was treated with supportive care and glucocorticoids with resolution of hypercalcemia and improved cardiac function. Unfortunately, serum 1,25 dihydroxy vitamin D was not successfully measured until after the first dose of prednisone and was found at the upper limit of our reference range 62.0 pg/mL (19.9-79.3).
Conclusion:
Immune checkpoint inhibitors are effective agents in treating various cancers. Adverse effects due to autoimmunity are common and early recognition of life-threatening complications is critical. Although cutaneous and pulmonary sarcoidosis have been described with ICI, to our knowledge, this is the first case report of ICI-related cardiac sarcoidosis presenting with PTH-independent hypercalcemia.

Adrenal

ADRENAL - CORTISOL EXCESS AND DEFICIENCIES

Characterization of the Adrenal Gland and Adrenal Rest Tissues in Congenital Adrenal Hyperplasia

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Background: Adrenonodular hyperplasia and tumor formation are common long-term complications of congenital adrenal hyperplasia (CAH) driven by chronic ACTH elevation. Clinical studies indicate that the majority of males with classic CAH have testicular adrenal rest tumors (TART). Ovarian adrenal rest tumors (OART) are less commonly observed. Little is known about the pathophysiology of adrenal rest, however both adrenal cortex and Leydig cell markers have been described in TART, suggesting a pluripotent embryological cell origin.
Objective: To characterize adrenals and adrenal rest tissues of patients with CAH in comparison with normal tissues.
Materials and Methods: Using immunohistochemistry (IHC) and, real-time qRT-PCR we investigated CAH-affected adrenals (n=5), adrenal rest tissues (n=2; 1 testicular, 1 ovarian), controls [normal adrenal (n=2), testis (n=1), and ovary (n=1)]. Tissue sections prepared from paraffin embedded tissue blocks were immunostained with adrenal [melanocortin 2 receptor (*MC2R*), delta-like homolog 1 (*DLK-1),* steroidogenic factor 1 (*SF-1*), steroidogenic acute regulatory protein (*StAR*) and other cytochrome P450 genes], inflammatory [interleukin 2 receptor *(IL-2R)*, B-lymphocyte antigen (*CD20)*, cluster of differentiation 3 (*CD3)*, tumor necrosis factor alpha (*TNFα),* interleukin 6 *(IL6)*], and gonadal markers [progesterone receptor (*PR*), androgen receptor (*AR*), insulin-like 3 (*INSL3)*]. RNA was isolated and gene expression studies were performed. High-throughput RNA sequencing technology was used to analyze the differential transcriptome profiles between the CAH adrenals, adrenal rest and normal tissues.
Results:
In contrast to the controls, CAH adrenals and adrenal rest tissues showed the following:
(i) IHC studies revealed 95% of tissue positive for adrenal zona-reticularis; (ii) significant nodular lymphocytic infiltration with a predominance of B and T lymphocytes and overexpression of lymphocyte markers *IL-2R, CD20, CD3,* and inflammatory cytokines *TNFα and IL6;* (iii) increased expression of adrenocortical specific genes *MC2R, DLK1.*
Conclusion: CAH-affected adrenals and adrenal rest tissue have similar predominance of zona reticularis and demonstrate lymphocytic infiltration. Active inflammation may play a role in the abnormal development of adrenal and adrenal rest tissue in CAH patients.

Steroid Hormones and Receptors

STEROID BIOLOGY AND ACTION

Brain Aromatase Is Essential for Regulation of Sexual Activity in Male Mice

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Introduction: The biologically active form of estrogen, estradiol (E_2), has important organizational roles in brain development and activational roles in adult brain physiology and behavior. It has been proposed that E_2 formation in the brain might regulate sexual activity in various species. The mechanisms that link estrogen formation in the brain and sexual behavior, however, remain unclear. Aromatase is the key enzyme that catalyzes the conversion of testosterone (T) to E_2 in the testis and brain of male mice. To determine the role of brain aromatase in male sexual activity, we generated a brain-specific aromatase knockout (bArKO) mouse model. Additionally, a newly generated total aromatase knockout (tArKO) mouse model served as a positive control. *Methods:* We generated the floxed aromatase mice ($Arom^{fl/fl}$), which flanked the transcription and translation start sites and the common splice acceptor site for the upstream brain promoter I.f of the aromatase gene. We then crossed Nestin-Cre mice with $Arom^{fl/fl}$ mice to generate bArKO mice. Using the same $Arom^{fl/fl}$ mice, we bred tArKO via crossing with ZP3-Cre mice. Circulating and tissue (brain and testis) E_2 levels were measured using liquid chromatography-tandem mass spectrometry. We assessed sexual activity in 12-14 week-old bArKO, tArKO and littermate control males over two 30-minute trials. The interactions were monitored and videotaped, and the videotape was scored for the sexual activity. To investigate whether the lack of estrogen production in the brain was causative for altered sexual behavior, 20 bArKO and 20 control mice were castrated at ~nine weeks of age and supplemented with exogenous sex hormone via 60-day time release pellet implantation. *Results:* E_2 levels are significantly decreased in the brain but not the testis of bArKO