

was followed very closely as an outpatient. Although the omega-3 fatty acids were titrated to 8g per day, the triglyceride level remained ~2000mg/dL. She remained asymptomatic and delivered a healthy baby boy weighing 3446 grams at 36 weeks 4 days, with no complications. She continues follow up with endocrinology with triglycerides 6 months later being 1618 mg/dL.

Conclusion: We present a patient with severe gestational hypertriglyceridemia with a known history of pancreatitis. Due to the rarity of this condition, there is limited data on the safety of treatments for hypertriglyceridemia in pregnant women. This case demonstrates the use of gemfibrozil is appropriate when the hypertriglyceridemia threatens the health of the mother and baby. Further studies are needed to establish efficacy and safety of the use of these treatments in pregnant patients.

Adrenal

ADRENAL CASE REPORTS I

A Sweet and Salty Milieu: The Utility of CT in Bilateral Adrenal Hemorrhage

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Introduction: Bilateral adrenal hemorrhage (BAH) is seldomly recognized as a cause of adrenal insufficiency due to nonspecific clinical manifestations within the milieu of major concurrent illnesses. CT abdomen is the investigation of choice to evaluate acute adrenal crisis.

Clinical Case: A 68 year old female with systemic lupus erythematosus, anti-phospholipid antibody syndrome (APS) complicated by multiple strokes, on warfarin, and recent hip fracture presented with confusion, lethargy, fever, and cough. On exam she was febrile, tachycardic, tachypneic, disoriented with right sided hemiparesis, and crepitations on lung auscultation. Lab results were significant for leukocytosis of 14K/uL, hemoglobin (Hb) 9.9g/dL, INR 3.8, azotemia, normal electrolytes, and glucose 67mg/dL. Blood and urine cultures were negative. Anti-dsDNA, C3, and C4 were normal. CT chest showed right lower lobe infiltrates and bronchial debris. She was treated with antibiotics and bronchoscopy with mucus plug removal. Her lethargy and confusion persisted. MRI brain was negative for acute event. Hb fell to 7g/dL; managed conservatively with i.v. iron. CT abdomen showed BAH both measuring 3.5x3.5cm; AM cortisol was 5.5 mcg/dL. Warfarin was reversed with vitamin K; hydrocortisone 50mg q8h was started with improvement in her mental status. ACTH levels were <5pg/ml; ACTH stimulation testing was deferred as steroids were started emergently. Repeat CT showed stable BAH, AM cortisol increased to 19.4mcg/dL, and Hb stable at 8g/dL. She was discharged on hydrocortisone 10mg twice daily.

Discussion: Trauma, corticotropin stimulation during stress, anticoagulation therapy, and APS inducing adrenal venous thrombosis have been identified as risk factors that predispose to BAH. There is a lack of consensus regarding normal cortisol levels in critical illness. Fluctuations in serum cortisol levels are frequent and not necessarily indicative of definite injury to the adrenal gland. CT abdomen,

the investigation of choice in the acute setting, has a heterogeneous, high density appearance; the presence of an underlying adrenal mass cannot be excluded. BAH appears as diminished attenuation of the adrenal gland with respect to the adjacent tissues, along with thickening of the ipsilateral crura due to retroperitoneal extension of blood (1). MRI has a greater accuracy for identifying BAH in comparison to CT as it can discern adrenal hematoma from adjacent necrotic tissue and determine the acuity of the hematoma.

Conclusion: The nonspecific clinical manifestations of BAH are frequently inseparable from those of the concurrent major illness. The diagnosis requires a high index of suspicion, initiation of prompt steroid replacement, and confirmation by CT abdomen.

References: (1) Fatima, Z., Tariq, U., Khan, A., et. Al. A Rare Case of Bilateral Adrenal Hemorrhage. *Cureus*. 2018 Jun; 10(6): e2830. doi: 10.7759/cureus.2830

Thyroid

THYROID DISORDERS CASE REPORTS I

A Case of Hyperthyroidism with Multiple Recurrences of Neutropenia After Stopping Methimazole

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Background: The adverse effects of methimazole usually occur in the first 6 months of treatment and they usually are dose dependent. The most severe ones are hepatotoxicity and agranulocytosis, the frequency of the latter is 0.1-0.5% and with a high mortality rate.

Clinical case: A 15-year-old female patient was sent to Endocrinology in May 2017 because of a 4-month history of tremor, palpitations and heat intolerance. Lab tests: WBC: 6,800, neutrophils: 36% (2,448/l), TSH: < 0.06 uU/ml (0.27- 4.7), T4: > 25 ug/dl (4.5 -12), FT4: >7.7 ng/dl (0.93 -1.7), TPO >1,000 UI/ml (<10), TRAb > 40 UI/L (<1.75) which confirmed Graves' disease. Propranolol 80 mg/day and methimazole 30 mg/day were prescribed. Two months later methimazole dose was increased to 40 mg/d, hematologic lab test was normal. Seven months after starting methimazole the patient presented with febrile neutropenia, methimazole was stopped, methylprednisolone 20 mg/d was prescribed and we increased propranolol to 120 mg/d, neutropenia improved. A month after the first episode of neutropenia, she presented a second episode with a pharyngeal infection, WBC: 6,300, neutrophils: 1%. In December 2017 radioiodine therapy was performed: 15 mCi. Hyperthyroidism was not resolved, she continued with methylprednisolone 20 mg/d and propranolol 120 mg/d, and 6 drops/d of Lugol solution was prescribed. From December 2017 to July 2018, the patient presented 9 episodes of febrile neutropenia, she had a good response to Granulocyte-colony stimulating factor. Serology tests for CMV, VDRL, HIV, Epstein Barr, Toxoplasmosis, hepatitis B and C were all negative. Lab tests for rheumatologic diseases: rheumatoid factor, C3 and C4, electrophoretic proteinogram, antiestriptyolysin O, anti-DNA, ANA, anti-Ro/SSA, anti-La/SSB were all negative, and immunoglobulins were normal.

