal glands, whereas MRI of the pituitary gland demonstrated asymmetry of pituitary with a presence of focal lesion centrally and posteriorly, 3x4 mm. Also a CRH Stimulation Test was performed (0’: Cortisol = 89.6 nmol/L, ACTH = 86.2 pg/ml, 30’: Cortisol = 932.0 nmol/L, ACTH = 175.0 pg/ml, 60’: Cortisol = 1100.0 nmol/L, ACTH = 190.5 pg/ml, 90’: Cortisol = 1369 nmol/L, ACTH = 345.9 pg/ml, 120’ Cortisol = 1550 nmol/L, ACTH = 436.9 pg/ml) in favour of Cushing’s disease. Blood pressure was above the reference values and treated with an ACE inhibitor (Tbl. Enalapril 5 mg 2x1) at the beginning of the investigations, and gradually increased to 10 mg 2x1.

After proving the diagnosis of Cushing’s disease, a radiosurgery with gamma knife was applied to the patient. During the postoperative monitoring of the condition, withdrawal of symptoms occurred. Normalized blood pressure values were recorded and the treatment with ACE inhibitor was discontinued.

CONCLUSION: The patient has been investigated for hypercortisolemia according to Cushing diagnostic algorithm and was diagnosed with Pituitary Cushing disease. Radio-surgical intervention led to the normalization of cortisol values, thus eliminating the cause of secondary hypertension.

KEYWORDS: hypercortisolemia, pituitary Cushing, secondary hypertension

P-05
Adrenal

CUSHING’S DISEASE AS A CAUSE FOR SECONDARY HYPERTENSION

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OBJECTIVE: Primary hyperparathyroidism is an endocrine disorder characterised with autonomous parathormone secretion. Currently most of the cases are recognised with a slight hypercalcemia and slightly increased parathormone levels instead of renal or bone disease. Brown tumor is a late manifestation of primary hyperparathyroidism and presentation with bone disease is rare nowadays. Here we present a rare case of multiple brown tumor associated with ectopic parathyroid adenoma.

CASE: 43 year old woman admitted to hospital with complaint of emerging swelling in the jaw to orthopaedic clinic. In the preoperative blood tests for the solid lesion operation hypercalcemia was detected and patient was consulted to endocrinology clinic. Laboratory parameters were: calcium: 12 mg/dl, phosphorous: 2 mg/dl, alkaline phosphatase: 609 u/l, albumin: 45 g/l, parathormone: 1284 ng/l, 25(oh)d: 10.7 mcg/l, 24 hour urine calcium: 488 mg/day. Parathyroid scintigraphy was performed with preliminary diagnosis of primary hyperparathyroidism. A 2.5 cm solid nodular lesion in the mediastinum was detected and multiple bone lesions were detected in both frontoparietal bones, maxilla, right ramus of mandible, left clavicle and were interpreted as brown tumor. The bone lesions were also screened with bone scintigraphy and also interpreted as brown tumor with the clinical signs. The patient was operated by thoracic surgeon for the ectopic adenoma and the follow up of the brown tumors were planned.

CONCLUSION: Brown tumor as the initial clinical manifestation of hyperparathyroidism is rare without classical symptoms of hypercalcemia. The initial management is the control of hyperparathyroidism and most of the lesions regress with this but surgical excision may be required for the large painfull lesions. The patients presenting with bone lesions with the possibility of brown tumor should be examined for hyperparathyroidism with blood test.

KEYWORDS: brown tumor, hyperparathyroidism, hypercalcemia
OBJECTIVE: Suppression of osteoclast with denosumab or bisphosphonates can cause hypocalcemia. The incidence of symptomatic hypocalcemia in primary osteoporosis is rare, usually associated with medical conditions that can cause hypocalcemia: vitamin D deficiency, malabsorption syndrome, chronic kidney disease.

METHODS: 82 years old women was hospitalised due to generalized seizures. She was treated with antiepileptic therapy for 14 years, last 3 years with carbamazepin and levetiracetam. Due to high fracture risk she received denosumab therapy. At the injection day she experienced pain at the jaw, tooth, palm, joints and tingling in limbs. In the following days frequent cramps at limbs occurred, after 10 days she developed generalised seizures.

RESULTS: Initial laboratory tests: s-Ca 1.32 mmol/L, s-iCa 0.73 mmol/L, GFR 90 ml/min/1.73m², i-PTH 592.2 pg/mL, 25-OH vit. D 7.5 nmol/L, s-AP 1.85 Ukat/L, s-P 0.55 mmol/L. She was treated with i.v. Ca-gluconate, vitamin D and oral calcium. After hospital discharge she was followed in outpatients endocrinology department. Last laboratory tests: s-Ca 2.38 mmol/L, s-iCa 1.24 mmol/L, s-P 1.04 mmol/L, 25-OH vit. D 95.1 nmol/L, i-PTH 85.6 pg/mL.

CONCLUSION: Severe vitamin D deficiency because of increased metabolism of vitamin D with long term antiepileptic therapy and limited sun exposure resulted in significant secondary hyperparathyroidism. Strong osteoclast suppression with denosumab caused life threatening acute hypocalcemia. It is necessary to correct vitamin D deficiency before starting treatment with antiosteoporotic drugs.

KEYWORDS: hypocalcemia, vitamin D deficiency, antiosteoporotic drug
Thalassemia is an inherited disorder of alpha or beta globin chain synthesis leading to ineffective erythropoiesis requiring chronic transfusion therapy in its most severe form. Osteoporosis is a prominent cause of morbidity in patients with thalassaemia major; it is present in approximately 40–50% of patients. The pathogenesis includes genetic factors as well as endocrine complications (mainly hypogonadism, hypoparathyroidism, hypothyroidism and diabetes mellitus), iron overload, desferoxamine treatment, bone marrow expansion, vitamin C and vitamin D deficiencies and lack of physical activity. Annual checking of BMD starting in adolescence is considered essential.

Case – 36 year old Iranian woman arrived our clinic with diagnosis of thalassemia major offering endocrinological evaluation. She was using oral vitamin D3 and parenteral desferrioxamine for years and was under blood transfusion every three weeks. She was anti-HCV(+) for three years besides thalassemia major, for which she is under screening with normal liver function tests in gastroenterology department. She was addressing no complaint such as chronic back pain or height loss. She was having regular menstrual cycle, had no cigarette, alcohol or history of bone fracture. Her height was 154 cm and weight was 58 kg. Her bone mineral densitometry Z scores were L1-L4:-6.2, L2-L4:-6.6, L2:-6.8, L3:-7.0. She had no compression fracture appearance in lateral vertebral radiograph. Her blood test values were: Hemoglobin: 9.4 g/dl, creatinine: 0.59 mg/dl, aspartate aminotransfarase(AST): 24 IU/L, alanine aminotransfarase(ALT): 9 U/L, Thyrotropin(TSH): 2.05 µIU/ml, free thyroxine(fT4): 1.01 ng/dl, FSH(follicle stimulating hormone):5.52 m IU/ml, LH(luteinizing hormone): 3.11 m IU/ml, prolactin: 16.2 ng/ml, Estradiol:68 pg/ml,parathormone:29.5 ng/ml, 25-0H-vitamin D3: 21 ng/ml.2mg dexamethasone suppression test result was 1.0 µg/dl. Since she was willing to get pregnant in the future bisphosphonates, denosumab or teriparatid could not be prescribed because of lack of safety data. She started combined oral 1000 mg Calcium carbonate plus 880 IU vitamin D3 and 900 IU/d vitamin D3.

CONCLUSION: Thalassemi major would usually end up with osteoporosis. The mean Z score of the lumbar spine of thalassemia major patients was documented to be -2.1 in one article. The BMD scores would fall under expected levels in thalassemia major patients when accompanied with other diseases such as HCV infection. Patient’s weight, age, duration of the disease and history of hypogonadism or concurrent hypothyroidism are significant contributory factors or predictors of bone mineral loss. Male thalassemia patients would be more frequently and more severely osteopenic/osteoporotic than females. Screeing and treatment of thalassemia major patients more carefully for prevention of bone fractures and of associated morbidity should be necessary.

KEYWORDS: thalassemia major, osteoporosis, HCV infection
blood test values were as follows: Ca: 8.4 mg/dl, albumin 42g/L, cre: 0.66 mg/dl, phosphorus: 3.5 mg/dl, TSH: 1.31µIU/ml, parathormone(PTH): 225.5 ng/ml and 25-OH-vitaminD3(25-vitD3):0.6 ng/ml. Calcitriol medication was ceased and she was prescribed with only high dose vitamin D3, calling for a visit after one month.

CONCLUSION: Hypoparathyroidism is a disease which must be diagnosed after confirmation of low blood values of PTH with low Ca levels. It is medicated with Ca preparations and sometimes vitD3 preparations. Although rarely, after some period the hypoparathyroidism would undergo remission or the clinician would not be sure about the diagnosis of the hypoparathyroid patient who is under medication. This time, the blood tests must be checked for the re-evaluation. Sometimes vitamin D insufficiency is the only real reason for manifestation of hypocalcemia.

KEYWORDS: hypoparathyroidism, hypocalcemia, vitamin D deficiency

INTRODUCTION: Hypoparathyroidism is a disorder which is characterized with hypocalcemia which can reach extremely low levels when untreated and/or accompanied with vitamin D insufficiency. The medication of choice is calcium and vitamin D3. Vitamin D levels should be checked in those patients regularly, and parathormone(PTH) level would be checked either if there is no assurance of the hypoparathyroidism diagnosis. There might be disachievement in optimization of calcium and 25 oh vitD3 levels despite the treatment with calcium and/or vitamin D preparations or the real diagnosis would be singly hypovitaminosis D which could not be replenished successfully in previous years.

Case-A 35 year old woman applied to our clinic with the history of idiopathic hypoparathyroidism which she is treated for 13 years. She had no history of thyroid operation or thyroid disease. She was using calcitriol 0.5 mcg/day and calcium carbonate 500 mg/day since the diagnosis time. 7 months before the admission her calcium(Ca) level was 7.0 mg/dl, creatinine(cre):0.78 mg/dl. Her recent
days and then denosumab 60 mg subcutaneously. Ten days after injection, her serum calcium was 6 mg/dl, albumin was 3.6 mg/dl, phosphorus was 2.5 mg/dl, and PTH was 669 pg/ml. She had mild numbness and tingling in her fingers but no other symptoms of hypocalcemia, however Chvostek and Trousseau signs were positive. She was initially managed with intravenous calcium and then oral calcium supplementation and calcitriol. One week after therapy serum calcium was 8 mg/dl, albumin was 3.8 mg/dl and PTH was 569 pg/ml. She was managed as an out-patient with close monitoring of calcium homeostasis. Three weeks after therapy serum calcium was 8.4 mg/dl, albumin was 3.8 g/dl, phosphorus was 3.3 mg/dl, and PTH was 380 pg/ml.

CONCLUSION: Denosumab is increasingly used to prevent skeletal-related events related with osteoporosis and metastatic bone disease. Hypocalcemia is a known side effect of denosumab but it is generally mild and can be avoided by simultaneous vitamin D and calcium supplementation. Patients with a low baseline GFR are at significantly increased risk for developing hypocalcemia. Clinicians should ensure special attention in recognizing patients at risk of developing this serious adverse effect, so that prompt treatment and preventive strategies can be implemented.

KEYWORDS: hypocalcemia, denosumab, chronic renal failure, parathyroid hormone

INTRODUCTION: Chronic kidney disease-mineral and bone disorder (CKD-MBD) is frequently seen in advanced stages of chronic kidney disease. These patients are at high risk of fracture. Denosumab, an injectable human monoclonal antibody with affinity for nuclear factor-kappa ligand, is an effective treatment for osteoporosis in postmenopausal women and men. In contrary to the bisphosphonates, the pharmacokinetics and pharmacodynamics of denosumab are not influenced by the renal function and are being increasingly used for patients having CKD-MBD with low bone mineral density to reduce the risk of fragility fractures. Hypocalcemia is a known side effect of this drug along with compensatory increase in parathyroid hormone [PTH]. Here, we present a patient with grade IV renal failure who developed severe symptomatic hypocalcemia and dramatic increase in PTH following denosumab therapy.

CASE: A 84 years old female patient with coronary heart disease, essential thrombocytosis, hypothyroidism and chronic renal disease was consultated to our clinic for osteoporosis. She had stage IV chronic renal disease for 7 years. Her serum creatinine, urea, glomerular filtration rate (GFR), calcium, phosphorus, albumin, and PTH were 1.8 mg/dl, 58 mg/dl, 25 ml/min/1.73 m2, 9.3 mg/dl, 4.7 mg/dl, 3.4 mg/dl, and 65 pg/ml, respectively. Dual energy X-ray absorptiometry revealed a femoral neck t score of -3.7 and lumbal vertebra t-score of -3.3. She was given vitamin D 7500 IU/day for 8
BACKGROUND: It is known that 85-90% of the parathyroid adeno-
mas (PA) are found in usual locations while 5-10% can be located
ecktopically in the thymic band or mediastinum. PAs are visual-
ized as oval and hypoechoic lesions generally parallel to the thyroid
gland in two dimensional ultrasonography (US) images. However,
adenomas with atypical locations can be in different forms in the	hree dimensional plane. The most common form is the bean grain
type. In this report we present four cases of atypical PA with differ-
ent US features and locations.

CASE-1: A 41-year old patient was referred to emergency service
with hypercalcemia crisis. His calcium (Ca) and intact parathyroid
hormone (iPTH) levels were 14.24 mg/dl and 735 pg/ml respectively.
His biochemical parameters were shown in table. Since Ca level did
not decrease with intravenous hydration and loop diuretics, hemodi-
alysis was performed and his Ca level decreased to 11 mg/dl. There
was no lesion compatible with PA in his first neck US. Technetium-
99m-sestamibi was compatible with PA. No adenoma was found in the
second US evaluation also. But when the US probe was changed from
13-5 MHz to 10-5 MHz and the tissue penetration was also changed,
a giant PA isoechoic with the thyroid gland was seen inferior to the
right thyroid lobe starting from the lower end extending to the cervi-
cal vertebrae. PA was removed successfully with minimally invasive
procedure (MIP) and the histopathological diagnosis was atypical PA.

CASE 2: A 52-year old woman was referred to our clinic because
of hypercalcemia. Her biochemical parameters were shown in the
table. US revealed a hypoechoic lesion (compatible with PA) with
macrocalcific areas, fibrous bands and partial cystic changes in the
inferior posterior part of the right thyroid gland. She underwent
MIP and atypical PA was detected histopathologically.

CASE-3: A 35-year old woman admitted to emergency clinic due
to the hypercalcemia crisis (biochemical parameters were shown
in table). A giant PA lesion in the right thyroid gland starting from
the middle part to the inferior part was detected in neck US. It was
iso-hypoechoic and had partial cystic areas. After the removal of
the PA, her Ca level was normalized and histopathologically atypi-
cal PA was observed.

CASE-4: A 82-year old man was referred to our outpatient clinic
due to hypercalcemia. His US finding was consistent with PA lo-
cated superior to the right thyroid gland. It was isoechoic and had
partial cystic areas. He underwent MIP and Ca levels decreased
to normal levels. The histopathological diagnosis was atypical PA.

CONCLUSION: The common US findings of these four atypical
PAs were either the anteroposterior diameter was longer than the
transvers diameter (in all of the four cases) or the PA was larger
than the longest diameter of the thyroid gland (case 3 and 4). Our
findings suggest that the location and the size of atypical PAs may
also be atypical.

KEYWORDS: Atypical parathyroid adenoma, parathyroid adenoma,
ultrasonography, histopathology

Figure 1. Ultrasonography images of the atypical parathyroid
adenomas

PARATHYROID ADENOMAS WITH ATYPICAL
HISTOPATHOLOGY HAVE ALSO ATYPICAL
ULTRASONOGRAPHY FINDINGS

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Table 1. Biochemical features and Technetium-99m-sestamibi results of the patients, sizes of the parathyroid adenomas and the longest diameter of the thyroid gland

<table>
<thead>
<tr>
<th>Variables</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
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<td>Calcium (mg/dl)</td>
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<td>25-hydroxy vitamin D (µg/L)</td>
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<td>Parathyroid adenoma size (mm)</td>
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<td>Anteroposterior</td>
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<td>Longest diameter of the thyroid gland (mm)</td>
<td>40</td>
<td>45</td>
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 Bone/Calcium

SEVERE AND LONG-STANDING HYPOCALCEMIA SECONDARY TO DENOSUMAB TREATMENT IN A PATIENT WITH POSTOPERATIVE HYPOPARATHYROIDISM, BREAST CANCER AND BONE METASTASIS

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INTRODUCTION: Denosumab is a monoclonal antibody, which is used to prevent bone-related outcomes in patients with solid tumor bone metastasis and reduces the transfer of calcium from bone into the blood. It rarely causes severe hypocalcemia as a side effect. Here we present a case of severe hypocalcemia lasting 8 months after administration of a single dose of denosumab given for diffuse bone metastasis. The patient’s concomitant surgical hypoparathyroidism has also contributed to the development of hypocalcemia.

CASE: A 57-year-old female patient who underwent left mastectomy for breast cancer in 2002 and received chemotherapy and radiotherapy was operated for multinodular goiter in 2013. Histopathological diagnosis was multifocal papillary thyroid carcinoma and it was in complete remission. In April 2018, she was diagnosed with postoperative hypoparathyroidism and her serum calcium levels were in normal ranges with calcitriol 0.5mcg/day and calcium carbonate 1000mg/day. In December 2018, she was given denosumab 60mg subcutaneously and capecitabine treatment due to disseminated bone metastasis of breast cancer detected in 18F-FDG-PET examination. Although her serum calcium was 9.3mg/dL a few days before denosumab, four days after injection her serum calcium was 6.9mg/dL. Her calcitriol and oral calcium supplementation doses were increased in course of time in another clinic. At the second month of denosumab, she was consulted to our clinic due to weakness, tingling in the body and numbness and a serum calcium was 6.2mg/dl (8.7-10.4), phosphorus was 4.3mg/dL (2.4-5.1), albumin was 36 g/L (32–48) and parathyroid hormone was 28.0pg/mL (18,5–88) despite treatment with calcitriol 2mcg/day and oral calcium 5000 mg/day. She was hospitalized and intravenous calcium infusion was given with oral active vitamin D and calcium supplementation. Since the patient had low calcium values with calcitriol, treatment was replaced by alphacalcidol. During hospitalization, intravenous calcium infusions were repeated and oral vitamin D and calcium supplementation doses were increased. Her serum calcium could be maintained between 7.5-8 mg/dl with high doses of vitamin D and calcium. She was on 3mcg/day alphacalcidol, 8000 mg/day calcium carbonate and she had a serum calcium of 7.6mg/dl when she was discharged at the 25th of hospitalization. She was followed weekly and then every 15 days in the outpatient clinic and vitamin D and calcium supplementation doses were reduced, gradually. Finally at the 8th month of denosumab injection, the treatment doses of alphacalcidol and calcium carbonate could be reduced to basal levels which were 0.5mcg/day and 1000mg/day, respectively.

CONCLUSION: Hypocalcemia is a known side effect of denosumab, however it is usually mild. In the case of coexisting hypoparathyroidism, severe and prolonged hypocalcemia that needs to be treated with intravenous calcium and very high doses of vitamin D and oral calcium supplementation may occur.

KEYWORDS: breast cancer, bone metastasis, hypoparathyroidism, denosumab, hypocalcemia
Hypercalcemia secondary to hypervitaminosis D is extremely rare. Vitamin D intoxication usually occurs as a result of inappropriate use of vitamin D preparations and can lead to life-threatening hypercalcemia.

Here we present a case of a 45-year-old female diagnosed with colon adenocarcinoma stage IV with liver, lung and bone (ribs) metastases, s/p FOLFOX x 6 cycles, s/p FOLFIRI x 2 cycles. She was admitted for 3rd cycle chemotherapy but hospitalization was complicated by development of pneumonia with worsening of kidney function and initiation of hemodialysis. Despite being on regular hemodialysis, her calcium levels were noted to be increasing. She was also noted to be feeling weaker, with decrease in sensorium attributed to hepatic encephalopathy. Workup for hypercalcemia revealed low normal PTH (21.50 pg/mL, N: 14.0-72), with a normal phosphorus level and elevated Vitamin D (104.28 ng/mL, N: 30-50). It was later revealed upon review of the patient’s medications that her mother was giving her various herbal supplements, the latest of which was one that contained an extract from Agaricus blazei Murrill, a mushroom native to Brazil that allegedly aids in the treatment of a variety of diseases such as cancer, chronic hepatitis, diabetes, atherosclerosis and hypercholesterolemia.

