

MON-277

Background There is augmented concern for dopamine agonists (DA) related risk to mood and impulse control disorders (ICD) in patients (pts) with pituitary adenomas (PA). In this study, we analyzed prevalence using two validated self-assessment screening surveys; PHQ-9 and BIS-11. **Methods** A retrospective review of pts from an IRB approved PA registry. Patients; DA treated group (DA-T) and DA nontreated controls (DA-C). Patients with previous psychiatric diagnoses, and taking anti-depressive or anti-psychotics, were excluded. BIS-11 score \geq 75thile (>61 points) was considered an increased ICD risk. DAs maximum standard dose low (MSDL) and high (MSDH), were calculated (2.0 and 3.5 mg/week for cabergoline (Cab) and 7.5 and 15 mg/day for bromocriptine; Bromo). Stats SPSS v.25. **Results** 103 pts (61 female, mean age 42.38 \pm 5.38 years) were included. 76 were DA-T (70 Cab, 6 Bromo) and 27 DA-C. Median MSDL was 0.5mg (IQR: 0.25-0.75), MSDH was 0.28mg (IQR: 0.14-0.42). Median prolactin was 12.7ng/ml (IQR: 4.35-51.6). Overall median PHQ-9 score was 4 (IQR=2-9) and median BIS-11 score was 52 (IQR: 47-61). Per **PHQ-9**, 11/103 pts had major depressive disorder (MDD); 10 (13.2%) DA-T, 1 (3.7%) DA-C, $p=0.28$. 12/103 pts had other depressive disorder (ODD); 7 (9.2%) DA-T, 5 (18.5%) DA-C, $p=0.19$. 8 pts had thoughts of self-injury; 6 (7.9%) DA-T, 2 (7.4%) DA-C, $p=NS$. Severe depression was found in 3, (3.9%) DA-T pts only, moderately severe in 7 (9.2%) DA-T and 2 (7.4%) DA-C, moderate in 8 (10.5%) DA-T and 1 (3.7%) DA-C, and mild in 18 (23.7%) DA-T, 12 (44.4%) DA-C, $p=NS$. For **BIS-11 (97 pts)** median score was 52.0 (23-104) for DA-T, 52.5 (38-77) for DA-C. 23 pts had a score \geq 75thile, 18 (26.1%) DA-T and 5 (20%) DA-C. Younger pts (36 \pm 14.8 vs 43.5 \pm 15.09 years; $p=0.043$) and lower DA cumulative doses had significantly higher ICD scores (median 18.27, IQR 11.5-313.98 vs 120.4, IQR 48.04-296.5; $p=0.022$). Differences in prolactin levels and sex were not significant. Per PHQ-9; 26.1% of pts with vs 5.3% without increased ICD risk had MDD ($p=0.013$). Depression severity and the total PHQ-9 score were higher in pts with increased ICD risk ($p\leq 0.001$). Pts with an increased ICD had higher odds of having thoughts of death or self-harm (OR=6.29 CI95% 1.37-28.86, $p=0.01$). **Discussion** The data shows a trend of higher impulsivity among DA treated pts. Pts with increased ICD risk had higher odds of MDD, self-harm ideation and thoughts about being dead. In contrast with previous studies, prolactin and male sex were non-significant for increased ICD, while a lower DA cumulative dose was significant. We suggest ICD is more likely to appear in DA naïve or pts recently taking DA. **Conclusion** Routine self-assessment questionnaires PHQ-9 and BIS-11 during office visits may be useful to identify patients at risk of depression and ICD in pts with DA treated PA.

Neuroendocrinology and Pituitary CASE REPORTS IN CLASSICAL AND UNUSUAL CAUSES OF HYPOPITUITARISM

Isolated Adrenocorticotrophic Hormone Deficiency Secondary to the PD-1 Inhibitor Pembrolizumab

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SAT-242

Background: Immune checkpoint inhibitors (ICIs) are now indicated in the treatment of several solid tumors and have improved the prognosis of patients with advanced malignancy. The expanded use of ICIs has led to the rise of otherwise rare autoimmune sequelae. The overall incidence of ICI-induced autoimmune hypophysitis has increased to approximately 10%, but is only estimated to be 0.4% with PD-1 inhibitors specifically (1). Isolated ACTH deficiency from immune checkpoint inhibitors is rare, and very few cases secondary to the PD-1 inhibitor pembrolizumab have thus far been reported.

