Conclusion:
- Levels of ACTH and cortisol can be suppressed for several months after intra-articular corticosteroid injections, placing the patient at subsequent risk for adrenal crisis
- In some cases, high doses of Triamcinolone administered by intra-articular injection can cause clinical Cushing syndrome

Diabetes Mellitus and Glucose Metabolism

LIPIDS, OBESITY AND METABOLIC DISEASE

Bile Acid Sequestration Synergistically Accelerates Glucagon Receptor-Stimulated Body Weight Loss in Diet-Induced Obese Mice

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Glucagon, an essential regulator of glucose and lipid metabolism, also promotes weight loss in obese mice. We have shown that hepatic Farnesoid X Receptor (FXR, a bile acid receptor) and bile acids (BA) play an important role in the anti-obesity effect of glucagon in mice. Specifically, glucagon-receptor (GCGR) agonism is a potent regulator of BA metabolism, increasing total plasma BA levels and preferentially raising cholic and chenodeoxycholic acid levels. These findings led us to hypothesize that BA, signaling via hepatic FXR, contributes to GCGR-stimulated weight loss. Furthermore, we reasoned that BA sequestration may impair GCGR-mediated weight loss by reducing the availability of BA to stimulate FXR-action. Thus, to elucidate the role of BA in GCGR-mediated weight loss, we utilized anion-exchange BA-binding resins (BARS; Cholestyramine and Colesevelam) to prevent intestinal (ileal) re-uptake and reduce plasma total cholesterol, LDL, and BAs via fecal excretion. Diet-induced obese (DIO) C57Bl/6J mice were randomized to groups matched for body-weight and administered daily GCGR agonism (IUB288, 10 nmol/kg, s.c.) or vehicle, in the presence or absence of BARS. Consistent with our prior findings, IUB288-treatment reduced body weight in DIO mice. Counter to our original hypothesis, IUB288+Cholestyramine (3% in high fat diet, HFD [58% kcal%]) enhanced IUB288-stimulated weight loss. Similar body-weight loss effects following combined IUB288 and BARS treatment were replicated both at a lower dose of Cholestyramine (1.5% in HFD), as well as in combination with both low- (2% in HFD) and high- (4% in HFD) dose Colesevelam. IUB288-stimulated weight loss is accompanied by suppression of food intake (FI), while Colesevelam alone did not significantly lower FI at either dose (2 or 4% in HFD). However, 4% Colesevelam with IUB288 completely suppressed FI, while 2% Colesevelam stimulated a reduced, though not complete suppression. GCGR agonism is a potent stimulus of weight loss; however, its impairment of glucose tolerance reduces its value as a monotherapy. Excitingly, Cholestyramine (3% in HFD) rescued IUB288-induced glucose intolerance, restoring glucose excursion to levels observed in control (vehicle-treated) mice. Together these studies suggest BARS may enhance the anti-obesity effect of GCGR agonism, beneficially regulate feeding behaviors, and prevent GCGR-stimulated glucose dysregulation in DIO mice. Furthermore, these studies argue that GCGR agonsim combined with BARS treatment may represent a novel therapeutic approach for obesity and obesity-associated glucose intolerance.

Neuroendocrinology and Pituitary

CASE REPORTS IN CLASSICAL AND UNUSUAL CAUSES OF HYPOPITUITARISM

Combination of Immune Check Point Inhibitors Causing Hypopituitarism

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Introduction: Immune Check Point inhibitors (ICI) have been associated with immune related adverse events including a wide array of Endocrinopathies particularly when a combination of ICIs is used. We present a case of Hypopituitarism secondary to CTLA-4 inhibitor Iplimumab and PD-1 inhibitor Pembrulizumab in a patient with Vulvar Melanoma.

Case Description: 49-year-old female with past medical history of Type 2 Diabetes and Vulvar Melanoma presented with nausea, vomiting and fatigue. The patient had surgical excision of Vulvular Melanoma and had been on chemotherapy with Pembrolizumab and Ipilimumab for 1 month. She was found to be hypotensive in the ER, but blood pressure improved after fluid resuscitation. Her blood sugar levels were 76 MG/DL. She denied using any insulin in the last 24 hours. AM Cortisol was <1 UG/ML. TSH was 0.205 UIU/ML with free T4 at 0.74 NG/DL. FSH was 2.5 MIU/ML. LH was 0.5 MIU/ML. Prolactin was 90.2 NG/ML. ACTH was less than 9 PG/ML. MRI of the brain showed mildly enlarged pituitary gland with suprasellar extension, measuring 10.5 mm in craniocaudal height and normal homogeneous enhancement. A diagnosis of Hypopituitarism secondary Ipilimumab and Pembrolizumab was made. She was started on steroids and thyroid replacement. The patient's symptoms resolved, and she was discharged home in a stable condition with outpatient Endocrinology follow up.

Discussion: Immune checkpoint inhibitors (ICI) includes PD1(Programmed cell death receptor 1) inhibitors like Pembrolizumab and CTLA-4 (Cytotoxic T Lymphocyte Antigen-4) inhibitors like Ipilimumab. CTLA-4 inhibitors have more frequently been associated with Hypophysitis leading to particularly ACTH and TSH deficiencies and causing secondary adrenal insufficiency and secondary hypothyroidism. Posterior Pituitary involvement is less common. MRI usually shows mild to moderate enlargement of the pituitary gland. ICI therapy usually does not need to be stopped. Patients commonly require long term glucocorticoid and thyroid replacement.