Mushrooms are one of the main dietary sources of vitamin D. The probable offending agent was discontinued and the patient was given IV hydrocortisone. Other therapies such as calcitonin and denosumab were not given due to the patient’s history of anaphylactic reactions. Serial monitoring showed that the calcium levels steadily decreased, as well as the Vitamin D levels, although at a slower rate. This case highlights the importance of assessing the intake of all substances, not only prescribed medications, and the potential danger of the ingestion of unlicensed herbal supplements.

**KEYWORDS:** Hypervitaminosis D, Hypercalcemia, Calcium Metabolism
Primary hyperparathyroidism is a state in which serum calcium and PTH levels increase concurrently and usually caused by a solitary parathyroid adenoma. Rarely, localization may not be found by conventional imaging methods including ultrasonography and parathyroid siringraphy. The presence of a thyroid nodule located posteriorly and close to the parathyroid gland’s localization causes diagnostic challenge. Parathyroid cells have a large amount of mitochondria which enables sestamibi to enter more intensely into the neighboring thyroid tissue. Fine needle aspiration gives poor results when parathyroid tissue is located within thyroidal tissues with most aspirates being misinterpreted as thyroid follicular neoplasms because of the similarity of cytomorphological features. Parathyroid fine needle washout may be helpful in distinguishing thyroid nodule from parathyroid adenoma but results may not be clear all time. We present a case in which giant parathyroid adenoma mimics a thyroid nodule.

A 53-year-old man with no remarkable history was evaluated for weakness and fatigue. Physical examination revealed a 5 cm nodule in thyroid region. In laboratory and radiological assessment, TSH and free T4 levels were normal. Corrected serum calcium 12.8 mg/dL (8.5–10.5) and parathormone (PTH) of 631 pg/mL (12–88) were markedly elevated with hypophosphatemia 2.2 mg/dL (2.5–5.5). Ultrasonography of the neck revealed a heterogeneous echo nodule of 51x38x43 mm with smooth contours, cystic openings extending from the inferior to the left lobe of the thyroid. Although, there was no history of nephrolithiasis and bone fracture, 24 h urine calcium level was detected increased (498 mg/day). Bone mineral density scores were normal including lumbar, femoral neck and distal third of radius. Parathyroid siringraphy and single-photon emission CT (SPECT)-CT did not confirm a parathyroid adenoma. A US-guided percutaneous fine needle aspiration of the dominant nodule was performed and reported as benign follicular thyroid nodule on cytologic examination. Parathyroid hormone washout from the suspected nodule was performed and examination is resulted compatible with serum PTH levels. Since, we couldn’t localize the source of elevated PTH, we performed parathyroid venous sampling. PTH levels were detected four times higher at left brachiocephalic vein than the right one. Based on these findings, the thyroid mass, in this patient with primary hyperparathyroidism, is presumed to be parathyroid adenoma so the patient underwent to left lobectomy. Histopathologic examination was revealed parathyroid adenoma. Postoperatively, serum calcium levels normalized and PTH levels declined.

Especially in the absence of a typical location on imaging or known hyperparathyroidism, besides conventional imaging techniques, parathyroid venous sampling can guide to surgical intervention. Parathyroid lesions can be reliably distinguished from thyroid nodules by cytomorphological methods after surgery. 

**KEYWORDS:** hypercalcemia, parathyroid nodul, thyroid nodul
A 72 year old female patient was examined by an internist due to diffuse vague pain lasting 2 months. On basic metabolic panel severe hypercalcaemia was detected (14.32 mg/dL corrected for albumin). Further tests were run and revealed phosphorus (P) 2 mg/dL, parathyroid hormone (PTH) 1337 pg/mL, 25 OH vitamin D (vit D) 67 ng/mL. Blood urea nitrogen (BUN) and creatinine (Cr) were within normal range. She was hospitalized in the internal medicine ward and hydrated. Diuretic therapy and zoledronic acid (5 mg) was administered intravenously along with steroid afterwards. Calcium (Ca++) level decreased to a nadir level of 13.7 mg/dL. Ultrasound revealed multiple isoechoic well demarcated nodules, the largest one measuring 17x15 mm in size. However the ultrasound was fruitless for detecting a parathyroid lesion. MIBI-technetium subtraction scan was planned. However she refused further investigation and was voluntarily discharged.

Ten days after discharge she was brought to the emergency room because of deteriorating consciousness and decreased oral intake. She was consulted with endocrinology specialist. On physical examination she showed signs of dehydration (decreased skin turgor and tonus). She was confused (Glasgow Coma Scale score 9). Her temperature was normal. Her blood pressure was 120/60 mmHg. She was significantly kyphotic. She had an operation scar over her anterior neck due to a previous thyroid surgery. No murmur was detected on cardiac auscultation, but rhythmic tachycardia was present. Her lungs were clear. Abdominal examination was normal peripheral oedema was absent. Laboratory tests were as follows: Ca++ 23.2 mg/dL, albumin 3.7 g/dL, P 3 mg/dL, BUN 39 mg/dL, PTH 1300 pg/mL, vit D 119 ng/mL, leucocyte count 18.300/mm3. TSH was within normal range.

She denied any chronic disease and kidney stone. She underwent thyroidectomy about 50 years ago, but the pathology report was missing. She was not on any regular medicine but taking non steroidal anti-inflammatory drugs and proton pump inhibitors on irregular basis. Since vit D level was high on 2 occasions, the patient was questioned for a possible injudicious use of vitamin D. It was discovered that she had been prescribed oral 300 000 U cholecalciferol.

PTH level was still very high despite vit D sufficiency, primary hyperparathyroidism was suspected. A lesion in the lower right of thyroid lodge on MIBI-Technetium parathyroid thyroid subtraction scan and a lesion neighbouring inferior to the residual thyroid tissue, which was 8x4 mm in size, compatible with parathyroid adenoma on contrast-enhanced computed tomography. She was referred to surgery. Before surgery, her final values were Ca++ 15.0 mg/dL, P 2 mg/dL, PTH 830 pg/mL, vit D 84 ng/mL. Post-surgical pathology report is pending.

Vitamin D therapy may uncover previously undiagnosed hyperparathyroidism and resultant hypercalcemia may lead to detrimental outcomes. Ca++ measurement is crucial before prescription.

**KEYWORDS:** malignant hypercalcemia, vitamin D intoxication, primary hyperparathyroidism
It has been described in the literature that parathyroid glands may be located ectopically. Parathyroid glands may have ectopic location, which has been described in the literature. Approximately 30% of ectopic parathyroid adenomas are asymptomatic and clinical and radiological diagnosis can be difficult. Ectopic localization within the thyroid is the result of abnormal complex migration of the glands during embryogenesis.

Intrathyroidal parathyroid adenomas can be evaluated as neck thyroid nodules in the USG, and FNA can be mistakenly diagnosed as follicular neoplasia. Because of their morphological similarities, it is difficult to differentiate parathyroid lesions from thyroid lesions based solely on FNA. Although there are studies showing that wash-out for PTH helps, the unstable structure of the hormone and the lack of standardization for testing are barriers to its usage.

Our case was diagnosed with intrathyroid parathyroid adenoma and thyroid papillary microcarcinoma in the other lobe of the thyroid. When the literature was reviewed, a case with intrathyroid parathyroid adenoma and thyroid papillary microcarcinoma were reported.

**KEYWORDS:** intrathyroid parathyroid adenoma, follicular thyroid neoplasia, thyroid papillary microcarcinoma
immediately and iv hydration, diuretic treatment and then hemodialysis treatment were applied. She got extubated after 3 days. Serum calcium levels were gradually decreased to 9.5 mg/dL in 4 days. 1,25-OH vitamin D3 level could be measured at third day of ICU admission, and it was 43 pg/mL (19-65 pg/mL). One week later the patient was well and discharged with normal calcium (9.2 mg/dL) and normal PTH levels (28 pg/mL) without calcium or calcitriol replacement.

CONCLUSION: The treatment of postoperative hypoparathyroidism can be challenging. In particular, calcitriol may play a role in the development of life-threatening severe hypercalcemia due to the narrow therapeutic range especially in patients who can not be monitored closely.

KEYWORDS: hypercalcemia, iatrogenic, thyroidectomy, hypoparathyroidism

**INTRODUCTION:** Iatrogenic injury of the parathyroid glands resulting hypoparathyroidism is a common complication of thyroidectomy. It can be permanent but it is mostly transient. We describe a case with severe hypercalcemia after early treatment with calcitriol due to hypoparathyroidism after thyroidectomy.

**CASE REPORT:** A 49 year-old woman was admitted to our emergency department with confusion and dizziness. In a short time, her level of consciousness decreased and she was intubated due to low GCS score and cardiac arrest. She was taken to intensive care unit (ICU) for further treatment and evaluation. The laboratory test results showed: serum calcium 17.8 mg/dL (8.5-10.5 mg/dL), albumin 4.9 g/dL (3.9-4.9 g/dL), phosphor 7.2 mg/dL (2.6-4.5 mg/dL), 25-OH vitamin D 28 ng/mL, PTH 5.6 pg/mL (15-65 pg/mL), creatinine 2.9 mg/dL (0.7-1.2). There was no significant abnormality with imaging tests of the brain. It was found out that she had undergone two thyroid surgeries about 3 months ago. The first operation was right lobe thyroidectomy and it was reported as a follicular variant of papillary thyroid carcinoma, and the report also said that tumoral tissue was present within surgery limits. Complementary thyroidectomy was a few weeks later and no malign tissue was reported. Post-operative first day laboratory test results after the second surgery were as follows; PTH 10.6 pg/mL, calcium 7.6 mg/dL, albumin 3.6 g/dL, phosphor 3.5 mg/dL. On the first surgery it was noted that parathyroid glands were preserved but the second surgery note did not mention anything regarding to parathyroid glands. The patient experienced muscle spasms after the second operation, and the surgery department started calcitriol 0.5 mcg b.i.d. and calcium carbonat 1000 mg plus vitamin D3 880 IU q.i.d. before discharge from the hospital. Three weeks after the surgery her TSH level was 49 IU/mL (0.27-0.42 IU/mL), PTH 6.2 pg/mL, calcium 12.05 mg/dL, phosphor 4.3 mg/dl, however interestingly no change in the patient’s medications was recommended. Two months after the surgery, she was treated with 100 mci radioactive iodine. We were consulted for symptomatic hypercalcemia while she was in ICU. Calcitriol and calcium carbonat was stopped immediately and iv hydration, diuretic treatment and then hemodialysis treatment were applied. She got extubated after 3 days. Serum calcium levels were gradually decreased to 9.5 mg/dL in 4 days. 1,25-OH vitamin D3 level could be measured at third day of ICU admission, and it was 43 pg/mL (19-65 pg/mL). One week later the patient was well and discharged with normal calcium (9.2 mg/dL) and normal PTH levels (28 pg/mL) without calcium or calcitriol replacement.

**CONCLUSION:** The treatment of postoperative hypoparathyroidism can be challenging. In particular, calcitriol may play a role in the development of life-threatening severe hypercalcemia due to the narrow therapeutic range especially in patients who can not be monitored closely.

**KEYWORDS:** hypercalcemia, iatrogenic, thyroidectomy, hypoparathyroidism

**FIGURE 1.** Overall timeline of the patient’s surgeries, laboratory values and treatments made
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Bone/Calcium

USEFULNESS OF VITAMIN D REPLACEMENT IN PRIMARY HYPERPARATHYROIDISM WITH CONCURRENT VITAMIN D DEFICIENCY-CASE REPORT

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INTRODUCTION: Hypercalcemia is the most common clinical presentation of primary hyperparathyroidism (PHPT). The diagnosis is usually first suspected because of the incidental finding of an elevated serum calcium concentration on biochemical screening tests. Concurrent vitamin D deficiency may cause confusion in course of diagnosis, follow-up and treatment. It is reported that individuals with vitamin D deficiency and hyperparathyroidism have more clinically significant disease, including larger adenomas, higher concentrations of PTH, increased bone turnover, and more frequent fractures.

We aim to present a case to impress the usefulness of vitamin D replacement in patient with hypercalcemia.

CLINICAL CASE: A female patient aged 42 applied to our outpatient clinic with difficulty in walking. She was a housewife who had 5 children. She ignored any trauma and known rheumatological disease. She had no history of any kind of medication. She reported regular cycles. Her last delivery was 2 years ago. Total lactation period was approximately ten years.

Laboratory findings were as follows at admission: Serum creatinine: 0.28mg/dL, PTH: 1672 pg/mL, albumin: 37.8g/L, calcium 11.0 mg/dL, phosphate: 1.53, vitamin D: 6.8 ng/mL, alkaline phosphatase activity(ALP): 2669 U/L, estimated glomerular filtration rate (e-GFR): 144mL/min/1.7m² ECG: normal sinus rhythm.

Bone mineral density(BMD) by dual energy x-ray absorptiometry (dxa) revealed osteoporosis (Z-score L2-L4:-2.4, femoral neck: -2.7,T-score L2-L4:-2.4, femoral neck: -3.0)

Primary hyperparathyroidism with vitamin D deficiency was diagnosed based on laboratory findings including elevated serum calcium and PTH levels. MIBI spect images revealed a lesion localized at inferior region of right thyroid lobe suggesting parathyroid adenoma.

The patient was discussed at our endocrinology council regarding to surgery indications. 1200 IU/day Vitamin D was given to replace deficiency prior to parathyroidectomy, mainly in order to prevent hungry bone syndrome that may be seen in such patients like our’s with severe osteomalacia.

At 3rd month of follow-up PTH, ALP, calcium levels decreased to: 610.7 pg/mL, 843U/L, 10mg/dL respectively 25 OH vitamin D level increased to19.7 ng/mL (Table 1)

CONCLUSION: It has shown that mild doses of vitamin D replacement improve serum 25-hydroxyvitamin D levels, while PTH levels remain unchanged without worsening of hypercalcemia in patients with concurrent vitamin D deficiency.. In our patient replacement of vitamin D not only improved clinical symptoms of osteomalacia, also normalized serum calcium levels. The benefits of vitamin D replacement in such patients, need further evaluation with larger numbers of patients.

KEYWORDS: vitamin D deficiency, primer hyperparathyroidism, hypercalcemia

Table 1.

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<th>Admission</th>
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<tr>
<td>PTH</td>
<td>1672 pg/mL</td>
<td>610.7 pg/mL</td>
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<tr>
<td>ALP</td>
<td>2669 U/L</td>
<td>843 U/L</td>
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<tr>
<td>Calcium</td>
<td>11 mg/dL</td>
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<tr>
<td>Vitamin D</td>
<td>6.8 ng/mL</td>
<td>19.7 ng/mL</td>
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ALP: alkaline phosphatase activity
INTRODUCTION: The causes of hypercalcemia may be PTH-mediated or non-PTH-mediated. It is mostly easy to find the etiology, however herein we presented a case in whom we couldn’t be successful in explaining the cause and also the mechanism.

CASE: A 21-year-old male admitted with nausea, vomiting, progressive weakness and bone pain. He had no remarkable medical and family history. On his physical examination, he was immobile, wheelchair-bound and his movements were painful. Laboratory evaluation revealed a calcium 16 mg/dL, PTH 4 pg/mL, phosphorus 4.2 mg/dL (2.2-4.4 mg/dL), ALP 192 U/L (40-129 U/L), creatinine 1.3 mg/dL (baseline 0.7 mg/dL), uric acid 10.8 mg/dL (2.5-7 mg/dL), CRP 3.8 mg/L (<5 mg/L), eritrocyte sedimentation rate 13 mm/h, 25OHD: 26 ng/mL, TSH: 2.1 mIU/L. PTHrP and 1,25 (OH)2D concentrations were low. Severe hypercalcemia with suppressed PTH was compatible with non-PTH mediated hypercalcemia. Protein electrophoresis, serum/urine immunofixations, serum concentrations of kappa, lambda, beta-2 microglobulin, immunoglobulin, vitamin A, ACE, IGF-1, urine catecholamine metabolites, 5-HIAA, NSE, CK, calcitonin and IL-6, also rheumatologic tests including ANA, ENA, anti-dsDNA, MPO-ANCA, PR3-ANCA, C3, C4, RF, anti-CCP were all normal. No sign of malignancy was detected with 18-FDG and Ga68-DOTA-TATE-PET-CT. Bone scintigraphy showed increased osteoblastic activity on cranium, axillary and appendicular skeleton, increased osteoblastic and osteoclastic activity in the long bones. Whole body MRI showed osteolytic changes in the diaphyseal region of femur, tibia, fibula and humerus, radius, ulna bilaterally. Also bilateral stress fractures were noted in the tibial plateau. All these findings led us to suspect that it could be a metabolic bone disease. Tru-cut bone biopsy of humerus which was not sufficient for diagnosis revealed trabecular bone formation with osteoblastic and osteoclastic activity with no tumor cell.

During these evaluations we administered iv saline infusion, zole- dronic acid (on admission and 2 months later) and achieved normocalcemia only for a short while (Picture 1). Due to insufficient and short-term calcium-lowering effect of bisphosphonate, methylprednisolone 32 mg/day was started and calcium level normalized in 15 days. On 4th week of glucocorticoid treatment, the patient started to be mobile, but we did not let him to walk without a walker to avoid a new fracture.

The dose of methylprednisolone was tapered gradually and stopped on day 20th. He is still on follow-up, his serum calcium level didn’t increase after cessation of glucocorticoid for 3 months and no new fracture occurred.

CONCLUSION: We could not highlight the exact cause of hypercalcemia and multiple fractures in the present case. We can speculate that increased osteoclastic activity and hypercalcemia which is responded to glucocorticoid treatment may be associated with malignant cells which may release local osteoclastic activating factors.

KEYWORDS: Hypercalcemia, metabolic bone disease, PTH-mediated, non-PTH mediated
A CASE OF PSEUDOPSEUDOHYPOPARATHYROIDISM WITH SEVERE HYPOCALCEMIA

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Pseudopseudohypoparathyroidism (PPHP) is a rare condition of pseudohypoparathyroidism which is caused by several alteration or mutation for the alpha subunit of the G protein (GNAS). It is characterized by the presence of Albright Hereditary Osteodystrophy (AHO) and the absence of any hormone resistance, serum calcium and PTH levels are normal.

CLINICAL CASE: 35 years old female patient admitted to the outpatient clinic with the complaints of paresthesia on face and especially on the lips, muscular twiching and contraction on hands. Chvostek’s and Trousseau’s sign were both positive, and she had carpopedal spasm. She had round face, short stature, short fingers, 4th short metacarsps on right hand and 3rd short metacarsps on left hand. The patient had severe hypocalcemia, hypomagnesemia, vitamin D deficiency, normal phosphorus and intact PTH level with normal renal functions. It was learned that she had diarrhea for three weeks and she gave birth a month ago. The patient has never had similar complaints before and during pregnancy.

CONCLUSION: Hypocalcemia etiology should be investigated in patients with probable PPHP diagnosis, as our patient had intestinal loss.

KEYWORDS: hypocalcemia, hypoparathyroidism, pseudopseudohypoparathyroidism
CASE 2: A 54 year-old women was diagnosed with colon cancer in 2004 and underwent total gastrectomy due to gastric lesion in 2014. Parathyroid scintigraphy was performed in 2009 due to a serum calcium of 10.4 mg/dL and PTH of 99pg/mL but no pathology was detected. In 2016 serum calcium, albumin, phosphorus, PTH and 25-hydroxyvitamin D were 10.7 mg/dL, 3.6 g/dL, 2.8 mg/dl, 12 g/dL and 202 pg/mL. She had nephrolithiasis and osteoporosis (lumbal vertebra t score was -3.5 in dual energy X-ray absorptiometry). A 15x5x3mm lesion inferior to the left thyroid lobe was detected in ultrasonography and it was confirmed to be a parathyroid lesion with scintigraphy. The patient underwent parathyroid adenomectomy in 2016 and histopathologic result was consistent with parathyroid adenoma.

CONCLUSION: We hypothesize that parathyroid adenoma secondary to chronic hypocalcemia may develop in patients undergoing gastrectomy for gastric cancer. However, parathyroid adenoma and gastric cancer may be just a coincidence. Further studies on pathogenesis are needed. It is important to keep in mind that calcium and vitamin D levels should be monitored in patients undergoing gastrectomy regardless of etiology.

