ACTH causes elevated levels of steroid hormone precursors & chronic stimulation of the adrenal glands resulting in hyperplasia. The most common form of CAH is due to 21OH deficiency (21OHD) with the classic, salt-wasting form causing glucocorticoid & mineralocorticoid deficiency & androgen excess.
Poorly controlled CAH causes increased production of androgens & progesterone & decreased fertility. Fertility in woman with 21OHD can be challenging due to decreased sexual interest & anatomical abnormalities. Despite these challenges, the pregnancy rate is not significantly lower in women with well controlled 21OHD. However, as these patients are uncommon recommendations for pregnancy can be challenging for endocrinologists.
Clinical Case:
A 27-year old G0P0 female with classic, salt losing CAH presented to discuss pregnancy. Her medications were hydrocortisone 10mg qAM & 5mg qHS & fludrocortisone 0.1mg daily. She denied symptoms of dehydration, nausea, vomiting, dizziness, or fatigue.
She was diagnosed with CAH while in-utero & started on steroid therapy after birth. She did not require any surgical genital reconstruction. Menarche occurred at age 11 and she had regular menses every 35-40 days, with no evidence of excessive androgen exposure including excess body hair, deepening of her voice, or cliteromegaly.
On physical exam she was normotensive & had no evidence of virilization or cushingoid features. She exhibited minor darkening of the palmar creases. Her labs were significant for free testosterone of 9.1 pg/ml (0.2-5.0 pg/ml), total testosterone of 115 ng/dl (2-45 ng/dl), ACTH of 780 pg/ml (6-50 pg/ml), androstenedione of 636 ng/dl (41-262 ng/dl), & 17 OHP of 1560 ng/dl (15-290 ng/dl).
Her hydrocortisone dose was increased to 20 mg qAM & 10 mg qHS & fludrocortisone 0.1mg daily was continued. Our objectives were to normalize the androgen level & suppress serum progesterone to less than 2 nmol/L. If the objectives were not reached she would be converted to prednisone BID.
Conclusion:
Endocrine providers are the primary resource for fertility recommendations for 21OHD patients & must understand the challenges in this very rare group of patients. Collaboration with the perinatologist is crucial for success. The goals of preconception endocrine assessment in a patient with classic CAH are to adjust hormone therapy to ensure optimal endocrine milieu for conception & risk assessment of having a child affected with 21OHD. The patient will need a higher dose of fludrocortisone during the later part of pregnancy. Counseling that stress doses of glucocorticoids for intercurrent illness and during labor and delivery are required for both the patient and the obstetrician.

Thyroid

THYROID CANCER CASE REPORTS II

Unusual Case of Metastatic Struma Ovarii Diagnosed at the Time of Hysterectomy

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MON-440
Introduction: Struma ovarii is rare ovarian teratoma composed of more than 50% mature thyroid tissue, which can rarely transform to malignancy. There are fewer than 200 cases reported and no established treatment approach. We present a case of metastatic malignant struma ovarii. Case Presentation: A 41 year old female was diagnosed with metastatic papillary thyroid carcinoma (PTC) after it was found on uterine histopathology. History was notable for remote left ovarian cystectomy of a mature teratoma with prominent thyroid component. She had no personal or family history of craniocervical radiation or thyroid cancer. Eight years later, she had a total hysterectomy for menorrhagia. Pathology showed subcentimeter serosal deposits of follicular variant PTC, staining positive for thyroglobulin, CK19, and HBME1. Endometrial and cervical pathology were normal; the myometrium had many leiomyomata. Post-hysterectomy TSH was 2.3 (0.34 - 5.66 μIU/mL), and thyroglobulin 44.3 (<=33.0 ng/mL). Thyroid ultrasound showed a 7 mm isoechoic nodule without lymphadenopathy. Whole body PET/CT showed multiple hypermetabolic masses in the pelvic peritoneum and liver. The right ovary had many cystic lesions and was enlarged to 5.3 x 4.5 cm. She underwent partial hepatectomy, oophorectomy, salpingectomy, and omental resection with no residual disease. Pathology showed follicular variant PTC in both ovaries, peritoneum, colonic mesentery, and omentum. Thyroglobulin fell to 6.9 ng/mL 3 weeks later. A 0.2 cm focus of follicular variant PTC with capsular invasion was found on pathology after total thyroidectomy. She underwent radioiodine ablation with 150 mCi. Postablative scan showed residual activity in the thyroid bed and right hemipelvis, but no new foci of activity. CT abdomen showed resolution of perihepatic lesions and thyroglobulin declined further to 0.5 ng/mL. Discussion: A low risk of recurrence (7.5%) has been reported in patients with malignant struma ovarii, with survival rates of 96.7% at 5 years and 84.9% at 20 years, despite a variety of surgical and adjuvant management strategies. Unilateral cystectomy, unilateral salpingo-oophorectomy, or total abdominal hysterectomy and bilateral salpingo-oophorectomy may be sufficient for patients with well differentiated thyroid cancer arising in struma ovarii without metastases. Thyroid ultrasound should be performed to exclude primary thyroid malignancy. Patients with distant metastases may benefit from aggressive treatment including resection of gross abdominal and pelvic disease and total thyroidectomy to facilitate radioactive iodine ablation and surveillance for recurrence. Conclusion: Due to its rarity, there is no consensus on optimal treatment of malignant struma ovarii. More research in this field is warranted.

