mice as compared to control mice (P < 0.05, n=6-12). As expected, E_2 levels in the brain and testis are significantly lower in tArKO mice compared with their WT littermates (n=6-9). Furthermore, we demonstrate that local aromatase expression and estrogen production in the brain is required for male sexual behavior and sex hormone homeostasis. Male bArKO mice exhibited significantly decreased sexual activity in the presence of strikingly elevated circulating T (n=5). In castrated adult bArKO mice, administration of E_2 together with T restored maximum sexual behavior (n=5). Thus, aromatase in the brain is necessary for T-dependent male sexual activity. We also found that brain aromatase is required for negative feedback regulation of circulating T of testicular origin. *Conclusion:* Our findings suggest T activates male sexual behavior in part via conversion to E_2 in the brain and provide the foundation for inhibition or enhancement of brain aromatase enzyme activity and/or utilization of selective estrogen receptor modulators in modifying sexual behavior.

DCB and HZ contributed equally to this work.

Adrenal

ADRENAL CASE REPORTS I

Silent Pheochromocytoma Complicated by Adrenal Insufficiency After Unilateral Adrenalectomy

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SAT-184

Background: Adrenal insufficiency (AI) following unilateral adrenalectomy for pheochromocytoma (PCC) is an exceedingly rare occurrence described previously in 1 study in only 4 out of 13 patients with unilateral PCC. We discuss an unusual case of a patient with incidentally discovered PCC who underwent unilateral adrenalectomy and subsequently developed AI.

Clinical Case: 61-year-old male in overall good health taking no medications presented with left flank and groin pain after a handlebar injury in a bicycle crash. CT angiogram Abdomen & Pelvis revealed a complex enhancing left adrenal mass with internal necrosis measuring 13 x 12 cm. He denied history of headaches, diaphoresis, chest pain or hypertensive crisis. He did endorse palpitations which had resolved with reduced caffeine intake. Labs showed plasma free metanephrine 3,295 pg/mL (ref range <57) and normetanephrine 68,472 pg/mL (<148), 24hr urine metanephrine 192,677 ug (52-341), 24hr urine normetanephrine 171,880 ug (88-444), 24hr urine vanillylmandelic acid (VMA) 182 mg (1.8-6.7), serum aldosterone 8.1 ng/dL (<39.2), serum free cortisol 0.47 ug/dL (0.07-0.93), 24hr urine cortisol 41.6 ug (<60), DHEA sulfate 37 ug/dL (42-290). He was started on phenoxybenzamine and underwent left adrenalectomy. Of note patient remained only minimally hypertensive with tumor manipulation intraoperatively. Pathology was consistent with PCC with no evidence of regional or distant metastases. Postop-labs showed plasma free metanephrine <25 pg/mL and normetanephrine 122 pg/mL. Calcitonin and parathyroid hormone levels were normal. Patient was evaluated in endocrinology clinic 4 weeks after surgery for complaint of severe fatigue, weight loss, anorexia and myalgias. Adrenocorticotropic hormone (ACTH) level was 31 pg/mL (7.2-63) with AM cortisol of 2.1 ug/dL (5-23) which increased to 7.4 ug/dL 1 hour after Cosyntoprin 250 mcg stimulation. He was started on prednisone 10 mg once daily with significant improvement in his symptoms.

Conclusion: PCCs typically manifest as sustained or paroxysmal hypertension, episodic headaches, palpitations or diaphoresis. Our patient was found to have a PCC with strikingly elevated levels of catecholamines without typical signs and symptoms of PCC. To the best of our knowledge this is the 5th reported case where a patient developed AI after unilateral adrenalectomy for PCC. There are case reports describing PCCs which secrete both catecholamines and ACTH. However, our patient lacked clinical or biochemical evidence of hypercortisolism preoperatively and his tumor cells in path sample stained negative for ACTH. Other possible pathophysiologic mechanisms include ectopic corticotropin releasing factor production leading to subclinical Cushing syndrome (SCS). Clinicians should have a high suspicion for SCS in the setting of PCC to promptly diagnose and treat AI after unilateral adrenalectomy.