KEYWORDS: Parathyroid adenoma, Operated gastric carcinoma, Hypocalcemia

BACKGROUND: The prevalence of bone disease is high after gastrectomy because of a change in the calcium metabolism. There are several reports about development of secondary hyperparathyroidism in patients operated for gastric cancer. We present two cases who underwent total gastrectomy for gastric cancer and developed parathyroid adenoma during long-term follow-up.

CASE 1: A 60 year-old woman with multinoduler goiter underwent gastrectomy due to gastric cancer 3 years ago. Her serum calcium was 8.3 mg/dL (8.6-10.2 mg/dl), albumin was 3.9 g/dL(3.9-4.9 g/dL) and 25-Hydroxyvitamin D was 5.9 ng/mL(30-100ng/mL) two months after the operation. Laboratory test results in 2019 was as follows; serum calcium 9.4 mg/dl, albumin 4.3 g/dl, parathyroid hormone (PTH) 123 pg/mL (15-65pg/mL) and 25-hydroxyvitamin D 20 ng/mL. Alkaline phosphatase was 94U/L(5-141U/L) and 24-hour urine calcium was 151 mg/day. Cervical ultrasonography revealed a 4x5.8x5.4 mm hypoechoic lesion inferior to the left thyroid lobe compatible with parathyroid adenoma. Parathyroid SPECT-CT revealed parathyroid pathology in the lower pole of the left lobe. She did not have osteoporosis and nephrolithiasis. Asymptomatic primary hyperparathyroidism was diagnosed and follow-up was recommended for the patient.
UNEXPECTED FINDING IN D VITAMIN INSUFFICIENCY; HYPERCALCEMIA WHICH DOES NOT INCREASE WITH REPLACEMENT THERAPY

KEYWORDS: Hypercalcemia, Vitamin D deficiency, vitamin D insufficiency

REPLACEMENT THERAPY: D vitamin deficiency is a common problem worldwide. It is characterized by hypocalcemia and/or hypophosphatemia. Hypercalcemia has not been reported in D vitamin deficiency. Here we report about 2 cases with hypercalcemia and viD deficiency.

CASES: CASE 1: A 58-year-old man admitted to our outpatient clinic for routine check-up. We analyzed 25-OH Vitamin D level, calcium level, phosphorus, albumin, PTH. Ca was slightly elevated. (Ca2+: 10.7 mg/dl; alb: 5.3 gr/dl; corrected Ca2+: 10.6 mg/dl; phosphorus: 4 mg/dl, PTH: 66; Chlorine:105 mmol/L). At the same time 25-OH vitamin D was 19 ng/ml. We administered vitamin D. After appropriate therapy the Ca level did not increase.

CASE 2: A 54-year-old woman attended our policlinic with the question whether she had osteoporosis. She had vitamin D insufficiency. 25-OH vitamin D: 15 ng/ml, Ca2+: 10.5, albumin: 4 g/dl, phosphorus: 2mg/dl. Vitamin D was administered intramuscularly for this patient due to stomach pain.

Moderate hypercalcemia was noticed and we checked for vitamin D level. We administered only vitamin D because the patient had no other complaint. There was no drug, other illness history that could explain the hypercalcemia.

CONCLUSION: During hypercalcemia etiology screening we have observed that some patients have slightly hypercalcemia as an unexpected finding in D vit deficiency. We have observed that this slightly increase of calcium did not deteriorate after replacement therapy. We have observed that some patients with vitamin D deficiency do not have any hypocalcemia. Some of these patients have surprisingly a slight increase in Ca which does not deteriorate after therapy. The underlying mechanism of this needs to be discussed.
After the diagnosis was clarified as LADA diabetes, the patient was given intensive insulin treatment with basal-bolus. Insulin Degludec 16 IU once daily subcutaneously + insulin aspart was given 8-10 IU subcutaneously.

When the patient was checked after a month, he was very good, had no complaints, was satisfied with the treatment and his HbA1C values were 7.1%.

**RESULTS:**
A1C first -12.3%
A1C -7.1% after 1 month

**DISCUSSION AND CONCLUSION:** Although rare, we should remember that LADA diabetes will occur in elderly patients who are always non-obese, with no family history, known as uncontrolled type 2 diabetes, and we want to remind the importance of this.

**KEYWORDS:** Anti-GAD, Insulin antibody, Islet antibody, LADA diabetes

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**INTRODUCTION:** LADA diabetes (Latent Autoimmune Diabetes in Adult) is a type of autoimmune diabetes that occurs in adults over the age of 30 years and is often confused with the classical types of diabetes. The importance of correct diagnosis of LADA in achieving glycemic control is mentioned in this case.

**METHOD:** The case was a 58-year-old female housewife with weight loss, frequent urination, dry mouth and fatigue. She had been suffering from type 2 diabetes for 10 years. In the patient’s family history, he reported that no one had diabetes. At night, we learned that he used 20 IU Insulin glargine + Gliclazide 120 mg + Vildagliptin 50 mg / metformin 1000 mg twice a day. Acute blood glucose was 265.7 mg / dl, C-peptide was 0.2 ng / mL, microalbumin (spot urine) was 228 mg / g, GFR was within normal reference ranges, apart from normal routine biochemistry, thyroid function tests and other assays. We found out that the diet fits, the patient watches her diet, but is not physically active.

HbA1C values and high blood sugar levels, despite the patient’s medication, led us to review the diagnosis again.

The patient’s non-obese (height-161 cm, weight-56 kg, BMI-21.6 m2 / kg), had low insulin reserve, no family burden of diabetes, lack of macro and microvascular complications due to diabetes for 10 years Two of the 3 antibodies were positive. Anti-GAD positive -82.31 IU / ml (0-5), Islet (Islet) antibody positive-7.02 IU / mL (> 1 positive), Insulin antibody -2.2 IU / mL negative (0-10.0).

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**KEYWORDS:** Anti-GAD, Insulin antibody, Islet antibody, LADA diabetes
BACKGROUND: Glucagon-like peptide-1 receptor agonists (GLP-1RA) are a new class of injectable therapy in Type 2 Diabetes (T2D) with proven efficacy in lowering blood glucose parameters and causing weight loss. Liraglutide (Victoza), the only available GLP1RA in Iran, has also been shown to be beneficial in reducing cardiovascular outcomes in T2D patients.

Victoza has been available in Iranian market for almost 4 years and proven to be effective in lowering blood glucose parameters and reducing body weight. Weight reduction, however varies among patients and we believe that this effect is highly dependent on patient’s compliance in modifying their lifestyle and respecting the diet and exercise.

CASE: A 45 years old Iranian woman with 10 years history of T2D, body weight of 103 Kg and uncontrolled blood glucose parameters (FBS =158 mg/dl, 2h PPG= 323 mg/dl and HbA1C= 8.4%) under current oral antidiabetic treatment (Metformin 1500 mg/day and Acarbose 100 mg BID), has been prescribed with Victoza 1.8 mg/day [starting dose of 0.6 mg per day with weekly dose escalation of 0.6 mg]. Acarbose was discontinued and Metformin dose was reduced to 1000 mg/day. She was also asked to change her lifestyle and exercise for at least 150 minutes per week along with reduced calorie intake. She was very compliant with her treatment and lifestyle modification and did not show any major side effects from the treatment apart from the sensation of satiety which is one of the well-known side effect of GLP1RAs.

RESULTS: Five months after the start of treatment with Victoza 1.8 mg/day, the blood glucose parameters were normalized to: FBG=90 mg/dl; 2h PPG= 90-100 mg/dl; HbA1C=6.8%; Her body weight reduced to 85 Kg; her systolic blood pressure reduced from 190 mmHg to 130 mmHg and diastolic blood pressure from 100mmHg to 80 mmHg

CONCLUSION: The above case is a great example of how modification of lifestyle together with proper treatment could change the course of diabetes in an uncontrolled T2D patient. Appropriate patient training for their new treatment and emphasizing on the importance of lifestyle change is necessary to increase patient’s compliance and achieve great outcomes.

KEYWORDS: GLP1RA, Lifestyle, Diabetes
A 69 year female patient with diabetes was referred to us for glycaemia regulation. After an extensive anamnesis the patient reported about a RS3PE syndrome 7 years before the diagnosis of pancreas cancer and secondary diabetes. RS3PE presents with edema of the hands and feet along with synovitis, and usually occurs in older adults. Concurrent malignancy is common with this condition; its prevalence among patients with RS3PE has been found to be from 16 to 30 percent. To the best of our knowledge our case is the first case in the literature presenting first as RS3PE and then revealing a pancreatic cancer and secondary diabetes after 7 years.

**CASE:** The patient had been experiencing swelling of her hands and arthritis before the diagnosis of diabetes and pancreatic cancer. She received prednisolone therapy for three months. After three months of steroid therapy she was on nonsteroidal anti-inflammatory on drugs demand. Her arthritis resolved after this treatment. After 7 years she suddenly experienced nausea and vomiting and stomach pain. She received proton pump therapy for these complaints. No resolution of these symptoms was observed. Further evaluation with computerized tomography revealed a 1 cm diameter mass in the pancreas. After operation of the mass she was diagnosed with pancreas adenocarcinoma. After removal of the distal pancreas she was started on insulin therapy for secondary diabetes.

**DISCUSSION:** Associations of rheumatic diseases and cancer have been described. The reasons for this are not well defined, but chronic inflammation may trigger malignancy and autoimmunity arising as a byproduct of naturally occurring anti-tumor immune responses. Patients with potentially paraneoplastic rheumatic syndromes, such as palmar fasciitis, leukocytoclastic vasculitis, hypertropic osteoarthropathy, and remitting symmetrical seronegative synovitis with pitting edema (RS3PE), should be evaluated for underlying malignancy. The evaluation and testing performed depend upon the particular rheumatic syndrome and the individual patient’s risk factor. This case report shows that clinical awareness is mandatory in treating elderly patients with RS3PE syndrome since this could be an opportunity to diagnose cancer at an early, curable stage. Further research should explore whether or not cancer screening should be systematically performed in these patients even in later years.

**KEYWORDS:** RS3PE syndrome, pancreas cancer, secondary diabetes.
back and increased in recumbent position, acute pancreatitis was suspected. Routine bloods showed mild leukocytosis, HbA1C 6.2%, total cholesterol 196 mg/dL, triglyceride 219 mg/dL, ALT was 88 (N: up to 45 U/L) and serum lipase was 450 (N: up to 160 U/L). Abdominal ultrasound showed mild free fluid in the abdomen with mild pancreatic edema. Following diagnosis of acute pancreatitis, patient kept nil by mouth and was given IV fluids. Blood glucose was monitored every 4 hours. Patient completely recovered after 72 hours. During her admission, her blood glucose was within (70-140 mg/dl) with no hypoglycaemic episodes.

CONCLUSION: Dulaglutide can rarely cause acute pancreatitis. Patients should be warned about symptoms of acute pancreatitis and advised to seek medical advice if they develop them.

KEYWORDS: Dulaglutide, Acute pancreatitis, type 2 diabetes

INTRODUCTION: Dulaglutide is a new once weekly GLP-1 analogue approved for treatment of type 2 diabetes. Acute pancreatitis is a rare side effect that occur in less than 1% in patients using it. Here we describe a case report of dulaglutide-induced pancreatitis.

CASE: A 48 years old female with type 2 diabetes presented to ER after injecting 6 mg of dulaglutide (4 Pre-filled pens of dulaglutide 1.5 mg/ml) as suicidal attempt. She had type 2 diabetes for 5 years and on was metformin, dulaglutide and rosuvastatin. She had nausea and vomiting of moderate intensity, also she was hemodynamically stable and rest of examination was unremarkable. Random capillary blood sugar was 107 mg/dl. She was commenced on pantoprazole 40mg IV twice daily, ondasetron 8mg/8h and IV glucose 5% /8 hours. Blood glucose measurement every two hours using a glucometer were done and no hypoglycemia occurred in the first day of hospitalization. Twelve hours later, the intensity of nausea and vomiting was increased and epigastric pain and tenderness started to appear. This pain was of severe intensity, radiating to
**INTRODUCTION:** Lithium, used to treat bipolar disorder, may cause multiple endocrinopathies. Nephrogenic diabetes insipidus (NDI) is its mostly seen renal side effect. Although NDI is accepted to be reversible, persisting cases are reported after cessation of therapy. Herein, we presented a case of lithium-induced NDI case responsive to l-deamino-8-D-arginine vasopressin (DDVAP) treatment.

**CASE:** A 55-year-old female patient was seen in consultation because of hypernatremia, polyuria and polydipsia. Her medical history revealed bipolar disorder of 39 years’ duration. She had been treated with lithium for 37 years and discontinued it for 2 years. She was normotensive and not edematous. Her laboratory findings are shown in Table 1. Based on the medical history and laboratory results, the patient was diagnosed with lithium-induced NDI and indapamid (1.5 mg) plus indomethacin (50 mg) treatment was started. Since the patient’s serum sodium level was 150 mEq/L, we couldn’t do water deprivation test. Hypotonic solution was started for hydration. Mild decrease was seen in the patient’s serum level but her polyuria continued so she was admitted to our inpatient clinic. On the 3rd day of her admission, her serum sodium level and urinary output were still high so a single dose of DDVAP (10 mcg) was administered. Although urine osmolality didn’t change (580mOsm/kg and 600 mOsm/kg before and after DDVAP, respectively), which confirmed the diagnosis of NDI, serum sodium level and urinary output of the patient decreased. Patient was started on DDVAP 120 mg. On the 7th day of treatment serum sodium level was 145 mEq/L. NSAID and diuretic treatments were stopped. On the 15th day of treatment the patient was prescribed 180 mcg DDVAP therapy and was discharged with serum sodium level of 143 mEq/L and urinary output of 2500 mL/24h.

**DISCUSSION:** Lithium therapy can cause many endocrinopathies. It interferes with renal collecting tubules and generates cyclic adenosine monophosphate in response to antidiuretic hormone secretion, which then results in a reduction of the kidneys’ capacities to preserve water leading to polyuria. However, Guirguis et al. reported eight cases of lithium-induced NDI persisting after cessation of lithium therapy. They related this continuous lithium effect to slow recovery from urinary concentrating defects and prolonged exposure to the drug (>10 years), as seen in our patient. The accepted treatment of NDI is amiloride, thiazide diuretics and NSAID. There are two case reports pointing out the importance of DDVAP in treatment of NDI with indomethacin. Although there is not enough evidence about the use of DDAVP in NDI, in the light of early studies we tried oral desmopresin therapy and gained successful results. The most likely explanation to this condition may be the defective vasopressin receptor and aquaporin-2 axis in the renal tubular cells in lithium-induced NDI causing partial vasopressin resistance which may be overcome by high doses of DDVAP therapy.

**KEYWORDS:** Desmopressin, diabetes, lithium

<table>
<thead>
<tr>
<th>Table 1. Sequential serum and urine measurements of the patient</th>
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<tr>
<td><strong>Factor</strong></td>
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<tr>
<td>Bun (mg/dL)</td>
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<tr>
<td>Creatinine (mg/dL)</td>
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<td>Sodium (mmol/L)</td>
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<td>Serum osmolality (mOsm/kg)</td>
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<td>Urine volume (mL/24h)</td>
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Body temperature was 36°C, pulse 110/min, Bp 90/60 mmHg, RR 20/min. She was oriented and examination of organ systems was unremarkable.

Laboratory examination revealed hyperglycemia (glucose: 346 mg/dL), metabolic acidosis (pH: 6.96, HCO3: 2.1 mEq/L, pO2: 74 mmHg and pCO2: 8 mmHg), hyponatremia and hyperkalemia (ALT: 15 U/L, AST: 12 U/L, creatinine: 0.93 mg/dL, Na: 130 mmol/L, Cl: 110 mmol/L, K: 5.59 mmol/L, Ca: 8.5 mg/dL, P: 5.1 mg/dL). Urinalysis showed 4+ ketonuria.

With the diagnosis of diabetic ketoacidosis, oral intake was ceased, hydration with 0.9% NaCl and iv insulin infusion was given. Acidosis, ketosis and hyperglycemia resolved. Then, oral intake was allowed and insulin dose was adjusted. Due to technical problems, basal insulin was skipped, and ketonuria and hyperglycemia recurred. Although oral intake was prohibited, severe vomiting occurred again, and DKAlk (pH: 7.55) emerged. The rate of iv hydration was increased and insulin was continued. At the 3rd day, alkalosis regressed, oral intake was allowed and intensive insulin was re-initiated.

CONCLUSION: Severe vomiting due to gastroparesis may lead to severe dehydration and hyperaldosteronism. Loss of gastric content, and secondary hyperaldosteronism causing paradoxic aciduria might culminate in DKAlk. Iv hydration improved alkalosis. However, overcorrection would cause hyperchloremic acidosis and should be avoided.

KEYWORDS: Diabetic ketoalkalosis, ketoalkalosis, acute complication, diabetic coma, alkalotic ketoacidosis.
Her skin biopsy findings were compatible with drug eruption. She was then started on oral methylprednisolone, 0.5 mg/kg day. Her symptoms quickly resolved, and steroids were tapered and stopped in a month. Her itching resolved in two days, and her papules and plaques did so entirely in a week.

She is now being followed with metformin + basal insulin with an HbA1c of 6.5 for four months and is free of all her dermatological symptoms.

CONCLUSION: DPP-4 inhibitors, including saxagliptin, are not devoid of side effects. Their dermatological safety seems to be a matter of concern. This case suggests saxagliptin can be a cause pityriasiform drug eruption. Whether this is related to saxagliptin itself or a class effect remains to be elucidated.

KEYWORDS: Saxagliptin, DPP-4 inhibitor, pityriasis rosea, drug eruption
INTRODUCTION: Diabetes is a chronic disease which can frequently lead to vision loss and neuropathy due to microvascular complications when not well controlled. Here we present a case of a diabetic patient presenting with vision loss and neuropathy due to a cause other than diabetes.

CASE: A 60-year-old female patient was admitted to our clinic with complaints of fatigue, loss of appetite, weight loss, severe pain, numbness and loss of strength in the right foot and difficulty in walking for the last month. She presented to a different medical center five months ago due to sudden vision loss in her right eye. Orbital MRI was normal. Due to the findings of fundus examination, her complaint was accepted to be associated with diabetic retinopathy and intravitreal ranibizumab (anti-VEGF) was injected at that center. However, her vision did not improve. Lumbar MRI revealed a lesion in L4 vertebra. An operation was recommended for it but the patient had refused. In another center, these symptoms were said to be associated with diabetic neuropathy but gabapentin did not resolve her symptoms. She was admitted to our clinic due to her continuing complaints. She had diabetes and hypertension for 20 years. Her treatment included insulin detemir, metformin, ramipril, gabapentin. Diabetic retinopathy, nephropathy and neuropathy were noted. There were no macrovascular complications. In physical examination; there were decreased breath sounds in the left lung, and muscle strength of the right lower extremity was 3/5.

On laboratory findings, glucose: 263 mg/dl, HbA1c: 9.6%, ESR: 34 mm/h, CRP: 2 mg/l, hemogram, creatinine, liver enzymes, electrolytes, thyroid function tests were normal.

There was an opacity in the left lung on her chest X-ray. Fundus examination revealed lesions compatible with choroidal metastases bilaterally. Thorax CT showed suspicious multiple lymph nodes, the largest being 27x13 mm in the mediastinum, a 10x6 cm mass-at-electasis complex in the left lung, nodular lesions thought to be metastatic in the bilateral lung parenchyma and pleural effusion in the left hemithorax. Cranial MRI showed multipl foci compatible with metastasis. 18-F-FDG PET/CT revealed that the lesion in the left lung (SUV:7.3) may be the primary focus and there were lesions with increased FDG uptake compatible with metastases in thyroid, bilateral lung parenchyma, liver, left adrenal and various parts of skeletal system. Consultation with neurology suggested paraneoplastic neuropathy and the repeated lumbar MRI revealed lesions compatible with metastases in D12, L4, and L5 vertebra and the L5 nerve root was observed to be significantly compressed. Diagnostic transthoracic fine needle aspiration biopsy resulted as primary lung adenocarcinoma. The patient was referred to the oncology department.

CONCLUSION: Findings like vision loss and/or neuropathy in a diabetic patient should not always be thought as complications of diabetes, as these findings may be due to different causes other than diabetes.

KEYWORDS: diabetes, retinopathy, neuropathy, malignity, vision loss
**INTRODUCTION:** Last few years, Sodyum Glukoz co-transporters-2 (SGTL2) inhibitors have been often used in diabetes treatment Canagliflozin, Ertugliflozin, Dapagliflozin and Empagliflozin are in this group. There are Dapagliflozin and Empagliflozin drugs in our country.