Adipose Tissue, Appetite, and Obesity

RARE CAUSES AND CONDITIONS OF OBESITY: PRADER WILLI SYNDROME, LIPODYSTROPHY

Presence of LMNA p.R582H Pathogenic Variant in Homozygous State Demonstrates Gene Dosage Effect on the Severity of Fat Loss in Lipodystrophy

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SUN-600

Background Classical heterozygous pathogenic variants of the lamin A/C (*LMNA*) gene cause familial partial lipodystrophy type 2 (FPLD2). However, recent reports indicate phenotypic heterogeneity among carriers of *LMNA* pathogenic variants, and a few patients have been associated with generalized fat loss. **Clinical Case** Here, we report a patient with lamin A specific pathogenic variant at exon 11 *LMNA* p.R582H present in homozygous state. Fat distribution was compared radiographically to a heterozygote *LMNA* p.R582H patient from another pedigree, female healthy control, a series of adult female subjects with congenital generalized lipodystrophy type 1 (CGL1, n = 9) and typical FPLD2 (n = 8). The whole body MRI of the index case confirmed near-total loss of subcutaneous adipose tissue with well-preserved fat in the retroorbital area, palms and soles, mons pubis, and external genital region. This pattern resembled the fat loss pattern observed in CGL1 with only one difference: strikingly more fat was observed around mons pubis and the genital region. Also, homozygous p.R582H *LMNA* variant was associated with lower leptin level and earlier onset of metabolic abnormalities compared to heterozygous p.R582H variant and typical FPLD2 cases. On the other hand, heterozygous *LMNA* p.R582H variant was associated with partial fat loss which was similar to typical FPLD2 but less severe than the patients with the hot-spot variants at position 482. **Conclusions** Our observations and radiological comparisons demonstrate a gene dosage effect of *LMNA* variants on the severity of fat loss and add to the body of evidence that there may be complex genotype-phenotype relationships in this interesting disease known as FPLD2. Although the pathological basis for fat loss is not well understood in patients harboring pathogenic variants in the *LMNA* gene, our observation suggests that genetic factors modulate the extent of fat loss in *LMNA* associated lipodystrophy.

Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS II

Multiple Endocrine Neoplasia Type 1- A Clarion Call for Clarity

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MON-922

A 35-year-old gentleman presented with epigastric pain and bilious emesis. He also endorsed urinary frequency, non-bloody diarrhea and diffuse bone pain. On physical examination he had epigastric tenderness and multiple hyperpigmented skin lesions.

An abdominal computed tomography (CT) scan revealed multiple diverticula with peri-colonic fat stranding in the descending and sigmoid colon, concerning for diverticulitis. He was started on a course of metronidazole and ciprofloxacin. A 3.1 cm mass was incidentally noted in the uncinate process of the pancreas. Bilateral adrenal nodules were also appreciated.

An endoscopic ultrasound (EUS) guided trans-gastric fine needle aspiration biopsy was performed, revealing a well differentiated pancreatic neuroendocrine tumor (pNET - pT3N1Mx, intermediate risk). Chromogranin A was elevated to 108 ng/ml (reference range <93 ng/ml). Serum and urine metanephrine, V-peptide, gastrin, glucagon and parathyroid hormone related peptide were all normal; indicating a nonfunctioning neuroendocrine tumor. He underwent a pancreaticoduodenectomy. Octreotide scan was unrevealing for residual uptake. Adrenal biopsy revealed adrenal adenomas.

Three years later, he presented with severe abdominal pain and a new pancreatic mass was noted on CT. Chromogranin A was elevated to 227 ng/mL. EUS revealed a 0.35 cm mass in the bed of the pancreatic head, encasing the superior mesenteric artery. Pathology was positive for recurrence of the neuroendocrine tumor.

He was hypercalcemic to 11.4 mg/dL and parathyroid hormone was elevated to 319 pg/mL. CT neck revealed a 0.1 cm nodule concerning for parathyroid adenoma. He underwent a subtotal parathyroidectomy.

Genetic testing confirmed Multiple Endocrine Neoplasia Type 1 (MEN1) with a heterozygous mutation of the menin1 gene.

MEN1 is a rare genetic syndrome with affected individuals at increased risk of developing pancreatic, pituitary, parathyroid gland and cutaneous tumors. With a kaleidoscope of presentations, clinicians must maintain a high index of suspicion for MEN1, particularly for cases with nonfunctioning pNETs which present insidiously and are the foremost cause of mortality in MEN1 patients.[1]

Further clarity is needed on MEN1 associated pNET prognostic risk stratification, surveillance and targeted immunochemotherapy.[2] Timely and algorithmic screening for MEN 1 syndrome in patients with pancreatic incidentalomas is essential to improving patient outcomes.

1.
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Thyroid

THYROID DISORDERS CASE REPORTS II

Transient Thyrotoxicosis with Immune Checkpoint Inhibitors Therapy: The Importance of Endocrine Evaluation

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