Thyroid

THYROID AUTOIMMUNITY AND BENIGN THYROID DISEASE

Effect of Teprotumumab on Proptosis Reduction Across Various Demographic Sub-Groups

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OR18-01

Introduction: Teprotumumab, an insulin-like growth factor 1 receptor inhibitory monoclonal antibody, was recently shown to significantly reduce proptosis in patients with active, moderate-to-severe thyroid eye disease (TED) in phase 2 and phase 3 clinical trials.[1,2] Prior analyses have demonstrated a combined trial proptosis response (≥2 mm reduction) rate of 77.4% in the teprotumumab group and 14.9% in the placebo group after 24 weeks of therapy (p < 0.001).[3] The current analysis was performed to investigate whether or not patient demographic characteristics influence the teprotumumab proptosis response.

Methods: Data from two 24-week randomized, double-masked, placebo-controlled, parallel-group, multicenter studies (Phase 2 [NCT01868997], Phase 3 [NCT03298867[) were combined. All patients had active TED associated with Graves' disease. The study eye designated at baseline manifested more severe TED and a clinical activity score of > 4. Subjects were divided into subgroups based on gender, smoking status, and age at baseline (younger: <65, older: ≥65). The percentage of proptosis (≥2 mm) responders and proptosis change from baseline were examined in each of these subgroups. Because most of both teprotumumab (85%) and placebo (87%) subjects were white, there were

insufficient numbers of subjects to examine the effect of race on the teprotumumab proptosis response. All analyses were performed on the intent-to-treat (ITT) population using data from the study eye.

Results: A total of 171 patients comprised the population from the two studies. Eighty-four and 87 patients were randomized to the teprotumumab and placebo groups, respectively, and the treatment groups had balanced baseline characteristics. At week 24, significantly more teprotumumab than placebo patients were proptosis responders in all examined subgroups (male: 73.1% vs. 5.0%, female: 79.3% vs. 17.9%, smokers: 70.0% vs. 23.1%, non-smokers 79.7% vs. 11.5%, younger: 76.1% vs. 16.2%, older: 84.6% vs. 7.7%; all $p < 0.001$). In continuous variable analyses, the mean proptosis reduction from baseline was also significantly greater at week 24 in teprotumumab-treated patients than placebo patients (male: -3.34 vs. -0.07 mm, female: -3.10 vs. -0.42 mm, smokers: -2.99 vs. -0.72 mm, non-smokers: -3.20 vs. -0.31 mm, younger: -3.10 vs. -0.39 mm, older: -3.55 vs. -0.22 mm; all $p < 0.001$).

Conclusion: Teprotumumab was effective across subgroups of age, gender, and smoking status in the pooled 24-week clinical trials.

Reference: (1) Smith TJ, et al. *N Engl J Med* 2017;376:1748-1761. (2) Douglas RS, et al. AACE 2019 late-breaking abstract. (3) Kahaly GJ, et al. *Thyroid* 2019;29(Suppl1):A-1 [abstract].

Cardiovascular Endocrinology

FROM BEDSIDE TO BENCH AND BACK AGAIN: LIPID METABOLISM & VASCULAR DISEASE

Changes in Hepatokines and Apolipoproteins Are Associated with Metabolic Response to Metreleptin in Partial Lipodystrophy

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OR17-02

Introduction Metreleptin treatment may improve the metabolic aspects of partial lipodystrophy; however, the treatment response is heterogeneous. This study aimed to explore changes in circulating apolipoprotein concentrations, as well as ANGPLT3, ANGPLT4, and IGF-1 levels in patients treated with Metreleptin as part of a clinical study investigating the efficacy of Metreleptin in non-alcoholic steatohepatitis (NASH) associated with partial lipodystrophy (ClinicalTrials.gov identifier: NCT01679197).