SGTL-2 inhibitors regulate glycemia by increasing urinary glucose excretion with insulin-independent mechanism. Besides blood glucose regulation, it has positive effects on blood pressure regulation in hypertensive patient and losing weight in obese, overweight patients.

The main side effects are increasing genitourinary tract infections, hypotension, euglycemic ketoacidosis, hypokalemia and hyponatremia. Its rare complications are bone fracture and extremity amputation.

**CASE:** 43 years old male patient has type 2 diabetes for 5 years. Patient has no history of chronic disease except diabetes. He was taking metformin + pioglitazone for five years in addition to empagliflozin, an SGLT-2 inhibitor, for one month.

The patient was admitted to dermatology department because of widespread skin rashes (palpable purpura and petechiae) on his body (Figure 1 and 2) a few days after starting to use empagliflozin in treatment. He was directed to Endocrinology and Rheumatology department. Blood tests and genetic tests were requested by rheumatologist. Laboratory tests results are summarized in Table 1.

Anti nuclear antibody was detected as positive at 1/100 dilution and proteinuria was detected in urinary test. Than, 24 hours urine was collected and 2547 mg/day proteinuria was detected. MEFV gene mutation analysis revealed pathogenic heterozygous mutations in M694V, P369S, R408Q, E148Q gene regions and was reported as pathognomonic for Familial Mediterranean Fever (FMF). Vasculitic skin rash can be seen in FMF patient. It can be FMF- associated vasculitis (IgAV, PAN) or co-occurrence of FMF and other vasculitic disease (e.g. drug related cutaneous vasculitis).

The patient refused the biopsy on the skin lesion. The skin lesions disappeared completely after discontinuation of empagliflozin.

It is thought that empagliflozin may cause vasculitic skin rashes or trigger the autoimmune process in the presence of underlying connective tissue diseases. This complication should be kept in mind when using these drugs on diabetes treatment.

**KEYWORDS:** Type 2 diabetes mellitus, empagliflozin, vasculitis, sodium-glucose co-transporter-2 inhibitors, skin rash.
INTRODUCTION: Ovarian hyperthecosis (OH) refers to an ovarian pathology characterized by stromal cells differentiated into luteinized cells in ovary. Due to excess of androgen production, hyperandrogenemia and hirsutism are manifested. Hyperandrogenism among postmenopausal women is uncommon. However, in the presence of OH, gonadotropin related testosterone production by theca cells is unveiled among these patients because of the loss of the aromatization of testosterone to estradiol. Therefore, OH should be considered especially in postmenopausal women to define etiology of hyperandrogenism.

CASE PRESENTATION: A 56-year-old multiparous woman was admitted to endocrinology clinic. She had normal menstrual cycles until hysterectomy was performed due to uterine fibroids 10 years ago. She complained about excessive hair growth and hair loss for two years. She had type 2 diabetes mellitus and hypothyroidism. Her physical examination revealed hirsutism and androgenic alopecia. Hormonal assessment indicated four-fold increase in testosterone levels (Table 1). Serum cortisol level after 1 mg overnight dexamethasone administration was 0.9 µg/dL. To exclude a putative adrenal neoplasia, an abdominal CT was performed. Adrenal glands were normal. Transvaginal sonography and pelvic MRI showed that right ovary was enlarged. No other finding was obtained. Unilateral salpingo-oophorectomy was performed and specimen was sent for pathological examination. After operation, serum testosterone returned to normal levels (0.2 ng/mL). Microscopically, ovarian stroma was hyperplastic and there were cells that were morphologically different than stromal cells which were located around perivascular areas and interstitium. These cells were stained positively with inhibin and calretinin but epithelial membrane antigen (EMA) stain was negative (Figure 1). These findings confirmed the diagnosis of stromal hyperplasia and hyperthecosis.

DISCUSSION: Evaluating clinical, laboratory and radiological findings are crucial to reach certain diagnosis. Basic differential diagnoses of OH are polycystic ovary syndrome (PCOS) and androgen secreting tumors. Patients with OH may present severe symptoms such as hirsutism, clitoromegaly, temporal alopecia which are not seen commonly in PCOS. Testosterone levels are high in both OH and androgen secreting tumors but in OH group, levels are not as high as expected in tumor group. In OH group, other hormonal results such as gonadotropins, dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulphate (DHEA-S), 17-OH-progesterone and cortisol are usually normal. Specifically in OH patients, both ovaries generally seem enlarged and more solid via ultrasonography.

After diagnosis of OH, elimination of underlying cause is the curative treatment. Bilateral oopherectomy is the gold standard in postmenopausal patients. But GnRH agonist usage may be an alternative treatment modality in women who are at high risk for operation.

KEYWORDS: ovarian hyperthecosis, postmenopausal hyperandrogenism, virilization

Table 1. Serum parameters of the patient before surgery.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Reference range</th>
</tr>
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<tbody>
<tr>
<td>FSH (IU/L)</td>
<td>15.3</td>
<td>3.5-12.5</td>
</tr>
<tr>
<td>LH (IU/L)</td>
<td>17.7</td>
<td>2.4-12.6</td>
</tr>
<tr>
<td>Estradiol (ng/L)</td>
<td>20.4</td>
<td>12.4-233</td>
</tr>
<tr>
<td>Total testosterone (µg/L)</td>
<td>1.82</td>
<td>0.03-0.41</td>
</tr>
<tr>
<td>DHEAS (µg/dL)</td>
<td>80.6</td>
<td>12-407</td>
</tr>
<tr>
<td>Prolactin (ng/mL)</td>
<td>6.1</td>
<td>4.8-23.3</td>
</tr>
<tr>
<td>TSH (µIU/mL)</td>
<td>4.4</td>
<td>0.3-4.5</td>
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BACKGROUND AND AIM: Nowadays fat tissue is considered as an endocrine organ, and its excess is accompanied by increased production of aggressive estrogen metabolites (16-hydroxyestrone), which promotes development of hyperproliferative syndrome: uterine leiomyomas, adenomyosis, hyperplasia of endometrium, tumor-like lesions of the ovaries, fibrocystic disease of the mammary glands. This case provides results of multitarget therapy of infertility with hyperproliferative syndrome and obesity.

MATERIAL-METHODS: The patient, 35 years old, has been diagnosed with primary infertility for 10 years, adenomyosis, obesity (III stage) and varicosis of the lower extremities (II stage), and the last one was contraindication to hormonal therapy. Investigative plan included complaints, anamnesis of diseases, physical examination (anthropometric indicators: BMI, waist/hip ratio), gynecological examination (laparo- and hysteroscopy), ultrasound examination of small pelvis organs and mammary glands, laboratory studies (carbohydrate and lipid metabolism indicators, HOMA-IR index). Patient has received multitarget therapy: combined drug - indole-3-carbinol - 200 mg, epigallocatechin-3-gallate - 45 mg - 2 capsules twice a day. Duration of treatment was 6 months.

RESULTS: Before treatment a the woman has been worried about infertility, painful menstruations, hypermenorrhea, increased sensitivity and soreness of the breasts in the second phase of the menstrual cycle, overweight. The waist circumference (a marker of excess visceral fat associated with the presence of insulin resistance) exceeded 92 cm. The presence of visceral obesity was associated with signs of dyslipidemia (hypercholesterolemia, increased levels of cholesterol of LDL), and a carbohydrate metabolism disorder (increased fasting glucose levels and the HOMA-IR index).

At the end of treatment there were absence of menstrual pain syndrome, decreasing of volume of menstruation, decreased sensitivity and pain in the mammary glands in the second phase of menstrual cycle. Levels of total cholesterol and cholesterol of LDL have decreased significantly. We also observed significant decline of the HOMA-IR index and weight reduction by 9%. In 2 months after the end of therapy the patient had uterine pregnancy, which ended with childbirth by herself of alive baby on the 39-th week.

CONCLUSION: Multi-target therapy (indole-3-carbinol-200 mg, epigallocatechin-3-gallate-45 mg) not only normalized lipid and carbohydrate metabolism in the obese patient, it provided a complex effect on the organism, which manifested as inhibition of pathological hyperplastic processes in hormone-dependent organs and restored fertility. We consider this therapy in to be useful such group of patients.

KEYWORDS: infertility, adenomyosis, obesity, multi-target therapy, epigallocatechin-3-gallate, indole-3-carbinol.
OBJECTIVES: The risk of metabolic syndrome and cardiovascular disorders is higher in the patients with polycystic ovary syndrome (PCOS). There are also several studies pointing out the association between the risk of arrhythmia and PCOS. We present a case of Wolff-Parkinson-White syndrome (WPWS) which is incidentally detected on baseline electrocardiogram (ECG) of a patient presented with PCOS.

CASE: Twenty-five-year-old female was admitted to our clinics with the complaints of menstrual irregularity and hirsutism. She had oligomenorrhea with menstruation at each 2 or 3 months, and hirsutism on face, arms and legs. She had no menometrorrhagia or amenorrhea. She also complained about weight gain, alopecia increasing recently, and acne on trunk. She had no history of chronic illnesses. There was no history of drug, cigarette or alcohol usage. Family history was unremarkable.

On physical examination; body height was 168 cm, body weight:64 kg, and body mass index (BMI):22.9 kg/m2. Vital findings and examinations of respiratory, cardiac and gastrointestinal systems were in normal limits. There was male-type hirsutism on arms, legs, face and intermammary region; and Ferriman-Gallwey score (FGS) was 14. Cushing stigmata such as buffalo hump, purplish abdominal stria, truncal obesity or moon face were not observed.

Laboratory findings were as follows: fasting blood glucose (FBG):86 mg/dL, creatinine:0.69 mg/dL, LDL:77.6 mg/dL, HDL:59.6 mg/dL, triglyceride:39 mg/dL, total cholesterol:145 mg/dL, ALT:15 U/L, AST:18 U/L, Na:138 mmol/L, K:4.31 mmol/L, Ca:9.2 mg/dL, TSH:1.17 mIU/L, sT4: 1.05 ng/dL, AntiTPO:<10 U/L, LH:26.15 mIU/mL, FSH:7.69 mIU/mL, prolaktin:6.64 ng/mL, progesteron:0.22 ng/mL, E2:23.96 pg/mL, DHEA-SO4:310 mcg/dL, total testosteron:71 ng/dL, HbA1c:6.1%, and 25(OH)D3:15.48 ng/mL. Hyperandrogenemia, prediabetes (according to HbA1c) and vitamin D deficiency were detected.

Sonographic examination revealed that bilateral polycystic ovary appearance was present.

With a clinical and laboratory diagnosis of PCOS according to Rotterdam criteria, we planned to initiate oral contraceptive (OC) drug, metformin and vitamin D. Before the initiation of OC, we questioned the patient about contraindications such as cardiovascular disease history. There was no contraindication, but she mentioned about intermittent palpitation but no chest pain, dizziness or syncope. Baseline surface ECG was obtained, and it demonstrated shortened PR, widened QRS and delta wave. WPWS was diagnosed. The patient was referred to cardiology. OC was suspended, and metformin and vitamin D were initiated.

CONCLUSION: WPWS might be detected incidentally in any clinical background besides PCOS. However, based on the knowledge that cardiovascular events are higher in the patients with PCOS, baseline ECG is a simple screening tool and should be obtained at diagnosis especially if the patient has a "cardiac" symptom such as palpitation, syncope, or dizziness.

KEYWORDS: wolff-parkinson-white syndrome, polycystic ovary syndrome, wolff parkinson white, polycystic ovary, arrhythmia
28 years old man presented with bilateral gynecomastia, developed since puberty and propagated to post pubertal period. He is a poor patient and a porter. On was in examination Height= 157 cm, weight= 59 kg BMI=23, Hair distribution tanner stage 3 to 4, Bilateral testes were in good volume one 12 ml and the other 10 ml. The phallus was about 8 cm. He occasionally abuses steroid in form of dexamethasone tablet or injectable betamethasone due to allergic bronchitis. He is unmarried and his brother also had the same condition of gynecomastia, He has no history of smoking or alcoholism.

**INVESTIGATION:** Testosterone at early morning done twice 800ng/dL, LH 6 (mIU/mL), FSH 7 (mIU/mL), Estradiol (67 pg/mL), 17OH progesterone (160 ng/dL), Prolactin 22 mmol/L, DHEA-S 137.7µg/dL, TSH 2.96, FT4 0.99, ACTH 1.00 (pg/mL), Serum cortisol (7 µg/dL), SHBG 69.6nmol/L, Free Testosterone 10.1 ng/dL, Serum electrolyte liver function test, and lipid profile were normal. Abdominal ultrasound revealed no ovaries, uterus, testicular anomalies or mass.

No history of the following drug use were present: aldosterone receptor blockers, anti-hypertensive drugs, psychotropic drugs, antacids, estrogen (male to female), anti-HIV agents, hypolipidemic agents, herbal medicines The diagnosis was familial aromatase excess syndrome.

Aromatase excess syndrome is a condition characterized by elevated levels of the female sex hormone estrogen in both males and females. Males with aromatase excess syndrome experience breast enlargement (gynecomastia) in late childhood or adolescence. The bones of affected males grow and develop more quickly and stop growing sooner than usual (advanced bone age), and short adult height is seen in affected males. This condition is inherited in an autosomal dominant pattern, which means a genetic rearrangement involving one copy of the CYP19A1 gene in each cell is sufficient to cause the disorder. In some cases, an affected person inherits the mutation from one affected parent. Other cases result from new genetic changes and occur in people with no history of the disorder in their family. Serum estradiol levels are elevated in 48% of affected males, but are not necessarily useful for diagnosis.

**CLINICAL DIAGNOSIS:** Four criteria for the clinical diagnosis of AEXS are as follows: bilateral gynecomastia (> stage 2), pre- or peripubertal onset of gynecomastia (>5 and <14 years old), exclusion of other well-known causes of gynecomastia (symptomatic gynecomastia) and pubertal gynecomastia, having a genetic trait (autosomal dominant). The first three criteria are indispensable for clinical diagnosis. The fourth criterion, a genetic trait, is not obligatory, but rather pathognomonic. Detection of a maternal genetic trait may be difficult to discern in a small family. A genetic trait is absent in sporadic cases.

**KEYWORDS:** gynecomastia, Aromatase excess syndrome, CYP19A1 mutations
BACKGROUND: Insulinoma is a rare endocrine tumor derived from pancreatic Beta cells. It is the most common cause of endogenous hyperinsulinemia and hypoglycemia. Severe hypoglycemia increases the risk of atrial fibrillation. This risk is increased especially in patients with a history of coronary artery disease in the elderly. We aimed to present a case of insulinoma with atrial fibrillation secondary to hypoglycemia and a history of paroxysmal atrial fibrillation.

CASE PRESENTATION: A 74-year-old male patient presented with complaints of palpitation, fatigue, weight gain and quick-on hunger. He had hypertension, coronary artery disease and paroxysmal atrial fibrillation in his medical history. He was admitted to our clinic because of hypoglycemia. Prolonged fasting test was initiated for the diagnosis of insulinoma in the patient with findings supporting the whipple triad. In the patient who complained of palpitation and sweating at the sixth hour of the beginning of the test, blood glucose was measured and ECG was taken. 1 mg glucagon was administered iv as the patient’s measured blood glucose was 37 mg/dl. Blood glucose monitoring was performed every 10 minutes. The patient was consulted with cardiology because of rapid ventricular response atrial fibrillation on the ECG. Anticoagulant and beta-blocker treatment were performed with the recommendation of the cardiology clinic. Heart rate was controlled after treatment. Insulin - 53.4 uU/mL and C Peptid - 9.51 ng/mL were measured at the time of hypoglycemia. The blood sugar was measured 58-82-107 mg/dl after glucagon injection. Prolonged fasting test results were consistent with insulinoma. Abdominal MRI was performed for tumor localization. At the head of the pancreas, there was a lesion that was compatible with insulinoma without diffusion restriction, approximately 15x13mm. The patient was operated on by the general surgery clinic and the mass in the pancreas was excised. After the operation, the patient’s low blood sugar level continued. Insulin - 23.1 uU /mL and C Peptide - 4.86 ng /mL levels were seen in the post operative period. A residual tumor was shown as 13x12 mm lesion at the level of the head and neck junction of the pancreas in the abdominal CT. Long-acting lanreotide treatment was initiated for the patient who did not want to be reoperated with hypoglycemia.

DISCUSSION – CONCLUSION: Insulinoma is a functional pancreatic tumor, usually seen after 50 years of age among adults. Hypoglycemia may cause severe rhythm disturbances, especially in elderly patients. In our patient who had previously had paroxysmal atrial fibrillation, atrial fibrillation with rapid ventricular response developed during prolonged fasting test. The patient was operated after tumor localization and hypoglycemia continued due to insufficient resection. Long-term lanreotide treatment was initiated to prevent hypoglycemia and cardiac arrhythmia. KEYWORDS: severe hypoglycemia, atrial fibrillation, insulinoma
Table 1. Prolonged fasting test results

<table>
<thead>
<tr>
<th></th>
<th>Glucose (mg/dl)</th>
<th>Insulin (uU/ml)</th>
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<td>0 Minutes</td>
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<td>9.51</td>
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<tr>
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<tr>
<td>30 Minutes</td>
<td>107</td>
<td>18.2</td>
<td>3.46</td>
</tr>
</tbody>
</table>
METHODS: This case series is a retrospective review of patients who were diagnosed with Insulinoma at Shaukat Khanam Memorial Cancer Hospital and research center between January 2017 to July 2019

RESULTS: A total of four patients were included in this case series. Three males and one Female. Median Age was 43 years. All four patients presented with recurrent episodes of hypoglycaemia and unconsciousness. Two patients had episodes of fits as well.

All patients showed evidence of endogenous hyperinsulinism by demonstrating failure of insulin secretion to fall to very low rates as plasma glucose concentration falls to hypoglycemics levels. Pancreatic lesion was identified on cross-sectional imaging in three patients, however in the fourth patient lesion was identified on Endoscopic ultrasound (EUS) only. EUS was done in three patients and identified the lesion in all of them.

All patients underwent whipple’s procedure with resolution of hypoglycaemia episodes. Median tumor size was 1.8 cm. Two patients developed Diabetes Mellitus post-surgery.

CONCLUSION: Insulinomas are rare pancreatic islet cell tumors. The diagnosis of insulinoma is established by demonstrating inappropriately high serum insulin concentrations during a spontaneous or induced episode of hypoglycaemia. In our case series lesion was localized in three patients by CT and MRI scan, whereas in one patient lesion was localized by EUS only.

KEYWORDS: Insulinoma, Neuroendocrine tumor, Spontaneous Hypoglycaemia in non diabetic patient
BACKGROUND: Nivolumab is a monoclonal antibody, which binds to a human programmed cell death protein-1 (PD-1) on the T-cells, and helps to restore T-cell mediated anti-tumor activity. There has been evolving observational data reporting autoimmune adverse events related to these immunotherapy drugs. In this case report, we present a patient who developed combined adrenocorticotropic hormone (ACTH) and growth hormone (GH) deficiency likely secondary to autoimmune (AI) Hypophysitis as an adverse event of Nivolumab therapy, which she had received for her malignant melanoma.

CASE: A 46-year-old female presented to the outpatient clinic in November 2018 with decreased energy, fatigue, myalgia, shortness of breath on exertion, recent weight loss of 60 lbs, progressively worsening over 3 months. She had a history of stage IIIIC malignant melanoma (BRAF Wild type) on her right face, for which she underwent excision of the lesion and started on immune checkpoint inhibitor (ICI)- Nivolumab [IV 240 mg q2 weeks] in March 2018. After 10 cycles of therapy, she developed optic neuritis which was presumed to be immune-mediated and immunotherapy treatment was stopped. After 2 months she was admitted to the hospital with a diagnosis of DKA, which after extensive workup was presumed to be immune-mediated secondary to Nivolumab. She was started on an insulin regimen for this diagnosis. However, failed to improve clinically and started to develop the above-mentioned symptoms. In the clinic, she denied any skin changes, dizziness, hair loss, menstrual changes and leg swelling. Physical examination was benign except for orthostatic hypotension. Her laboratory analyses showed Cortisol <1.0 [3.0-16.0 µg/ml], ACTH <5.0 [7.2-63 pg/ml], IGF-1 37 [49-240 ng/ml], FSH 6 [3-33 mIU/ml], LH 4 [<17 mIU/ml], Prolactin 8 [<30 ng/ml], TSH 0.76 [0.34-3.00 µIU/ml], free T4 1.1 [0.6-1.6 ng/dl]. High dose ACTH (0.25 mg IV Cosyntropin) stimulation test revealed subnormal response with baseline cortisol level <1.0, 30-minutes cortisol level of 1.2 and 60-minutes cortisol level of 1.6, indicating primary/secondary adrenal insufficiency. Based on undetectable ACTH, secondary adrenal insufficiency and GH deficiency were diagnosed. She was treated with oral prednisone with remarkable improvement in her symptoms within a few days.