Bone marrow aspiration was normal. We could not perform flow cytometry of anti-neutrophil cytoplasmic antibodies (C-ANCA). Hyperthyroidism persisted and a second I-131 treatment was performed (20 mCi) in June 2018. A month later she presented hypothyroidism, levothyroxine was indicated. She continued with episodes of febrile neutropenia until March 2019, 23 months after the diagnosis of hyperthyroidism, 16 months after stopping methimazole and 8 months after having initiated levothyroxine treatment and having normal thyroid levels.

Conclusion: We presented a young female patient with persistent and recurrent neutropenia despite having stopped methimazole, and regardless of her thyroid hormone levels. Although neutropenia usually appears in the first months of treatment, it seldom occurs much later and almost never after stopping the drug. We could not reach an etiological diagnosis of neutropenia, but it is probable that methimazole had triggered an immune-hematological illness associated to Graves' disease.

Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS II

Susceptibility Genetic Testing and Functional Imaging Modalities in the Management of Bladder Paragangliomas

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Introduction: Bladder Paragangliomas (PGLs) are rare neuroendocrine tumors derived from sympathetic paraganglionic tissue within the bladder wall, accounting for <1% of all Pheochromocytomas and Paragangliomas (PPGLs). >40% of PPGLs are associated with inherited syndromes through mutations affecting citric acid cycle enzymes (commonly SDH). Susceptibility gene identification has important implications for long-term care and facilitates targeted cascade genetic screening. Functional imaging using MIBG, Gallium DOTATATE and FDG-PET have become important tools in both diagnosis and treatment (Peptide Receptor Radionuclide Therapy).

Clinical Cases: We report the demographics, clinical characteristics and novel features of 7 patients with bladder PGLs. The series includes 2 females and 5 males, median age 38 years (range 14-68). 5 presented with hematuria and 2 were detected incidentally (1 found on radiological imaging and the other during cystoscopy surveillance). Other symptoms reported were headaches, sweating and palpitations which were relieved by urination. Only 1/7 had a known family history of PGLs. 5/7 patients had elevated plasma normetadrenaline levels and 2 had non-elevated catecholamine metabolites (these 2 patients were asymptomatic).

6/7 patients had genetic testing performed and pathogenic variants were identified in 4 (Fumarate hydratase (FH),

SDHA, SDHB*2 genes) and no pathogenic variant identified in 2 patients in our genetic panel of 10 PPGL genes. All primary tumors demonstrated MIBG avidity and in 2 patients assessed there was PGL FDG-PET avidity. Metastatic disease was present in 2 patients (2 SDHB mutations; with 1 MIBG avid bone and 1 FDG-PET avid nodal metastasis). SDHB immunostaining on resected histology was available for 3 cases - absent SDHB immunostaining in the patient with SDHA mutation and strongly positivity in 2 patients (1 with no genetic mutation and in 1 with FH mutation).

Conclusions: The majority (>65%) of patients with bladder PGL have a germ line mutation in a susceptibility gene involving the citric acid cycle. An extended gene panel should be performed in all patients diagnosed with bladder PGLs including SDHA and FH gene mutations. SDH immunostaining of tumour can indicate SDHx gene defects but can be normal in FH mutations. SDHB is associated with increased risk of malignant/metastatic behavior. All 3 modalities of functional imaging (Ga DOTATATE, FDG PET, & MIBG) have a role in the assessment and treatment decision making in the management of bladder PGLs.

Bone and Mineral Metabolism

BONE DISEASE FROM BENCH TO BEDSIDE

Low Dose Ethinyl Estradiol in Women with Cystic Fibrosis Does Not Preserve Bone Mass

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BACKGROUND: Cystic fibrosis-related bone disease (CFBD) affects 26% of adults with cystic fibrosis (CF). CFBD increases the risk for fractures, which in turn limits patients' ability to effectively perform daily therapies necessary to maintain health. Factors contributing to CFBD include nutritional deficiencies, inflammation, glucocorticoid use, CF-related diabetes and untreated hypogonadism. Hypogonadism in CF is thought to be functional, although the distribution of etiologies of female hypogonadism in the modern era of CF therapies is unknown. Estrogen supplementation is commonly prescribed in the form of oral contraceptives to women with low bone mineral density (BMD). At our CF center, the average dose of ethinyl estradiol prescribed to women is 20 mcg. Recent evidence suggests that oral estrogen is ineffective for restoring bone health in women with functional hypogonadism and specifically that doses < 30 mcg oral ethinyl estradiol are inadequate. It is unknown if estradiol supplementation will restore and/or maintain BMD in women with CFBD.

METHODS: The purpose of this study was to examine the skeletal health of a cross-section of premenopausal women seen at a single CF center taking 20 mcg or less of ethinyl estradiol daily (low-dose estrogen) compared to women not taking estrogen supplement. As screening for an IRB-approved intervention study, we collected health information by chart review.