Methods Serum samples of 18 patients with partial lipodystrophy who underwent a full metabolic evaluation and paired liver biopsies before and after Metreleptin were studied. Patients were tested at baseline, month (M) 3, M6, and M12. Glycemic response was defined as "more than 1% HbA1c reduction from baseline". Lipid response was defined as "more than 30% decrease in triglycerides from baseline". The hepatic response was defined as "a decrease of 2 points or more from baseline in NASH score, without an increase in fibrosis". Patients with "any 2 of 3 above" at M12 were defined as metabolic responders. **Results** Metreleptin treatment resulted in significant reductions in triglycerides (346 mg/dL vs. 253 mg/dL; F: 8.474; $p < 0.001$), apo B (145.24 mg/dL vs. 111.09 mg/dL; F: 9.266: $p < 0.001$), apo CII (18.65 mg/dL vs. 15.95 mg/dL; F: 6.663: $p = 0.001$), apo CIII (62.95 mg/dL vs. 49.33 mg/dL; F: 5.640, $p = 0.002$), apo E (8.16 mg/dL vs. 6.52 mg/dL; F: 11.056, $p < 0.001$), and ANGPLT3 (14.36 ng/mL vs. 12.00 mg/dL; F: 4.348; $p = 0.008$) over time. IGF-1 levels significantly increased at M3 (134 ng/mL vs. 139 ng/mL; $p = 0.001$), however the difference was not significant over time. Metabolic responders had lower baseline leptin (12.4 ng/mL vs. 27.8 ng/mL; $p = 0.024$) and IGF-1 (95 ng/ml vs. 151 ng/mL; $p = 0.008$), and higher apo CII (39.06 mg/dL vs. 17.90 mg/dL; $p = 0.011$), apo CIII (173.57 mg/dL vs. 51.51 mg/dL; $p = 0.015$), apo E (18.41 mg/dL vs. 5.89 mg/dL; $p = 0.002$), and ANGPLT3 (17.33 ng/mL vs. 10.06 ng/mL; $p = 0.04$). Metabolic responders had a significant increase in IGF-1 (95 ng/mL vs. 134 ng/mL; $p = 0.019$), which was statistically distinguished from non-responders ($p = 0.004$). Responders also had a greater reduction in apo CII (20.51 mg/dL vs. -1.84 mg/dL; $p = 0.001$), apo CIII (32.59 mg/dL vs. -7.83 mg/dL; $p = 0.007$), apo E (8.17 mg/dL vs. 0.22 mg/dL; $p = 0.001$), and ANGPLT3 (6.08 ng/mL vs. -0.16 ng/mL; $p = 0.005$) early after treatment at M3. **Conclusions** Metreleptin treatment lowers levels of apolipoproteins associated with triglyceride metabolism as well as ANGPLT3 in patients with partial lipodystrophy. Metabolic response to Metreleptin appears to be correlated with early changes in these factors and an increase in IGF-1 levels.

Adrenal

ADRENAL CASE REPORTS II

Intra-Articular Triamcinolone Injections - a "Slipped" Cause of Cushing's Syndrome

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SUN-188

Background:
Triamcinolone injections are used to treat various orthopedic and rheumatologic conditions; their effects on the hypothalamic pituitary adrenal axis have not been well characterized.
Clinical Case:
A 14 yo female was referred to our clinic for evaluation of low TSH (0.16 μIU/mL) and possible hyperthyroidism. There was no goiter and she appeared euthyroid and had normal free T4 (1.01 ng/dl) but she had typical features of Cushing syndrome (CS), including round facies, thinning of hair, fatigue, truncal adiposity, violaceous striae, facial hirsutism and oligomenorrhea. She was previously healthy and participated in many sports. She did not report any history of exogenous glucocorticoid use but the fasting ACTH (4 pg/ml) and cortisol (0.1 μg/dl) levels were suppressed. Subsequent chart review revealed that she received intra-articular Triamcinolone (TA) to treat "slipping rib" syndrome. This included 3 injections of Kenalog 40 mg/mL, the last in July 2019. Her cumulative TA dose was 440 mg, the equivalent of prednisone 550 mg. Triamcinolone acetonide 1.4 mcg/dL (normal 0-0.1, analyzed by LC-MS/MS) was detected in the urine over 3 months after her last injection.