CONCLUSION: AI Hypophysitis secondary to immunotherapy is an established entity. The objective of our report is to highlight a rare but life-threatening entity called combined ACTH and GH deficiency secondary to Nivolumab induced AI Hypophysitis, where only ACTH pathway is affected amongst all the available endocrine pathways in the anterior pituitary. Oncologists, endocrinologists, primary care physicians need to be familiar with this potentially life-threatening and easily correctable adverse event.

KEYWORDS: Nivolumab, ACTH, GH, hypophysitis, autoimmune
Conclusion: Anosmia and hyposmia, the inability or decreased capability to smell, is approximated to affect 3–20% of the population. Risk of olfactory dysfunction increases with old age and may result from chronic sinonasal diseases, severe head trauma, and upper respiratory infections, or neurodegenerative diseases. ES develops when cerebrospinal fluid (CSF) fills the sella turcica and compresses pituitary tissue until it lines the sellar floor and walls. Primary ES occurs when CSF enters the sella through a tear in the sellar diaphragm that may or may not be associated with increased intracranial pressure. Secondary ES is a result of an injury to the pituitary itself (e.g., pituitary apoplexy) or the result of surgical or radiation treatment. Anosmia and empty sella, two conditions concerning neighboring structures, when accompany each other, would be supposed to develop from identical reasons such as an unrecognized head trauma or a simple sinusitis when leading to hypothalamopituitary infection.

Keywords: anosmia, empty sella, etiology

Introduction: Olfactory groove obstruction, olfactory mucosal atrophy, fractures in the anterior cranial fossa, or diseases involving the olfactory pathway may all lead to decrease or lack of olfactory sensation. In the postoperative period of pituitary adenoma surgery or following operations on anterior circulation aneurysms, olfactory nerve dysfunctions were reported. We introduced a case with acute anosmia who was recognized to have empty sella (ES). We suggest there would be relationship between two occasions, anosmia and ES, most probably upon sharing the same etiological factor.

Case: A 53 year old female arrived at our clinic for the consultation from neurology department regarding the empty sella appearance in her cranial magnetic resonance imaging (MRI). She had anosmia for six months with no other accompanying symptoms. She had no history of any operation, trauma or medication usage, or consumption of cigarette or alcohol. She had type 2 diabetes mellitus for several years with optimized blood glucose levels. Otolaryngology department had treated her for the suspicion of sinusitis but it was not beneficial for healing of the smelling sensation. Her blood pressure was 110/70 mmHg. In her blood tests creatinine: 0.78 mg/dl, alanine aminotransferase (ALT): 21 U/L, glycated hemoglobin (HbA1c): 6.75%, fasting plasma glucose: 134 mg/dl, sodium (Na): 141 mmol/L, potassium (K): 4.66 mmol/L, thyrotropin (TSH): 2.41 µIU/ml, free thyroxine (T4): 1.06 ng/dl, follicle stimulating hormone (FSH): 44.90 mIU/ml, luteinizing hormone (LH): 19.88 mIU/ml, prolactin: 13.15 ng/ml, cortisol: 13.2 µg/dl, urinary density: 1024 kg/L were found. She was visualized with pituitary MRI and empty sella was also shown by this imaging technique.
DISCUSSION: Acromegaly disorder results from uncontrolled hypersecretion of GH and secondary increase in IGF-1 level. The most common cause of acromegaly is somatotropinoma (99%) and is invariably visualized on sellar imaging. However, some patients with acromegaly who present with empty sella are more likely to have small-sized tumors that are not detected on the MRI, and the causes include silent apoplexy, ectopic GHRH-secreting neuroendocrine tumors, McCune–Albright syndrome, and rarely ectopic pituitary adenoma. Because of their rarity, the origin and pathogenesis of the coexistence acromegaly and empty sella remain unclear. Several explanations have been proposed and the issue remains debatable. One explanation is that in the course of tumor growth, the intrasellar adenoma undergoes necrosis, resulting in secondary empty sella.

KEYWORDS: Acromegaly, Empty sella, Lanreotid

INTRODUCTION: Empty sella (ES) means an enlarged sella turcica that is not completely filled with pituitary tissue. This syndrome has also been classified into a ‘primary’ form in which there has been no prior pituitary irradiation or surgery, and a ‘secondary’ form in which the empty sella is found after such procedures. Most patients with the primary empty sella syndrome are found to have normal pituitary function while about 30% have varying degrees of hypopituitarism. It is not widely appreciated, however, that the primary empty sella may harbour a pituitary tumor with resultant acromegaly. In this report we describe such patient who presented with active acromegaly.

CASE REPORT: A 61-year-old woman noticed gradual enlarging of his hands and feet for ten years. She also had hyperhidrosis, arthralgia, and hyperglycemia difficult to control. (HbA1c: %13.6) She did not have any visual symptoms. Physical examination revealed typical acromegalic features and no visual field defects. Laboratory data showed elevated serum growth hormone (GH; 11.7 ng/ml) and insulin-like growth factor-1 (IGF-1; 612 ng/ml). Since DM was diagnosed, OGTT-GH suppression test was not performed. The other pituitary hormone profile was in normal range. T1-weighted magnetic resonance imaging (MRI) revealed an empty sella and no sellar mass [Figure 1]. Computed tomography of thorax and abdomen were performed in case of ectopic focus, no pathology was found. Routine colonoscopy revealed a 4x5 cm mass in the ascending colon and endoscopic biopsy was reported the lesion as adenocarcinoma and segmental colon resection was performed. Lanreotid autogel 90 mg/ 28 day was started and six months later, IGF-1: 189 ng/d L and diabetes mellitus was resolved (A1c:%6.3)
CONFOUNDING THYROID FUNCTION TESTS IN A PATIENT WITH PITUITARY MASS

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DEPARTMENT OF ENDOCRINOLOGY, ESKISEHIR CITY HOSPITAL, ESKISEHIR, TURKEY

**CASE:** A 52 year old male patient was admitted due to preoperative evaluation for a sellar mass measuring approximately 2.5 cm in size. His past medical history was significant only for type 2 diabetes mellitus. He denied any thyroid disease. He was on daily 2 g metformin and 60 mg gliclazide therapy. His pulse rate was 120 bpm, rhythmic. Exophthalmus was absent. His physical examination revealed no stigmata of Cushing’s disease, acromegaly, and exophthalmus.

Initial TSH value was suppressed and free T4 and T3 were high (Table). Other hormones were as follows: ACTH 10 pg/mL, IGF-1 was 129 ng/mL, prolactin 8.14 ng/mL, LH 3.99 mIU/L, total testosterone 7.78 ng/mL (upper normal range 7.15 ng/mL), morning cortisol 8.5 mcg/dL. Free thyroid hormones were high and TSH was not suppressed as expected from primary hyperthyroidism; secondary hyperthyroidism due to a pituitary tumour was the most probable diagnosis. Since pituitary surgery was scheduled and combination of T3 suppression-TRH test was time consuming in the current situation, only TRH test was employed to differentiate TShoma from thyroid hormone resistance. TRH Ferring® 200 mcg was administered intravenously. Blood samples were obtained before injection and 30 and 60 minutes afterwards. TSH values were 0.44 mIU/L, 0.51 mIU/L, and 0.47 mIU/L, respectively. Resistance was excluded and a diagnosis of TShoma was made. Therefore methimazole 5 mg/day was commenced along with propranolol 40 mg/day.

He underwent surgery on 29th July. He stopped methimazole immediately after the surgery as advised. Three weeks following surgery and cessation of methimazole, thyroid function tests were re-run. We expected 3 possible profiles: 1) normalisation of thyroid function tests, 2) sustained secondary hyperthyroidism due to incomplete resection, 3) secondary hypothyroidism due to surgery. However in contrast to these scenarios the thyroid hormone profile was compatible with T3 thyrotoxicosis. Thyroid autoantibodies, thyroid ultrasound, thyroid scintigraphy, and immunohistochemical staining of the surgical material were ordered and the results are pending.

**DISCUSSION:** Most TSHomas are larger than 1 cm. Our patient had a mass approximately 2.5 cm in size. TSH response to TRH stimulation was flat and blunted compatible with TSHoma or primary hyperthyroidism. Thyroid function tests were normalized before surgery with low dose anti-thyroid therapy as expected in primary and some cases of secondary hyperthyroidism. Post-operative high free T3 with suppressed TSH value suggest primary hyperthyroidism. Nevertheless TSH level higher than 0.01 mIU/L still needs to be elucidated. Differential diagnoses are primary hyperthyroidism due to an intervening thyroiditis and laboratory artefacts due to heterophil antibodies against free T3 or T4 or TSH. Tests for heterophil antibodies were not feasible. Pending results regarding thyroid antibodies and imaging studies would aid making a definite diagnosis.

**KEYWORDS:** pituitary adenoma, hyperthyroidism, discordant thyroid tests, tshoma, trh test

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**Table 1. Thyroid hormone values before and after surgery**

<table>
<thead>
<tr>
<th>Date</th>
<th>TSH</th>
<th>Free T4</th>
<th>Free T3</th>
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<tr>
<td>4 July</td>
<td>0.66</td>
<td>1.73</td>
<td>6.93</td>
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<tr>
<td>19 July</td>
<td>1.09</td>
<td>1.14</td>
<td>3.47</td>
</tr>
<tr>
<td>20 August</td>
<td>0.07</td>
<td>1.01</td>
<td>3.76</td>
</tr>
</tbody>
</table>

Thyroid hormone values before and after surgery. Normal reference range for TSH: 0.35-4.94 IU/L, free T4: 0.7-1.48 ng/dL ng/dL, free T3: 1.71-3.71 pg/mL.
Pituitary metastasis is a rare condition, the most frequent primary tumors being lymphoma, breast and lung cancer. Metastasis from renal cell carcinoma (RCC) is rare, a small number of cases were described to date. It is a life-threatening condition with shortened life span because of pituitary dysfunction, in addition to primary tumor’s clinical behaviour. We report a case and discuss the clinical diagnosis and follow-up. A 71 year-old man was hospitalized because of nausea, vomiting and weakness. 18 months ago, he had right radical nephrectomy. Pathologic examination showed clear cell RCC. Three months ago, cranial BT showed a large suprasellar lesion, measuring 25x35 mm in diameter and multiple hyperdense lesions in the brain parenchyma. He had transcranial incomplete surgical resection of pituitary lesion. Histology confirmed a clear cell RCC. At immunohistochemistry, cancer cells were positive for cytokeratin, RCC, PAX2 and PAX-8. The morphology, immunohistochemistry and microscopic findings were similar with nephrectomy materials. This result was consistent with the diagnosis of a metastasis from the clear cell RCC. At that time, hormonal assessment revealed panhypopituitarism. He was given glucocorticoid and thyroid hormone replacement therapy. Subsequently the patient underwent radiotherapy for pituitary and brain metastases. But finally he was admitted to our clinic because of aforementioned symptoms. In addition to hypopitutarism, he had hyponatremia because of in appropriate ADH syndrome. Fluid restriction and hormone replacement therapy resulted in clinical improvement. Pituitary metastasis is rare and occurred in %1-4 of all cancer patients. It is usually asymptomic unless pituitary dysfunction is present in relation to invasion of primary tumor cells. Pituitary anterior lobe involvement is seen with multiple brain metastases. Pituitary posterior lobe involvement is frequent because of its wide contact with the adjacent dura mater and its direct supply from the hypophyseal arteries, contrasting with the anterior lobe. Diabetes insipidus (DI) is the most common symptom of pituitary metastases if the posterior lobe is affected. Frequently bilateral hemianopsia due to cranial nerve II defect follows DI. As a result, our case underlines the importance of pituitary metastases and their clinical presentation. Apropriate therapy is as important as the primary tumor therapy.

**KEYWORDS:** pituitary, metastasis, renal cell, carcinoma
Neurofibromatosis type 1 (NF1) is a rare genetic disorder with an increased susceptibility to develop both benign and malign tumors. NF1-related clinical complications include neurological, cardiovascular, gastrointestinal, endocrine and orthopedic features.

Herein, we report a case with NF1 who was presented with pituitary macroadenoma.

CASE: A 57-year old male presented with five months of headache, nausea and decreased libido for a year. Due to the addition of visual complaints such as blurred vision, cranial MRI was performed and a pituitary lesion was detected. He was referred to neurosurgery department of our hospital. We consulted the patient and hospitalized him for further evaluation. Physical examination revealed hypotension, fibromas especially on his face and in the gluteal region and multiple café-au-lait spots, body hair loss on his legs and scoliosis. There were scars on the back and left lumbar region due to surgical operation for skin lesions.

When family history is asked, we learned that his 26 years old son had died because of neurofibrosarcoma one year before.

Biochemical evaluation was consistent with hypocortisolemia, hypogonadotrophic hypogonadism and low prolactin level. Pituitary MRI showed a 39x35x27 mm sellar mass with suprasellar extension and slight optic chiasm compression. Bitemporal hemianopia was observed in visual field evaluation. Also Lisch nodules on the iris bilaterally were detected.

The diagnosis was NF type 1 and pituitary macroadenoma. No signs and symptoms of acromegaly, Cushing’s syndrome, hypertension, flushing, sweating, palpitations, hypoglycemia, diarrhea, abdominal pain were noted. 24-hour urine catecholamines levels were normal. The patient underwent transsphenoidal pituitary surgery due to pituitary mass.

The pathology was consistent with atypical pituitary adenoma. Immunohistochemical studies demonstrated PIT1 [-], GH [-], PRL [-], TSH [-], ACTH 2% [+, LH: [+] in 1-2 cells, FSH [-] CrgA [+], synaptophysin [+] and the Ki-67 index was 10%. Abdominal MRI showed adenomatous lesion 2x1.5 cm in the right adrenal gland and 13x6 mm in the left adrenal gland. Physiologic uptake was observed in adrenal glands with [68] Ga-DOTATATE PET.

Neck MRI and thorax HRCT imaging were normal. Cranial MRI showed glial tumor of the medulla oblongata and neuroma was detected on sacral MRI.

CONCLUSION: Neurofibromatosis type 1 may present with different clinical findings. Pituitary adenoma was described in several patients with NF type 1 in the literature. It should be remembered that benign and/or malign lesions may be accompanied with NF-1. Complications can be widespread and variable.

KEYWORDS: neurofibromatosis, macroadenoma, pituitary
ACTH-dependent Cushing’s syndrome (CS) is characterized by ACTH excess, arising either from tumors of the pituitary or ectopic tumors like small cell lung carcinomas, medullary thyroid carcinomas, pheochromocytomas, thymic, pancreatic, and bronchial carcinoids. The tumors are often indolent. High dose dexamethasone suppression and CRH stimulation tests, magnetic resonance imaging (MRI) and inferior petrosal sinus sampling (IPSS) are the diagnostic tests for distinguishing between pituitary and ectopic ACTH-secreting tumors. A 18 year old women presented with the symptoms of hypertension, weight gain, stria on the abdomen. Basal ACTH and cortisol levels were 123 pg/ml and 36.19 mcg/dl, respectively. The diagnostic 2 mg and 8 mg dexamethasone suppression are resulted with serum cortisol levels 15.7 and 25.5 mcg/dl, respectively. On MRI scan, a hypo-intense 2.2x1.8 mm adenoma was found in the right lobe of the pituitary. Abdominal tomography displayed bilateral adrenal gland hyperplasia. DOTA 68 GA scintigraphy showed lymph nodes in the right hilus that were smaller than 1 cm and not strongly visualized. Bronchoscopic biopsy and mediastinoscopy weren’t suitable for the lesions and broncho-alveolar lavage was not diagnostic. IPSS was performed two times and it’s results supported ectopic ACTH syndrome (EAS).FDG PET was negative for localization of the ectopic ACTH secretion. Ketoconazole was given for blocking of adrenal corticosteroid synthesis before operation. The patient underwent bilateral adrenolecctomy and the pathology was bilateral adrenal cortex hyperplasia. Prednisolone and fludrocortisone were started and the patient has followed up for the origin of EAS. Skin color darkening and ACTH increase started 3 years after bilateral adrenolecctomy, ACTH level was 1197 pg/ml. On DOTA 68 GA scintigraphy, 2.5x1.2 cm pathological lymph nodes were observed in the right hilar region (metastasis?) and increased Ga-68 peptide uptake. Excisional biopsy of pathological lymph nodes by thorocotomy resulted in malignant epithelial tumor metastasis. Since there was no decrease in ACTH levels at postoperative period, sondastatin treatment was started 3 months later. When ACTH increases again during the one year follow-up period, latest DOTA 68 GA scintigraphy displayed millimetric lymph node in the right hilar region and increased Ga-68 peptide uptake. The patient was reevaluated and no lesion was detected that can be removed. The patient is currently being monitored regularly under sondastatin treatment. Localization of ectopic ACTH-secreting tumors is often frustrating. Up to 50% of these neoplasms are not initially detectable, despite complete radiological screening and venous ACTH sampling. Long-term follow-up is often necessary, and the primary lesion is generally discovered within 2–5 years of follow-up. Particular attention is required to check the lung and thymus where epithelial or carcinoid tumors are the main causes of ectopic ACTH production.

**KEYWORDS:** ectopic cushing disease, cushing disease, surrenal adenoma
ACROMEGALY AND ANDROGEN PRODUCING ADRENAL MASS IN A WOMEN PRESENTED FOR EVALUATION OF MULTINODULAR GOITER

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The patient is a 39 years old woman who presented for evaluation of multinodular goiter. She complained of recent rapidly increasing facial and chest hair also.

Physical examination was remarkable for a MNG (Grade III WHO classification), but there were also some coarse features in favour of acromegaly in face and fingers and hirsutism (ferriway Gallman score 28).

Lab. data showed high (660 ngr/ml) IGF1 and basal GH (5.3 ng/ml) that did not suppress with glucose. There were also high serum level of Testosterone (2.1 ng/ml) and DHEAS (>1000 micgr/dl).

Brain MRI showed a 0.8 cm pituitary mass and abdominal CT scan was remarkable for a 2 cm mass in left adrenal.

TSS operation was performed initially and after one month a laparoscopic adrenalectomy was done.

Pathologic features were in favour of pituitary adenoma and androgen producing adrenal adenoma.

Operations were successful and after 3 months there was significant disappearance of hirsutism and soft tissue coarse changes of acromegaly. IGF1 level decreased to 164 ngr/ml, basal GH to 0.05 ng/ml, Testosterone to 0.025 ng/ml and DHEAS to 12.7 micgr/do.

KEYWORDS: acromegaly, adrenal androgen producing adenoma, hirsutism
Glucocorticoids are drugs that exhibit immunosuppressive and antiinflammatory effect at appropriate therapeutic doses. Many side effects are encountered during glucocorticoid treatment. Osteoporosis is a common side effect on bone metabolism, while avascular necrosis is a rare side effect. Osteonecrosis, commonly known as avascular necrosis (AVN) of bone, is one of the universally recognized side effects of high-dose steroid and commonly involves femur head leading to significant morbidity. However, AVN of femur head due to low-dose oral corticosteroid and a relatively shorter span of time is a rare occurrence.

Our case is a 34-year-old male who had been operated for non-secreting pituitary macroadenoma four years ago and eventually developed panhypopituitarism that needs levothyroxine and corticosteroid replacement. He did not come to regular follow-ups either in the surgery or endocrine unit for 3 years. He started to have pain in his hips bilaterally associated with limping, after approximately 3 years of prednisolone therapy (daily dose 5 mg). He was diagnosed with osteonecrosis of femoral head 3 months ago and stopped prednisolone and thyroxine treatment by himself. He was admitted to our clinic with bilateral hip pain, weakness, fatigue, nausea for the last three months. The patient was using crutches and had difficulty in walking. He does not drink alcohol or smoke cigarette. Biochemical examinations revealed panhypopituitarism (Table-1). Bone X-ray and hip magnetic resonance (MR) imaging showed avascular necrosis at femur neck (Figure 1 and Figure-2). Hydrocortisone (10 mg/day) was given for secondary adrenal insufficiency, as it is believed to be the more physiological preparation of glucocorticoids. Levothyroxine was initiated one week after corticosteroid replacement, initially at 100 µg/day and later increased to 125 µg/day. Monthly intramuscular testosterone (250 mg) was also initiated. The patient underwent core decompression surgery and was given vitamin D supplementation. Significant improvement was achieved in the patient’s clinic after the treatment. In addition, his hip pain was subsided and he started walking without crutches. He continues on low-dose glucocorticoid replacement which will continue lifelong.