Clinical Case: A 75-year old woman with history of Stage IV lung adenocarcinoma presented to oncology clinic in July 2019 with progressive weakness, weight loss, and confusion for several weeks. She was found to be hypotensive and dehydrated in the clinic and subsequently was admitted to the hospital. A comprehensive infectious work-up was non-contributory. History revealed that after treatment failure with carboplatin, she was treated with pembrolizumab from January 2017 to June 2019 with excellent response. Laboratory evaluation on admission demonstrated an undetectable AM cortisol level of < 1 ug/dL (n 5-25 ug/dL) with concomitant ACTH < 5 pg/mL (Roche cobas, n 7.2-63 pg/mL), consistent with central adrenal insufficiency. Testing of the remainder of the pituitary axis, including TSH (0.83uU/mL, n 0.4-4.6 uU/mL), FSH (34.7 mIU/mL, n <150 mIU/mL), LH (12.6mIU/mL, n <60 mIU/mL), and IGF-1 (33ng/mL, n 34-245ng/mL), all returned within normal limits. Further chart review verified that she had not been exposed to any form of glucocorticoids within the past 6 months. MRI brain with contrast demonstrated no obvious pituitary disease. The patient was started on 5mg of prednisone daily, with significant improvement in mental status, appetite, and blood pressure. She was discharged home on maintenance prednisone for adrenal insufficiency due to presumed isolated corticotroph destruction.

Conclusions: Isolated ACTH deficiency is a very rare but potential consequence of pembrolizumab use. It can be especially difficult to diagnose in patients on chemotherapy who are at higher risk for dehydration and failure to thrive. Duration of pembrolizumab therapy should not preclude the diagnosis of isolated ACTH deficiency, as it can occur even as late as 2.5 years into therapy.

Reference: (1) Chang, L., Barroso-Sousa, R., Toloney S., Hodi F.S., Kaiser, U.B., Min, L. Endocrine Toxicity of Cancer Immunotherapy Targeting Immune Checkpoints, *Endocr Rev.* 2019;40;17–65.

Pediatric Endocrinology

PEDIATRIC ENDOCRINE CASE REPORTS I

Polymicrobial Suppurative Thyroiditis Masquerading as Thyroid Storm

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SAT-063

Introduction:

The thyroid gland is highly resistant to infection due to a robust blood supply, good lymphatic drainage, and high

iodine concentration. Suppurative thyroiditis (ST) often presents with fever, tachycardia, leukocytosis, tenderness, and euthyroid labs. However, when ST occurs with thyrotoxicosis, it can meet criteria for thyroid storm, which presents a diagnostic dilemma.

Clinical Case:

A 17 year old female with family history of Graves' disease presented to the ER with a sore throat. She was diagnosed with viral pharyngitis and treated with dexamethasone. Over the next 2 weeks, she developed fatigue, body aches, nausea, vomiting, and chills. She returned to the ER and was found to have tachycardia, hyperthyroidism [free T4 5.64 ng/dL (0.8 - 2.0 ng/dL), TSH <0.015 uIU/mL (0.5 - 4.5 uIU/mL)], and WBC 11 k/uL (3.5 - 11.5 k/uL). She was prescribed atenolol and referred to Endocrinology. Three days later she developed fever, diaphoresis, ear pain, vomiting, and abdominal pain. In the ER, she was febrile to 101.2°F with a heart rate (HR) of 117 BPM. Labs showed a free T4 6.14 ng/dL, TSH <0.015 uIU/mL, and WBC 20 k/uL. She was treated with methylprednisolone, propylthiouracil, and labetalol with improvement and transferred for concern of impending thyroid storm. Exam showed left-sided thyroid enlargement with tenderness. Thyroid ultrasound showed an enlarged heterogenous left thyroid lobe with 2 nodules, one 25 x 33 x 21 mm heterogenous and one 19 x 11 x 19 mm homogenous, without discrete abscess. That night she developed vomiting, hand tremors, HR in the 130's BPM, fever to 104.1°F, and a headache. Treatment was initiated with methimazole, SSKI drops, propranolol, and dexamethasone. Symptoms improved save persistent neck tenderness and dysphagia. CT neck demonstrated a left-sided 25 x 17 x 90 mm abscess with concern for 4th branchial apparatus abnormality. She underwent incision and drainage with drain placement. Cultures grew *Streptococcus anginosus* and *Fusobacterium necrophorum*. Broad spectrum antibiotics were started and later narrowed to ampicillin-sulbactam. Betablockers and methimazole were discontinued and thyroid labs nearly normalized by discharge [T4 11.8 mcg/dL (4.5-11.5 mcg/dL), free T4 2.0 ng/dL (0.8-2 ng/dL), and total T3 78 ng/dL (100-210 ng/dL)]. Thyroid auto-antibodies were negative.

Discussion:

In patients with ST, only 11% present with hyperthyroidism. Current thyroid storm scoring systems are sensitive but not specific so an acute bacterial infection with thyrotoxicosis can easily meet criteria. While ultrasound is standard for assessing for thyroid abscesses, in the setting of high clinical suspicion, further imaging with contrasted neck CT is warranted.

Adipose Tissue, Appetite, and Obesity MECHANISMS AND TREATMENT OF OBESITY IN HUMANS

Amino Acid Signature of Abdominal Obesity in the TwinsUK Cohort

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OR33-05

Background and aim: Metabolomic studies have shown that circulating amino acid levels are altered in the context of obesity. The branched-chain amino acids (BCAAs, namely leucine, isoleucine and valine) have been the most studied because of their consistent positive association with adiposity and their ability to prospectively predict type 2 diabetes and cardiovascular diseases (1). Circulating glutamate has been much less investigated, but some have shown that its specific association with central fat accumulation was stronger than that of BCAAs (2). This study aimed to evaluate the relationship between circulating glutamate and abdominal obesity and the impact of genetic factors on this association. **Methods:** In the TwinsUK cohort, we selected individuals for whom both metabolomics and DXA trunk fat measurements were available (n=4 665). We used linear regression to assess the correlation between glutamate level and trunk fat. Those with a trunk fat mass greater than 15 kg were considered abdominally obese. We compared the odds of presenting abdominal obesity in each circulating glutamate quintile with logistic regression models. Monozygotic twin pairs discordant for trunk fat were selected to identify analyte differences driven by non-genetic factors. All analyses were also performed with BCAAs for comparison. **Results:** Circulating glutamate was positively and significantly associated with trunk fat (β : 0.28, 95%CI: 0.26-0.31). Individuals in the highest circulating glutamate quintile had a more than 8-fold higher risk of being characterized by abdominal obesity compared to those in the lowest quintile (OR: 8.44, 95%CI: 6.17-11.55). In the 54 monozygotic twin pairs discordant for trunk fat, the heavier twin had significantly higher glutamate level compared to the leaner co-twin (p-value: 4.05e-07). In all these analyses, the results for glutamate were more significant than with any of the BCAAs. **Conclusion:** There is a positive relationship between circulating glutamate and trunk fat that is partially independent of genetic background. This often-overlooked metabolite might represent an interesting biomarker of abdominal obesity. **References:** (1) Newgard (2017). Metabolomics and Metabolic Diseases: Where Do We Stand? *Cell Metab*, 25(1), 43-56, (2) Kimberly et al. (2017). Metabolite profiling identifies anandamide as a biomarker of nonalcoholic steatohepatitis. *JCI Insight*, 2(9).

Tumor Biology

NOVEL REGULATORS OF BREAST CANCER PROGRESSION

The Androgen Receptor Is a Tumour Suppressor in Estrogen Receptor Positive Breast Cancer

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