In conclusion, when hip pain develops in patients receiving steroid therapy, AVN should be considered in the differential diagnosis. Because Early diagnosis of hip AVN is critical, as all treatments geared towards the preservation of the femoral head are more successful early in the course of the disease. Management by stopping steroid can be challenging in many cases due to adrenal crisis. In such cases, standard management is done by reducing steroid to the lowest possible dose. This report intends to highlight the occurrence of AVN of the femur even with a small dose of glucocorticoid used for the treatment of panhypopituitarism.

**KEYWORDS:** Avascular necrosis, corticosteroid, steroid side effect; hypopituitarism
Figure 2. Anteroposterior view of the pelvis

Table 1. Hormonal analysis of patient at the time of admission

<table>
<thead>
<tr>
<th></th>
<th>Values</th>
<th>Reference Range</th>
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<td>TSH (mIU/L)</td>
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**INTRODUCTION:** Acromegaly is a rare disease almost always caused by a growth hormone-secreting adenoma of the pituitary gland. The goals of therapy in patients with acromegaly are to lower the serum insulin-like growth factor-1 (IGF-1) concentration to within the normal range, control adenoma size and improve symptoms. First line treatment option is transsphenoidal pituitary surgery; however, in recent years, some have suggested that medical treatment may be the first choice in selected patients. Here, we present a case who responded very well to medical treatment after ineffective surgical treatment resulting in panhypopituitarism.

**CASE REPORT:** A 27 year-old man was diagnosed with acromegaly, with excessive facial and other soft tissue growth along with headache, dizziness and concentration problems existing for over two years. His voice was hoarse, lips and nose were noticeably enlarged and shoe size had progressively increased over time, as typically seen in acromegaly. IGF-1 level was 826 ng/mL (83-259 ng/mL). For diagnosis, oral glucose tolerance test (OGTT-GH suppression test) was made with 75 grams of glucose solution and no growth hormon supression was detected as all GH levels were >40 ng/mL. MRI of the hypophyseal gland also revealed a mass of 8x14x16 mm that was reaching out to cavernous sinus on the left side of hypophysis gland (fig 1). As the first choice of treatment, he underwent transsphenoidal surgery by an experienced neurosurgeon. Pathology report showed hypophyseal adenoma with immunohistochemical staining positive for growth hormone and prolactin. Post-operative MRI scanning was consistent with changes regarding surgery with no residual mass (fig 2). The patient developed panhypopituitarism and replacement therapy was started with levothyroxine, prednisolone and testosterone propionate. However, postoperative third month IGF-1 levels (711 ng/mL) and serum GH levels (14 ng/mL) were still very high and octreotide acetate treatment was started with 20 mg/month. He responded to medical therapy well and IGF-1 level decreased to 40 ng/mL gradually and the dose of octreotide was reduced to 10 mg/month. Three months later, the patient started to have complaints of joint pain and IGF-1 level also increased to 274 ng/mL, therefore octreotide dose was increased to 20 mg/month again. At the first postoperative year, the patient is stil being followed-up with 20 mg octreotide and hormone replacement therapies with normal IGF-1 levels and no symptoms.

**CONCLUSION:** Transsphenoidal pituitary surgery is generally the first-line therapy in acromegaly. However, not all patients achieve remission after surgery. Medical treatment has been usually suggested as a first line treatment option for patients who don’t want surgical treatment or can’t undergo surgical treatment due to complication risks. But maybe it would be effective enough and safer if we had used somatostatin analog therapy as first line for this case.

**KEYWORDS:** acromegaly, treatment, surgery, panhypopituitarism
Timeline

Figure 3. Overall timeline of the case with IGF-1 levels and treatments made.
CONCLUSION: In patients with diagnosis of hemochromatosis, endocrinologic functions should be evaluated carefully. Gonadotropic cells are mostly affected cells in the pituitary. Somatotropic and lactotrophic cells are rarely affected. Even if, somatotropic cells are not affected, IGF-1 synthesis may decrease due to hepatic failure. Although, the frequency of hypothyroidism in hemochromatosis is around 1.7%, thyroid axis should be evaluated carefully. Untreated cases may result in clinical worsening and progression of disease.

KEYWORDS: Hemochromatosis, Hypogonadotropic Hypogonadism, Hypothyroidism, Diabetes Mellitus

RESULTS

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INTRODUCTION: Hemochromatosis is a disorder of iron overload and subsequent organ damage. Early studies showed a frequent involvement of the endocrine glands where diabetes and hypogonadism are the most common encountered endocrinopathies. Hypogonadism is mainly secondary to selective deposition of iron on the gonadotropin-producing cells of the pituitary gland, leading to impaired hormonal secretion. Cases of hypopituitarism or selected tropin defects, and abnormalities of adrenal, thyroid and parathyroid glands, even if rare, are reported.

CASE: A 19-year-old male patient with diagnosis of Thalassemia major was admitted to our clinic with weakness. In blood analysis serum TSH level:441 mU/L, FSH:0.8 IU/L, LH:0.23 IU/L, Total Testosterone:0.11 (1.75-7.8) µg/L, GH:1.47 ng/mL, IGF-1:24.5 µg/L, ACTH:14.3 ng/L, cortisol:14.2 µg/L, A1C:6.6 %, Hgb:9.7 g/dL, ferritin:8005 (23.9-336) µg/L, Iron:218 (70-180) µg/dL, iron-binding capacity:4 (155-355) µg/dL, fasting blood glucose:102 mg/dL, ALT:153 (5-50) U/L, AST:122 (5-50) U/L, ALB:34 (35-55) g/L, INR:1.28, vitamin D:6.9 µg/L. On pituitary magnetic resonance imaging (MRI), no adenoma and mass lesion were observed. Neurohypophysial signal change was observed on MRI. Thyroid autoantibodies were negative in the patient with severe hypothyroidism. On ultrasound (USG) thyroid gland was shrunken and had regular margins and heterogeneous parenchymal appearance. Sixtieth minute cortisol level was 22 mg/dl after ACTH stimulation test. Adrenal insufficiency was ruled out and L-Thyroxine replacement was started. The growth hormone response to insulin tolerance test was 6.2 ng / ml. The cause of low serum IGF-1 level was thought to be due to hepatic failure secondary to hemochromatosis. On abdominal MRI, the longitudinal size of liver was 187 mm and had hyperintense parenchymal appearance which is compatible with hemochromatosis. Scrotal USG showed both testes intrascrotally and the volume was smaller than normal. Choriogonadotropin alpha was added to the treatment. At follow up, the dose of L-Thyroxine replacement was increased, since TSH and T4 level were 249 mIU/L and 0.33 (0.61-1.12) ng/dl, respectively. Finally, thyroid function tests along with patient clinic were improved.

DEPARTMENT OF ENDOCRINOLOGY AND METABOLIC DISEASES, UNIVERSITY OF HEALTH SCIENCES, ADANA CITY TRAINING AND RESEARCH HOSPITAL, ADANA, TURKEY
Subclinical Cushing disease with bilateral adrenal nodules and pituitary adenoma

Tuğçe Apaydın, Dilek Gogas Yavuz
Department of Endocrinology and Metabolic Diseases, Marmara University, Istanbul, Turkey

Introduction: Subclinical Cushing syndrome has been defined in patients with autonomous glucocorticoid adenoma who lack clinical symptoms and signs of hypercortisolism. Here we present a case of subclinical Cushing syndrome with bilateral macronodular adenoma and pituitary adenoma.

Clinical Case: A 63-year-old woman with no chronic disease was admitted to our clinic in 2017, for incidental detection of bilateral adrenal nodules on abdominal computerized tomography (CT), which was performed for chronic constipation and abdominal pain. Abdominal tomography displayed bilateral adrenal adenoma; 44*19*21 millimeters (mm) on the right side, 42*29*26 mm on the left side. In physical examination, her BMI was 21.62 kg/m², she didn’t have a facial plethora, moon-face, central obesity, purple striae, and supraclavicular fat pads. In laboratory examination; 1-mg overnight dexamethasone suppression test (DST) was 5.5 µg/dl, urine free cortisol (UFC) was 139 µg/day, midnight serum cortisol test was 7 µg/dl, 2 days low-dose DST was 4.7 µg/dl, ACTH level was 5.91 pg/mL, urinary fractionated metanephrines were normal, aldosterone was 3.7 ng/dl, renin plasma activity was 0.24 ng/ml/h. Other laboratory examinations were at reference ranges.

Pituitary MRI was normal. And she was also investigated for aberrant receptors. Serum cortisol levels increased >50% only in response to ACTH. Inferior petrosal sinus sampling demonstrated a maximum central to peripheral ACTH gradient of 15 indicating Cushing disease. A dual-energy x-ray absorptiometry (DEXA) showed a T-score of −1.67 in the spine and of −2.3 in the femoral neck areas, respectively.

The patient was not scheduled for surgery because there was no obvious cushingoid clinic. On the last visit, Pituitary MRI has revealed a 4-mm lesion on the right side of the pituitary. The size of the adrenal adenomas were the same. Her metabolic profile was stable.

Conclusion: Among corticotroph adenomas, approximately 20% are silent corticotroph adenomas causing subclinical Cushing syndrome. The choice between surgery and conservative management is the major therapeutic dilemma. Subclinical Cushing can transform into clinical Cushing syndrome. Consequently, silent corticotroph adenomas need long-term follow-up.

Keywords: Subclinical Cushing, bilateral adrenal nodules, Cushing disease
INTRODUCTION: Tuberculous meningitis (TBM) can occur in isolation or along with a pulmonary focus. The clinical spectrum of TBM is broad and may be non-specific making early diagnosis difficult. Hypopituitarism has been reported due to pituitary or hypothalamic abnormalities in TBM, and it may become evident years after recovery, apparently due to progressive scarring of either the hypothalamus itself or adjacent tissues. Here, we present a case of hypopituitarism thought to have developed after tuberculosis meningitis during a multisystemic tuberculosis infection approximately 40 years ago.

CASE PRESENTATION: A 60-year-old male was sent to our endocrinology clinic because of low FT4 and TSH levels. Physical examination revealed pale skin and hypogonadal facial appearance. Axillary and pubic hairs were very scarce. The blood pressure was 90/60 mmHg. He had a scar on his left cervical region. He was diagnosed with colon carcinoma and received radiotherapy and chemotherapy after surgery in 2015 and was in remission thereafter. He indicated that he had decreased sexual function for more than 25 years. He gave the information of a long lasting treatment when he was 20 years old for left cervical masses without neck pain and/or stiffness. But there was discharge from these masses and hearing loss developed after an injection therapy, which was a part of the treatment. Based on past medical history, we thought that the patient was most probably treated for tuberculous lymphadenitis. His pituitary function tests were as follows: FT3: 2.8 pmol/L (3.1-6.8), FT4: 9.4 pmol/L (12-22), TSH: 2.6 mIU/L (0.27-4.2), IGF-1: 27.5 ng/mL (43-220), LH: 0.1 mIU/mL (1.7-8.6), FSH: 0.25 mIU/mL (1.5-12.4), Total Testosterone: 0.025 ng/mL (1.32-8.92), PRL: 16 ng/mL (4-15), basal cortisol: 4.77 ug/dL and 1 mcg ACTH stimulation test showed insufficient adrenal response. The patient denied to have polyuria or polydypsia, and his blood Na+ level was 141 mmol/L. These results showed central hypogonadism, central hypothyroidism and secondary adrenal insufficiency. Pituitary MRI revealed disseminated calcification compatible with sequelea of pulmonary tuberculosis. During current evaluation, active tuberculosis was excluded. Based on this data, early diagnosis and treatment of multisystem tuberculosis probably caused the symptoms of TBM to be mild. The patient begun to receive replacement therapies with glucocorticoid and thyroid hormone. He was warned about stress conditions and recommended to receive steroid protection.

CONCLUSION: Although hypopituitarism associated with meningitis is rarely reported, these cases may be more recognizable by careful physical examination and questioning of the patient’s medical history.

KEYWORDS: Tuberculous meningitis, hypopituitarism, central hypothyroidism
The patient is a 42 years old man who presented with headache and palpitation. On physical examination there was mild tremor and tachycardia. Laboratory examination showed high serum level of total and free thyroid hormones in presence of normal TSH.

Brain MRI showed a 2 cm pituitary mass 3 mm away from optic chiasma. Other pituitary hormones and perimetry were normal.

A Transsphenoidal adenectomy was planned for the patient but he denied operation. He treated with methimazol 20 mg daily. Thyroid hormones decreased to normal levels but after 6 months increased to a higher level and did not respond to maximum dose of methimazol. Monthly injection of sandostatin LAR 20 mg began with good response and he was followed with Brain MRI and thyroid function tests for 3 years. Tumor size decreased slowly and disappeared after 2 years. Now he is continuing his injections and is happy for his decision.

**KEYWORDS:** TSH producing adenoma, Thyrotoxicosis, sandostatin LAR
INTRODUCTION: Lymphocytic hypophysitis is a rare inflammatory disease of the pituitary gland predominantly affecting women at the end of gestation or during early postpartum. Its natural history is variable and its therapeutic approach is controversial. We report a rare case of lymphocytic hypophysitis where recovery of gonadal function was followed by an uncomplicated pregnancy.

CASE: A 31-year-old woman was admitted to our clinic for fatigue, depression, appetite loss, cold intolerance, and amenorrhea. About a year ago in her medical history, she experienced severe headaches, nausea and hypotension during the last trimester of her first pregnancy. In last trimester, the non-contrast pituitary MRI scan showed a large pituitary mass with suprasellar extension and it was interpreted as the pituitary enlargement of pregnancy. The patient was given analgesics and uncomplicated delivery was achieved with epidural anesthesia at term. Following this, the patient stated that she could not breastfeed her baby and had no menstruation. On physical examination she appeared pale. The blood pressure was 85/60 mmHg. She had reduced axillary and pubic hair. Hormonal evaluation revealed hypopituitarism and a repeat MRI scan a year after the initial presentation revealed a marked reduction in anterior pituitary gland size highly suggesting inflammation regression of the pituitary gland. Her thyroid autoantibodies were positive. Based on a presumptive diagnosis of hypopituitarism secondary to peripartum hypophysitis, replacement with prednisolone (5 mg/day) and L-thyroxine (50 µg/day) were instituted. Over the next four months regular menstruation resumed, therefore she regained normal gonadal function. Two years later, she became pregnant spontaneously and delivered a second healthy baby without lymphocytic hypophysitis recurrence. She could not be able to breastfeed, but her menstruation began in the first month after birth. Our patient has been followed-up for seven years from pituitary clinic and she is in good health under thyroid and steroid replacements.

Conclusion. Although hypogonadism due to lymphocytic hypophysitis can be recovered spontaneously or under steroid replacement, we believe that spontaneous pregnancy is very important in these patients following the normalization of long-term hypogonadism.

KEYWORDS: Lymphocytic hypophysitis, spontaneous recovery, pregnancy
adenoma. He underwent second operation via an endonasal endoscopic transsphenoidal approach in 2018. Focal prolactin was positive in immunostaining and immunohistochemistry was positive for Pit-1 and pathological examination was evaluated with the first pathology material and reported as plurihormonal adenoma. After second operation, pituitary MRI detected an operation-related defect in the central parts of the macroadenoma which was invasive to the cavernous sinus, the sphenoid bone, and the anterior section of the left temporal lobe. In laboratory examination, prolactin was 163.6 µg/L (4.04-15.2), total testosterone was 55.6 ng/dL (280-800), GH 1.06 µg/L, IGF-1 216 (44.7-210) and the other hormones were normal. Although IGF-1 level was high, on physical examination he had no signs of acromegalic features. He was taking cabergoline totally 4 tablets once week when these hormone levels were detected, and owing to hyperprolactinemia, cabergoline was increased to 6 tablets once a week. We were not able to start testosterone treatment due to lymphocytosis. He took radiotherapy which was decided in council. After radiotherapy and dopamine agonist treatment IGF-1 level was in normal ranges. We consult him with hematology and according to their decision we would like to start testosterone replacement treatment.

We should perform a complete biochemical and histologic evaluation in all patients with pituitary adenomas.

**KEYWORDS:** Pit-1, plurihormonal adenoma, macroadenoma

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PIT-1 - Positive PPAs expressing growth hormone, thyrotrophin and prolactin are rare. Because of this reason, we would like to share our case having giant macroadenoma secreting GH, TSH and PRL.

A 62 year-old male was consulted to our department before his operation in 2016. Neurosurgery department planned his operation because of giant macroadenoma which was detected in head MRI after his visual loss. In preoperative pituitary MRI, the diffuse homogeneous mass lesion originating from pituitary gland was observed and having grade 4 invasion into bilateral cavernous sinus and eroded the base of the sella. It extended to the anterior temporal convexity on the left side. In laboratory examination, pituitary hormone levels were within normal ranges except testosterone levels (total testosterone 0.27 ng/mL[2.8-8]). Pathological findings revealed a pituitary adenoma which displayed focal TSH and PRL immunoreactivity. Immunostaining of GH was rare positive, TSH and PRL were focally positive. Postoperatively, pituitary MRI demonstrated the component of the adenoma extending in the anterior to temporal convexity and the component extending towards the suprasellar area to be operated but the rest of the tumor remained. Pituitary hormone levels displayed low fT4, total testosterone, high prolactin but the other hormone levels were normal. He received cabergoline due to hyperprolactinemia and L-thyroxin due to central hypothyroidism. In surveillance, in 2017 pituitary MRI demonstrated pressure on optic chiasma and no difference in the size of the adenoma. He underwent second operation via an endonasal endoscopic transsphenoidal approach in 2018. Focal prolactin was positive in immunostaining and immunohistochemistry was positive for Pit-1 and pathological examination was evaluated with the first pathology material and reported as plurihormonal adenoma. After second operation, pituitary MRI detected an operation-related defect in the central parts of the macroadenoma which was invasive to the cavernous sinus, the sphenoid bone, and the anterior section of the left temporal lobe. In laboratory examination, prolactin was 163.6 µg/L [4.04-15.2], total testosterone was 55.6 ng/dL [280-800], GH 1.06 µg/L, IGF-1 216 [44.7-210] and the other hormones were normal. Although IGF-1 level was high, on physical examination he had no signs of acromegalic features. He was taking cabergoline totally 4 tablets once week when these hormone levels were detected, and owing to hyperprolactinemia, cabergoline was increased to 6 tablets once a week. We were not able to start testosterone treatment due to lymphocytosis. He took radiotherapy which was decided in council. After radiotherapy and dopamine agonist treatment IGF-1 level was in normal ranges. We consult him with hematology and according to their decision we would like to start testosterone replacement treatment.

We should perform a complete biochemical and histologic evaluation in all patients with pituitary adenomas.

**KEYWORDS:** Pit-1, plurihormonal adenoma, macroadenoma
When all the clinical findings of the patient were evaluated, we diagnosed Van Wyk and Melvin M. Grumbach syndrome due to the presence of severe clinical hypothyroidism, hypophysar hyperplasia due to severe TSH stimulation, and consequently macroadenoma, short stature, obesity, and premature puberty. The patient was given iron replacement and levothyroxine (FT4 replacement) treatment. When he came to the follow-up visit one week later, the patient showed clinical improvement within the week. TSH-349.21 mIU / ml and FT4-0.5 ng / dl were determined in one week control. When he came for a follow-up visit a month later, the patient’s general condition improved completely and he lost 10 kg of weight for 1 month.

The patient became euthyroid (TSH-1,703 mIU / ml. FT4-0.89 ng / ml). Prolactin levels decreased to 11 ng / ml. After 3 months, the patient was euthyroid, and the tumor size decreased significantly on the control pituitary MRI. Adenoma sizes decreased to 9 * 8 * 8 mm when compared with MR results 3 months ago. Abdominal ultrasonography showed complete loss of peritoneal fluid.

**CONCLUSION:** Although it is rarely seen, in such cases that suggest Van Wyk Grumbach syndrome with all parameters clinically, it is important to consider the patient in a large tuning fork and to provide correct diagnosis and treatment.

**KEYWORDS:** Myxedema, hypothyroidism, early puberty

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**INTRODUCTION:** To present the case of Van Wyk Grumbach syndrome with myxedema clinic, pituitary lesion and early puberty findings due to severe hypothyroidism.

**PRESENTATION:** 14.5-year-old female patient presented to the clinic with weakness, generalized edema, slowing speech, obesity, constant drowsiness, difficulty in walking, menstruation at an early age (9.5 years old), short stature, increasing problems in vision, pain and swelling in the legs, constipation, dry skin, hair loss, forgetfulness, memory loss. There was no consanguineous marriage between the parents. There was no feature in her history. His mother always said that the child was slow moving, prone to sleep. He applied to the health institution from time to time with these complaints but did not get any results. Endocrinology said it was his first time at the outpatient clinic. The patient was admitted to the cardiology outpatient clinic and ECO examination revealed significant pericardial fluid. Pleural and peritoneal fluid was also detected in thorax and abdominal CT scans. He was referred to the endocrinology clinic due to his short stature and obesity. TSH was measured as > 500 mIU / ml, FT4- 0.24 ng / dl and anti-TPO-669.9 IU / ml. Biochemical tests showed no pathological findings except iron deficiency anemia. Prolactin level was found to be 64 ng / ml. 1 mg DST Cushing screening test was negative. Thyroid ultrasonography showed a severe heterogenous, pseudonodular appearance of the thyroid parenchyma, decreased echo significantly, extending to the suprasellar cistern on the pituitary MRI, showing a pathological contrast enhancement, compressing the optic chiasm and measuring 20 * 18 * 12 mm solid lesion. Patient height 140 cm (<3p), weight 79 kg (> 97 p) and severe weight shortness and obesity predominates. Pelvic ultrasonography showed no pathological features except ovarian follicle cysts. Ophthalmology consultation was performed. Although there was no atrophy in spite of pituitary compression at the visual margins, perimetric visual field contraction was observed. Bone age was 11.5 [-3SD] and was below the calendar age.
INTRODUCTION: Thyroid function tests (TFT) are among the most frequently ordered tests in clinical practice. The presence of heterophile antibody, unesterified free fatty acids, drugs, pregnancy, non-thyroid diseases may lead to deviations in thyroid hormone measurements. In a small but important group, test results may show clinical discordance. Hereby, we present a case with acute pancreatitis whose TSH level is high without signs and symptoms of hypothyroidism.

CASE: A 35-year-old male patient with hypertension, type-2 diabetes mellitus and hyperlipidemia was admitted to the emergency department with abdominal pain. The patient was diagnosed as non-biliary acute pancreatitis with typical abdominal pain and elevated serum amylase-lipase levels. Triglyceride (TG): 3753 mg/dl (0-150) were detected in the tests. Since he had hyperlipidemia, to exclude hypothyroidism fT4 and TSH were ordered. TSH was elevated 21.084 uIU/ml (0.38-5.33) and free thyroxine (fT4) level was normal: 0.82 ng/dl (0.54-1.12) consistent with subclinical hypothyroidism. He had no signs and symptoms of hypothyroidism. The patient was administered glucose-insulin-potassium (GIK) solution and fenofibrate for three days. Control blood tests revealed TG: 1319 mg/dl (0-150), because of the discrepancy between his thyroid function test and clinical situation thyroid function tests were also repeated. Both TSH: 1.627 uIU/ml (0.38-5.33) and fT4: 0.97 ng/dl (0.54-1.12) level were normal.

CONCLUSION: Acute pancreatitis has a wide clinical spectrum ranging from a mild self-limited clinical circumstance that requires supportive therapy to severe life-threatening disease. In this case, the patient was followed with mild edematous acute pancreatitis. Since the signs and symptoms were not consistent with hypothyroidism, determining the TSH level of 21.084 uIU/ml was confusing. In this respect, we investigated the relationship between triglyceride elevation and its effect on TSH measurement. Positive correlation between hypertriglyceridemia and serum TSH elevation has been shown in many studies. In a study, it was found that m-RNA expression of TRH was increased and serum TSH level was increased 3.7-fold in mice fed high fat diet for 8 weeks. In the epidemiological study of Yang et al., it was shown that serum TSH levels were significantly higher (approximately 1.5 times) in patients with isolated hypertriglyceridemia compared to the control group, whereas serum fT4 was lower. When serum triglyceride levels were taken under control in our patient, serum TSH level was in normal limits. In this case, we would like to emphasize that high serum triglyceride levels may alter thyroid function tests particularly TSH. And this interference may be considered when interpreting TFT in patients with hyperglyceridemia whose clinical picture is not concordant with laboratory test results.

KEYWORDS: thyroid stimulating hormone, interference, hypertriglyceridemia

<table>
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<tr>
<td><strong>1st Day</strong></td>
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<tr>
<td>Triglyceride</td>
</tr>
<tr>
<td>TSH</td>
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<tr>
<td>fT4</td>
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OBJECTIVE: Thyroid disease is associated with changes in the skin while may sometime be the first clinical sign. So we report a case of dirty elbow which characterized by abnormal darkening of the extensor surface of right elbow without any erythema or scaling. Hypothyroidism is an unusual cause of dirty elbow.

METHODS: We report a case of 65-years-old woman presented with one month history of fatigue and malaise, that become apparent when the patient has episodes of atrial fibrillation for six months with darkening of skin of her left elbow unresponsive to topical keratolytic and corticosteroids. Laboratory evaluation revealed an autoimmune thyroiditis with hypothyroidism.

RESULTS: Dirty elbow is a darkening skin of elbow. Other causes of dirty elbow were excluded. After hormonal replacement therapy a gradual improvement of skin was observed.

CONCLUSION: The diagnosis of dirty elbow due to hypothyroidism is a very rare association. Hypothyroidism must be suspected in patients with dirty elbow, particularly when it occurs in association with systemic symptoms.

KEYWORDS: TSH thyroid stimulating hormone, US ultrasound, FADES fractional a symptomatic darkening of the extensor surface
INTRODUCTION: Struma ovarii (SO) is a type of ovarian germ cell tumor and a specific form of mature teratoma. It is defined as an ovarian teratoma that is composed predominantly of thyroid tissue (>50%). Malignant struma ovarii (MSO) occurs only in 5% of SO cases. Diagnosis of MSOs by imaging methods and clinical findings is difficult and most of them are diagnosed incidentally. We present here an interesting case of MSO which has been also diagnosed with acromegaly.

CASE REPORT: Transvaginal ultrasonography of a 61-year-old female patient with the complaint of inguinal pain revealed a mass of left ovary 4 cm in diameter containing solitary and cystic areas with septas and was initially considered as malignant (Figure-1). Pelvic MRI revealed 41x35 mm heterogeneous mass with irregular contrast enhancement of originating from the left ovary. Serum CA 125, CA19-9, CA15-3, CEA, TSH and LDH levels were normal.

It was decided to perform laparotomy and frozen procedure during operation. When the abdomen was entered by laparotomy, the mass was seen as 6x4 cm in diameter, lobulated, white, with multiple cystic areas on its surface. Pathologic examination of frozen section was reported as mucinous cystadenoma. Upon this result, total abdominal hysterectomy and bilateral salpingooophorectomy were performed. Pathologic examination of mass reported as struma ovarii and papillary carcinoma follicular variant on the background of struma ovarii. Papillary carcinoma was a microcarcinoma with 5 mm in diameter and intact struma ovarii capsule was reported. TTF-1, Thyroglobulin and Galectin-3 were found to be positive in the immunochemical examination.

The patient was evaluated by the endocrinology department and physical examination revealed acromegalic features such as frontal bossing, prognathism, skin thickening and growth of hands and feet. IGF-1 was found 637 ng/ml (44-220 ng/ml). Growth hormone suppression was not observed after 75 gr oral glucose load and so acromegaly was diagnosed (Table-1). The other pituitary hormone profile was in normal range: Prolactin 16,59 ng/mL, FSH 92,69 mIU/mL, LH 31,61 mIU/mL, estradiol <5,00 pg/mL, TSH 3,55 uIU/mL, free T4 1,24 ng/dL (0,93 - 1,7), cortisol 15,35 ug/dL. Pituitary MRI revealed a 5 mm microadenoma on the right side of pituitary gland. Meanwhile, thyroid ultrasonography was performed and a mildly hypoechoic nodule with a size of 5x8x15mm (EU-TIRADS 4) was detected in the isthmus. Total thyroidectomy was recommended because of atypia of undetermined significance reports of two consecutive fine needle aspiration biopsies. The total thyroidectomy was reported as benign. After total thyroidectomy, the patient was referred to the neurosurgery department for surgical treatment of acromegaly.

CONCLUSION: It has been reported that thyroid malignancy is increased in acromegaly, but the coexistence of MSO and acromegaly has not been reported in the literature before.

KEYWORDS: struma ovarii, acromegaly, thyroid papillary carcinoma

**Table 1. 75 gr oral glucose growth hormone supression test**

<table>
<thead>
<tr>
<th>Time</th>
<th>Glucose, mg/dl</th>
<th>Growth Hormone, ng/ml</th>
</tr>
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<tr>
<td>0. minute</td>
<td>113.4</td>
<td>7.73</td>
</tr>
<tr>
<td>30. minute</td>
<td>159.6</td>
<td>6.45</td>
</tr>
<tr>
<td>60. minute</td>
<td>164.4</td>
<td>5.91</td>
</tr>
<tr>
<td>90. minute</td>
<td>114.1</td>
<td>6.14</td>
</tr>
<tr>
<td>120. minute</td>
<td>136.3</td>
<td>5.43</td>
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**OBJECTIVES:** Thyrotoxic periodic paralysis (TPP) is associated with thyrotoxicosis and distinct from familial hypokalemic periodic paralysis (FPP) (Table 1). Graves’ disease is the most common etiology. We present two cases of Graves’ disease which were presented with TPP.

**CLINICAL CASES:** Case 1: Twenty-nine-year-old male patient was admitted to emergency ward with a complaint of sudden muscle weakness in all extremities. He had no comorbid illness, usage of medication, alcohol or smoking. Family history was unremarkable.

He was alert and oriented. Vital findings and examination of organ systems were unremarkable. Muscle strength was 1/5 in all four extremities.

Laboratory findings were as follows: glucose: 96 mg/dL, creatinine: 0.9 mg/dL, ALT: 17 U/L, AST: 27 U/L, Na: 147 mmol/L, K: 2 mmol/L, Ca: 8.6 mg/dL, P: 3.2 mg/dL, TSH: <0.004 mIU/L, fT4: 2.79 ng/dL, fT3: 8.32 pg/mL, AntiTPO: 854 IU/mL, and AntiTSH receptor antibody: 17.52 IU/L. Blood count and gas analysis were normal.

After correction of hypokalemia, muscle strength recovered. Perthecnetate scintigraphy confirmed bilateral diffuse hyperplasia of thyroid gland. Final diagnosis was Graves’ disease and TPP. Methimazole 15mg/d and propranolol 40mg/d were initiated. Radioactive iodine (RAI) was offered but the patient rejected. TPP did not recur.

**CASE 2:** Thirty-one-year-old male patient was admitted to emergency ward with a complaint of sudden muscle weakness in all extremities. He also complained with sweating, tremor, hair loss, and palpitation for 3 months. He had been taking analgesics during migraine attacks. He used to smoke but did not consume alcohol. He had been making an intense physical effort at work. His mother had hypertension.

He was alert and oriented. Vital findings and examination of organ systems were unremarkable. Muscle strength was 3/5 in upper, 1/5 in lower extremities.

Laboratory findings were as follows: glucose: 96 mg/dL, creatinine: 0.9 mg/dL, ALT: 17 U/L, AST: 27 U/L, Na: 147 mmol/L, K: 2 mmol/L, Ca: 8.6 mg/dL, P: 3.2 mg/dL, TSH: <0.004 mIU/L, fT4: 2.79 ng/dL, fT3: 8.32 pg/mL, AntiTPO: 854 IU/mL, and AntiTSH receptor antibody: 17.52 IU/L. Blood count and gas analysis were normal.

After correction of hypokalemia, muscle strength recovered. The clinical picture was not consistent with FPP. Perthecnetate scintigraphy confirmed bilateral diffuse hyperplasia of thyroid gland. With a final diagnosis of Graves’ disease and TPP, propylthiouracil 30mg/d and propranolol 160mg/d were initiated. At 3 months after admission, thyrotoxicosis was resolved, and RAI was given. TPP did never recur.

**DISCUSSION:** TPP was the first manifestation of Graves’ disease in our cases. Intense physical performance at work might be a precipitating factor in the second case. Definitive treatment of Graves’ disease is obligatory for prevention of recurrence of TPP.

**KEYWORDS:** Thyrotoxic periodic paralysis, periodic paralysis, hypokalemic periodic paralysis, Graves’ disease

| Table 1. Comparison of clinical features of TPP and FPP. |
|----------------|----------------|
| **TPP**        | **FPP**        |
| Attack duration| hours to days  |
| Attack frequency| not frequent   |
| Gender         | male preponderance |
| Etiology       | thyrotoxicosis (mostly Graves) |
| Accompanying features| thyrotoxicosis chronic thyrotoxic myopathy |
| Precipitating events| carbohydrate load stress heavy exercise |
| Age at presentation| >20 year-old |
| Hypokalemia    | present         |
| Prevention     | propranolol constitution of euthyroid state |
|                | carbonic anydase inhibitor K-sparing diuretic |
OBJECTIVE: Hypothyroidism is a common disorder and generally treated successfully with a dose of 1.6-1.8 mcg/kg daily levothyroxine. Absorption of levothyroxine is effected by foods, drugs and some gastrointestinal diseases. Nonadherence to the medication is a major challenge and levothyroxine pseudomalabsorption has been used for this situation when the patient does not report the nonadherence and mimics decreased gastrointestinal absorption of the drug.

CASE: 40 year old women with a history of subtotal thyroidectomy in 2013 with the diagnosis of toxic multinodular guatr was referred to endocrinology clinic with uncontrolled hypothyroidism. In outpatient clinic visits her levothyroxine dosage was increased gradually as her TSH levels were 40-50 mIU/ml up to 600 mcg/day. She reported taking the medication regularly, in the morning, with water and 30 minutes-1 hour before the breakfast. She was taking no other medication. Her hemogram and biochemical parameters were between normal ranges. Her celiac antibody tests were negative. For differential diagnosis of malabsorption or pseudomalabsorption she was admitted to inpatient clinic. Her TSH level was 32,4 mIU/ml and free T4 level was 0,65 ng/dl before test and free T4 level increased gradually up to 2,32 ng/dl. Her TSH levels suppressed and T4 levels elevated with high dose levothyroxine and her results were compatible with diagnosis of levothyroxine pseudomalabsorption syndrome.

DISCUSSION: Here we report a case of levothyroxine pseudomalabsorption documented with 2 hour levothyroxine supression test. Absorption of levothyroxine was demonstrated with subsequent elevated T4 levels. In the case of higher levothyroxine requirement than expected, clinician should consider pseudomalabsorption syndrome.

KEYWORDS: pseudomalabsorption, levothyroxine, high dose
INTRODUCTION: Primary hyperparathyroidism (pHPT) is characterized by hyperactivity of one or more parathyroid glands, a consequent increase in serum calcium (Ca) along with elevated or inappropriately present circulating levels of PTH. Besides this, normocalcemic primary hyperparathyroidism has been recently recognized as a distinct pHPT phenotype. Additionally, in the literature, a new phenotype with high serum Ca and consistently normal PTH levels has been documented. This type of pHPT comprises the so-called normohormonal variant. In the literature, there is no case of pHPT with normal Ca and PTH levels together. We recently defined normocalcemic and normohormonal variant of disease as a new type of pHPT.

CASE REPORT: The patient is a 28-year-old gentleman, who referred to our clinic in April 2019 after being found to have normocalcemia and incidental parathyroid adenoma seen at neck ultrasound (US) on routine laboratory work. He was a soldier and hasn’t any symptom and complaint. The patient had no specific past medical or family history. US at that time revealed a large well-defined hyperechoic nodular lesion seen related inferior to the lower pole of the left thyroid lobe measuring 7.8 x 5.8 x 3.1 mm, most likely representing enlarged left inferior parathyroid gland as nearly 3 grams. His corrected calcium (c.Ca) level was 9.8 and 9.5 mg/dL (NR 8.8-10.6). His serum PTH level was 63.4 ng/L (NR 15-65). 25 OH D vitamin was 23.8 µg/L (NR 30-80). GFR was 129 mL/dk/1.73m², ALP was 139 U/L (NR <128), P was 3.2 mg/dL (NR 2.6-4.5). Urinary calcium excretion was 320 mg/day. Thyroid function tests and the other laboratory tests were in the reference ranges. He had no nephrolithiasis on urinary US. Preoperative Sestamibi scan localized the adenoma in the left inferior thyroid gland. While he was no high Ca and PTH, we performed PTH washout with fine needle aspiration biopsy. It revealed 3470, as 50 fold of serum PTH and benign cytology. 24 hour urine metanefrines were normal. While he was a young man we offered operation. He was operated with minimally invasive parathyroidectomy and the pathology revealed parathyroid adenoma. Post operation first day his c.Ca was 8.93 mg/dL, PTH decreased to 9.7 ng/dL however after one week c.Ca was 9.4 mg/dL and PTH was 20.8 ng/L. He had no complication and then had been discharged from the hospital.

DISCUSSION: Hitherto classic, the normocalcemic and the normohormonal variants of pHPT were defined although the last two are topics for future investigations. We reported a case with normocalcemic and normohormonal status with pHPT. Normal parathyroid glands are not visualized on routine imaging, but parathyroid disease typically results in enlargement of the glands. There is no case in the literature of normocalcemic and normohormonal parathyroid adenoma.

CONCLUSION: Even though biochemical tests are normal there is need to investigate the parathyroid lesions if the localization is compatible with parathyroid adenoma.

KEYWORDS: primary hyperparathyroidism, calcium, parathyroid hormone
CONCLUSION: Superior vena cava syndrome is mostly seen in the cause of mediastinum localized malignancies. A giant goiter is an extraordinary reason for this syndrome, especially in the 21st century. The slow enlargement of retrosternal goiter permits to develop venous collaterals and the patients may stay asymptomatic for many years. The resection of the thyroid gland is adequate to relieve symptoms and physical signs of this syndrome in most of the patients.

KEYWORDS: retrosternal goiter, superior vena cava syndrome, thyroidectomy

INTRODUCTION: Retrosternal goiter may make compression on mediastinal structures but superior vena cava syndrome is an uncommon complication. The most common symptoms of this syndrome include dyspnea, plethora, facial swelling, and venous distension of the neck. Surgery resolves the sign and symptoms of this syndrome in most of the cases. We presented an exceptional giant goiter case that causes superior vena cava syndrome.

CLINICAL CASE: A 41-year-old female patient presented with dyspnea and venous distension of the neck. Personal history of patient stated no chronic disease and drug use. Physical examination showed a massive, firm, and painless thyroid gland and prominent enlargement of jugular and innominate veins [Figure 1]. Thyroid ultrasonography revealed multinodular goiter with 12-cm longitudinal size of right and 10-cm size of left thyroid lobes. The thyroid gland was extended to retrosternal area. Chest radiography revealed a widened mediastinum. Contrast-enhanced computerized tomography demonstrated an enlarged thyroid gland with intrathoracic extension, which makes compression to the trachea. The patient was euthyroid and other laboratory parameters were in the normal reference range. The patient underwent total thyroidectomy through cervical approach. The 615-g weighted thyroid gland excised totally with its capsule. Histopathological evaluation was compatible with nodular hyperplasia. The patient had a trouble-free recovery period and any surgery-related complication was not seen after surgery. The visible collateral veins resolved in 4 weeks after surgery [Figure 1]. We remain to follow the patient under levothyroxine treatment in the postoperative first year.

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Papillary thyroid cancer represents a small percentage, around 5%, of thyroid nodules. Thyroid ultrasound is very sensitive in detecting malignant nodule features and the necessity of Fine Needle Aspirate. Thyroid Scintigraphy differentiates between cold and hot thyroid nodules but cannot predict malignancy in the cold nodules thus FNA is needed. On the other hand, almost all hot nodules on Scintigraphy are benign hyperfunctioning adenomas thus eliminating the need of biopsy.

We present the case of a 22yo man, previously healthy, presented to the ophthalmology clinic for left periorbital edema. During his work up a CT scan showed periorbital cellulitis. TSH was done <0.05 FT4: 25.52 pmol/L, FT3: 7.11 nmol/L, thyroid receptor antibodies were done to rule out Grave’s disease, it was slightly positive 2.1 (normal <1). A Thyroid scintigraphy (attached) was done 1 month after the injected scan and showed a right toxic adenoma rather than Grave’s disease diffuse uptake. The patient was started on anti thyroid drug methimazole 15 mg/day and presented to us for a second opinion.

On physical exam, the periorbital edema was not affecting the patient’s sclera, no exophthalmos (picture attached). Thyroid exam showed hard palpable right thyroid nodule. To complete the work up and shape up the diagnosis an US thyroid was requested and showed a 1.9 cm Right lower thyroid nodule hypoechoic with irregular margins and few microcalcifications (TIRADS V). This single nodule had the same location of the toxic adenoma found on Scintigraphy.

FNA of the thyroid nodule was done and the result was highly suspicious for malignancy. Patient underwent total thyroidectomy with prophylactic central LN dissection, pathology post op showed single focus of papillary thyroid cancer 2.1 cm with no capsular invasion with 2 positive central Lymph nodes.

He received 100 Mcurie of I131 for remnant ablation and then he was started on levothyroxine 150 mcg daily to follow up closely.

In Summary our patient presented with hyperthyroidism due to a toxic adenoma but carrying papillary thyroid cancer. The thyroid ultrasound remains the most sensitive test to detect thyroid cancer. Being non-invasive, it is very important to always couple the US with the Scintigraphy in the diagnosis of hyperthyroidism.

**KEYWORDS:** Toxic adenoma, papillary thyroid cancer, radioactive iodine
INTRODUCTION: Takayasu’s arteritis is a rare disease involving inflammation in the walls of the largest arteries in the body: the aorta and its main branches. The disease results from autoimmunity which causes inflammation in the arterial Wall. Irregular inflammatory response is known to play an important role in the initiation, development and progression of tumours. The most common thyroid malignancy is papillary thyroid carcinoma (80% of all types of thyroid cancers). Papillary thyroid carcinoma is well known for its low malignant potential and good prognosis. Although Takayasu arteritis was associated with graves and hashimoto diseases, it is presented for the first time in association with thyroid papillary carcinoma.

CASE: A 42-year-old female patient was admitted to our clinic with the complaint of neck swelling. On physical examination, radial and brachial pulses could not be obtained in the right arm, the difference in systolic blood pressure between the left and right arms was 40 mmhg and the thyroid examination revealed a palpable nodule of approximately 2 cm on right side. Thyroid doppler ultrasonography (USG) showed an 18 mm hypoechogenic margin with irregular microcalcified nodule on the right, level 3 pathologic lymphadenopathy on the right cervical region and advanced intima thickening on the right carotid artery. Serological tests, sedimentation, bt angiography, and dopler usg were performed on suspicion of Takayasu’s arteritis. Sedimentation rate was 56 mm / h and serological tests were negative. Imaging results were consistent with takayasu’s arteritis. Takayasu’s arteritis was diagnosed and anti-inflammatory, antiaggregant and antihypertensive treatment were initiated. Thyroid fine needle biopsy was also performed. Upon suspicion of papillary carcinoma, bilateral total thyroidectomy and right lateral cervical dissection were performed. The pathology was a follicular variant of thyroid papillary carcinoma. The patient was given adjuvant radioactive iodine treatment postoperatively. The patient is in remission and being followed up with medical treatment.

KEYWORDS: Thyroid papillary carcinoma, Takayasu arteritis, Hypertension
SEVERE BILATERAL ORBITOPATHY IN PATIENT WITH HASHIMOTO THYROIDITIS CASE REPORT

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INTRODUCTION: Thyroid associated orbitopathy (TAO) is originated by immune related inflammation of orbital tissues, in which etiopathogenesis cannot clearly be explained. TAO is usually seen in hyperthyroid patients with Graves disease (GD). On the other hand, severe orbitopathy cases related to Hashimoto Thyroiditis (HT) were rarely published within the literature.

CASE: Here we report a case of Hashimoto’s ophtalmopathy. A 50 years old woman was admitted to our hospital with an acute onset of bilateral red and swollen eyes. She denied eye pain and photophobia. She had a history of Hashimoto’s Thyroiditis and was on levothyroxine treatment for 10 years. Her physical examination was normal. Ophthalmological examination showed bilateral proptosis, swelling of the eyelids and conjunctival injection. The degree of exophthalmos on the Hertel exophtalmometer was 27 mm for the left eye and 25 mm for the right eye. Intraocular pressure was normal in both eyes. Ten point clinical activity score (CAS) was 5. Laboratory data revealed normal thyrotropin (TSH) levels (1,8 µIU/ml; ranges 0,35-4,94 µIU/ml), negative TSH receptor antibody (8,4 U/L, ranges 0-14U/L) and high titers of thyroid peroxidase antibodies (anti-TPO) (>1200 IU/ml(<35 IU/ml) and antibodies to thyroglobulin (anti-TG) (>500 IU/ml(<20 IU/ml). Thyroid ultrasonography showed small thyroid volume with heterogeneous parenchyma. Orbital magnetic resonance (MR revealea increased thickness of bilateral, medial, lateral, superior oblique, inferior and superior muscle diffuse contrast, exophthalmos and compression of optic nerve sheath by medial and lateral rectus(Figure 1). Along with these findings thyroid ophtalmopathy associated with HT was the diagnosis. Pulse steroid therapy (500 mg/week for 12 weeks) was given due to her CAS was 5. During the follow up period her ophtalmopathy responded to the treatment.

CONCLUSION: Being aware of this atypical form of ophtalmopathy is important, since glucocorticoid treatment improves this disorder immedaately.

KEYWORDS: Hashimoto Thyroiditis, ophtalmopathy, orbitopathy

Figure 1. Orbital MR imaging of the patient
**RESULTS:**
October 2018: TSH <0.05 mU/l. T4 >60.0 pmol/l
May 2019: TSH <0.05. T4 48.0. T3 11.8 pmol/l
June 2019: TSH <0.05. T4 12.7. T3 4.8.
July 2019: TSH 0.06. T4 7.9. T3 4.6. TSH-R antibodies 33.4

**DISCUSSION:**
The association between thyrotoxicosis and peptic ulcer formation is highly debated. A link between thyroid hormone levels and stress ulcer formation is evident, yet the direction of correlation is uncertain; as shown by animal studies. Results of the few human studies conducted are less clear, yet case reports associating thyrotoxicosis and peptic ulcer formation exist. Some have highlighted that the similarity in developmental origin of the thyroid and gastric mucosa may be what drives their association in disease profiles. Potential theories underlying this connection include effect of thyroid hormones on parietal cell antibodies and parietal cell mass, and thus gastric acid secretion. If this is so, potentially further treatment options need to be investigated. Thorough treatment of thyrotoxicosis to reduce the risk of peptic ulcer formation may be relevant; Medical management with antithyroid drugs/radioactive iodine, or surgical treatment may be the key.

**KEYWORDS:** Thyrotoxicosis, thyroid hormone, graves disease, peptic ulcer, gastric ulcer

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**INTRODUCTION:** The association between thyrotoxicosis and peptic ulcer formation is unclear. Once considered extremely rare, previous reports reveal their presentation together to be more common than expected. It is uncertain how this occurs; hyperthyroidism is associated with high sympathetic drive, whilst peptic ulcer formation with high parasympathetic drive; there is thus a contradiction. We describe a patient presenting with a peptic ulcer, with a background of thyrotoxicosis, driving us to investigate the relationship and possible mechanisms underlying.

**CASE REPORT:** A 34-year-old man was referred to hospital due to coffee ground vomit. His PMHx includes thyroid over-activity, diagnosed in October 2018 by his GP, when he presented with weight loss (>2 st), shaking, sweating and palpitations. He was then started on Carbimazole 20mg OD and Propranolol. Yet his symptoms only slightly improved.

In May 2019, he presented to ED with haematemesis. He reported heat intolerance and palpitations for ~1/52.

Observations displayed high BP and tachycardia.

Examination revealed abdomen to be soft with a tender epigastrium. Blood tests displayed a stable Hb with raised urea and inflammatory markers. Gastroscopy showed a bleeding duodenal ulcer associated with gastritis. He also had elevated T3 and T4, with low TSH. Therefore, he commenced Carbimazole 40mg OD and Propranolol 40mg QDS to control his thyrotoxicosis, and Omeprazole 20mg BD for 6/52 for the gastric ulcer.

He was then reviewed in Endocrine clinic. Examination demonstrated regular pulse. There was no goitre and no signs of thyroid eye disease.

TSH receptor antibodies returned elevated, confirming his diagnosis of Graves’ disease. His Carbimazole dose was reduced to 10 mg as his thyroid function improved and his Propranolol dose was slowly decreased.
INTRODUCTION: Total thyroidectomy is the only successful option for treatment of medullary thyroid carcinoma. Elevation of calcitonin postoperatively is indicative of metastatic or residual disease. Here we present medullary thyroid carcinoma with persistent mild elevated calcitonin levels after surgery.

CLINICAL CASE: A 54-year-old woman referred to our endocrinology clinic after her sister diagnosed as having MEN2A. RET mutation was positive. Calcitonin (Ctn) and CEA levels found 222 pg/mL, 9.24 ng/mL, respectively. A 17*14 mm hypoechoic nodule in the right lobe, a 16*12 mm hypoechoic nodule and a 15*14 mm hypoechoic nodule in the left lobe of thyroid were detected. Left lobe inferior nodule biopsy was consistent with medullary thyroid carcinoma. Total thyroidectomy left and central neck dissection performed. The pathology revealed medullary carcinoma 1.6 cm on the left side and 2.1 cm on the right side, the mitotic index was 5/10. Lymphatic, tumor and thyroid capsule invasion were positive. Pathologic staging was pT2 (s), pN1a, cM0, stage III.

Calcitonin level was 50 pg/mL at the 3rd month, postoperatively. Neck MRI showed bilateral 1 cm level 1 b and millimetric lymph nodes in the cervical chain. Thorax and abdominal CT were normal. Ga-68 DOTATATE detected approximately 1 cm diameter lymphadenopathy, in the bilateral jugular chain and the posterior cervical triangle at level 2b and 5 (SUV max: 1.4). Right, and left neck dissection was performed because of elevated calcitonin level in the postoperative 11th month. 3/15 on the left side and 1/9 on the right side malignant positive lymphadenopathies were detected.

Two years after the second surgery calcitonin level was 129 pg/mL. A round-shaped 7*5 mm residue, 8.5 mm diameter lymph node at bilateral level 1B and 2, and 5*9 mm lymphadenopathy with increase in size compared to previous review (SUVmax 0.9) at left cervical level 5B were detected. And neck dissection performed again. The pathology was 3 benign lymphadenopathy and soft tissue. Three months after the third surgery, Ga-68 DOTATATE was similar to preoperative imaging (Figure 1). Fine needle aspiration biopsy of the left zone residue reported as non-diagnostic. Left level 5, 12*3 mm lymph node biopsy was benign. The last two calcitonin levels were 172 and 131 pg/mL (Figure 2). Following-up planned for the patient whom calcitonin doubling time was low [4 years] and no size increase was detected in the imaging.

CONCLUSION: The presence of somatic RET mutations correlates with lymph node metastases, persistent disease, and lower survival. The 10-year survival in the patients with postoperative high calcitonin was lower compared with patients who biochemically cured. But most asymptomatic patients with elevated serum Ctn levels and occult metastatic disease are not surgical candidates. In particular, patients with doubling time of the Ctn and CEA levels more than 2 years, have a relatively good prognosis.

KEYWORDS: Thyroid cancer, medullary carcinoma, calcitonin
Central neck lymph nodes are typically the first site of regional spread of papillary thyroid cancer (PTC). For PTC located in one lobe, lateral node metastasis firstly occurs ipsilateral to the primary lesion, although bilateral lateral node metastasis can be detected in advanced cases. However, PTC located in one lobe showing contralateral but not ipsilateral lateral node metastasis is not common. A healthy 46-year-old woman was presented with a neck mass. Her medical and family history was unremarkable. On examination, she appeared well, and her vital signs were normal. Physical examination revealed a palpable mass on the right side of the neck. An excisional biopsy was performed in the Otolaryngology department, in which pathology confirmed metastasis of papillary thyroid carcinoma. The patient was referred to the endocrinology and metabolism clinic. An ultrasound of the neck confirmed the presence of a 11x9x11-mm solid and hypoechoc nodule in the left mid thyroid with microcalcifications, irregular borders and, two solid and hypoechoc nodules with the largest diameter of 6mm in the right thyroid gland. Neck ultrasonography revealed 10x12x15 mm, 5x7x8 mm and 7x9x12 mm right cervical lymph nodes without central echogenicity and, an 8x10x12 mm right cervical lymph node with microcalcification. Fine-needle aspiration cytology (FNAC) of the right cervical node was consistent with metastasis of papillary thyroid carcinoma and thyroglobulin washout result was greater than 500 ng/mL. FNAC of the left lobe of thyroid was non-diagnostic. Neck ultrasonography also revealed a 5x9x13 mm left lymph node without central echogenicity. FNAC and thyroglobulin washout result of the left lymph node was negative for papillary thyroid carcinoma. The patient subsequently underwent a total thyroidectomy with bilateral level VI; right levels IIa, IIb, III, IV, VII lymph node dissection. Histopathology confirmed a thyroid papillary carcinoma, 5 mm, which was confined to the left thyroid gland with extrathyroidal and lenfovascular invasion. Forty-five lymph nodes were negative for malignancy while 4 right lymph nodes (2 in level II, III, IV and 2 in level VI) were positive for malignancy. 150 mCi radioactive iodine (RAI) treatment was performed after the surgery. PostRAI total body iodine screening and postoperative ultrasound of the neck was negative, and thyroglobulin was <0.2 ng/mL. Although PTC generally metastasizes to ipsilateral lymph nodes, contralateral lymph nodes should be carefully evaluated for metastases by ultrasonography preoperatively. Direct metastasis of carcinoma cells from primary lesions to the contralateral lateral nodes is possible. In these patients, total thyroidectomy with bilateral central node dissection and therapeutic modified radical neck dissection of the contralateral side is an acceptable surgical design and bilateral modified radical neck dissection may not be necessary.

**KEYWORDS:** Papillary thyroid carcinoma, metastasis, ultrasonography
It is well established that in euthyroidism TSH has a distinct circadian rhythm to maintain normal circulating levels of T3 and T4. On the other hand, it is distinctly and totally suppressed in latent and overt hyperthyroidism. Methimazole and propylthiouracil are the main antithyroid drugs (ATD) in hyperthyroidism. ATD treatment have some major side effects, including granulocytopenia or agranulocytosis. If the number of neutrophils (granulocytes) is at least 1800 neutrophils per mcl of blood, it is called normal absolute neutrophil count (ANC). If ANC is between 100-1800 per mcl of blood it is called granulocytopenia and if it is less than 100 per mcl of blood then it is called agranulocytosis. During ATD treatment, when granulocytopenia or agranulocytosis exists, after excluding the other causes, the ATD should be stopped. But it should be remembered that circadian rhythm also effects the neutrophil count as most of the biological systems. Circadian variations of neutrophil levels in healthy people exhibit a trough at 8:00 am, and a progressive increase in the afternoon with peak at 8:00 pm. The possible explanation for this increment is based on the the diurnal variations of cortisol levels, considering exogenous glucocorticoids administration increases ANC. In addition, physiological increases in epinephrine levels due to daily activities increases ANC in the afternoon.

**CASE:** A 63 years old women was admitted to our clinic because of thyrotoxicosis. She lost 10 kilograms during the last 3 months with palpitations. Thyroid hormones were consistent with thyrotoxicosis. TSH receptor antibody and anti-TPO were positive. Thyroid scintigraphy showed enlarged thyroid gland and homogenously increased tracer uptake (Tc-99m pertechnetate) in both of the lobes with faint background activity. She was diagnosed as autoimmune hyperthyroidism. She was given methimazole and propranolol. At the beginning of the therapy white blood cell count and ANC were normal but after 3 weeks of ATD, ANC was 1500 per mcl of blood. She did not have any signs of infection and any other causes of granulocytopenia other than ATD. After consultation with Haematology department, ANC was done in the afternoon. We observed a significant difference between morning and afternoon ANC in our patient. Our case underlines the importance of the neutrophil count performed in the afternoon which allows many hyperthyroid patients taking ATD to be excluded from the neutropenia threshold and unnecessary managements.

**KEYWORDS:** hyperthyroidism, methimazole, circadian rythm, absolute granulocyte count
Two years later, the patient represented to the Emergency Department with flushing and abdominal pain, her triglycerides were elevated at 29mmol/L. She had ceased her fenofibrate and fish oil due to gastrointestinal intolerance and changed to a statin. The patient self-ceased the statin several months prior due to gastrointestinal intolerance. During this admission to hospital, assessment for an underlying genetic diagnosis was sought. A metabolic gene panel identified a likely pathogenic PPARG gene missense mutation (c.551G>A) and a common APOA5 gene missense polymorphism (c.56C>G). Pathogenic PPARG mutations are implicated in familial partial lipodystrophy (FPL) type 3, and described as a monogenic cause of metabolic syndrome, with clinical features including hypertriglyceridaemia, insulin resistance, diabetes, hypertension, central adiposity and varying degrees of lipoatrophy of the buttocks and limbs.

CONCLUSION: We have identified a rare case of severe hypertriglyceridaemia, hepatic steatosis, insulin resistance and central adiposity related to a mutation in the PPARG gene. To our knowledge, the variant identified in our case has only been identified in two other patients, one of which is described to have FPL type 3 and the other to have severe hypertriglyceridaemia. The underlying genetic diagnosis in our patient will have implications to her ongoing therapy, including consideration for use of pioglitazone, comprehensive complications screening, management in future pregnancies and family screening.

KEYWORDS: hypertriglyceridaemia, PPARG, mutation

INTRODUCTION: Prevalence of severe hypertriglyceridaemia in adolescents and young adults is rare. When encountered in clinical practice, assessment for underlying genetic aetiology is beneficial to guide management, complications screening and predict potential disease course.

CASE: A 19-year-old female presented to the Emergency Department with an eruptive rash and severe dyslipidaemia, with triglyceride level of 110mmol/L [ref <1.7mmol/L] and total cholesterol level of 30mmol/L (<4mmol/L). Examination confirmed the presence of tuberous and eruptive xanthomata in addition to hepatomegaly. She had centrally distributed adiposity and her BMI was 31kg/m2. There was no obvious lipodystrophy. The patient was normoglycaemic and there was no complicating pancreatitis. The patient’s past medical history included hepatic steatosis identified two years prior, but was otherwise unremarkable. Her medications included the combined oral contraceptive pill and recent completion of a short course of prednisone. The patient was fasted and placed on an insulin/dextrose infusion. On discharge from hospital eight days later, her triglyceride level reduced to 25mmol/L; she was placed on fenofibrate and fish oil with good response. The patient’s lipoprotein electrophoresis demonstrated presence of chylomicrons and a significantly elevated VLDL level of 22.9 mmol/L [ref: <0.9 mmol/L]. She did not have a family history of dyslipidaemia, premature coronary artery disease or pancreatitis. Her oral glucose tolerance test did not demonstrate impaired glucose tolerance, but there was hyperinsulinaemia.

PPARG MUTATIONS: A RARE MONOGENIC AETIOLOGY FOR SEVERE HYPERTRIGLYCERIDAEMIA

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EXCELLENT RESPONSE TO PASIREOTIDE THERAPY IN AN AGGRESSIVE AND DOPAMINE-RESISTANT PROLACTINOMA

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Prolactinomas are the most commonly encountered pituitary adenomas in the clinical setting. While most can be controlled by dopamine agonists, a subset of prolactinomas are dopamine-resistant and very aggressive. In such tumors, the treatment of choice is neurosurgery and radiotherapy, with or without temozolomide. Here, we report a patient with an highly aggressive, dopamine-resistant prolactinoma, who only achieved biochemical and tumor control during pasireotide long-acting release (PAS-LAR) therapy, a second-generation somatostatin receptor ligand (SRL). Interestingly, cystic degeneration, tumor cell necrosis or both was observed after PAS-LAR administration suggesting an antitumor effect. This case shows that PAS-LAR therapy holds clinical potential in selective aggressive, dopamine resistant prolactinomas that express somatostatin (SST) receptor subtype 5 and appears to be a potential new treatment option before starting temozolomide. In addition, PAS-LAR therapy may induce cystic degeneration, tumor cell necrosis or both in prolactinomas.

KEYWORDS: prolactinomas, pituitary, adenoma
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