Adrenal
ADRENAL - CORTISOL EXCESS AND DEFICIENCIES

Efficacy and Safety of Prenatal Dexamethasone Treatment in Offspring at Risk for Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency
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MON-156
Objective: To assess the efficacy and safety of prenatal dexamethasone treatment in offspring at risk for congenital adrenal hyperplasia. Methods: MEDLINE, EMBASE, the Cochrane Library, the clinicaltrials.gov website databases was systematically searched from inception through March 2019. WMD and SMD with 95%CI was calculated using random or fixed effects models. Results: There was a significant reduction of virilization in the DEX-treated group (WMD: -2.39, 95%CI: -3.31,-1.47). No significant differences were found in newborn physical outcomes for birth weight (WMD: 0.09, 95%CI: -0.09, 0.27) and birth length (WMD= 0.27, 95%CI: -0.68, 1.21). Concerning cognitive functions, no significant differences in the domains of psychometric intelligence (SMD: 0.05, 95%CI: -0.74, 0.83), verbal memory (SMD: -0.17, 95%CI: -0.58, 0.29), visual memory (SMD: 0.10, 95%CI: -0.14, 0.34), learning (SMD: -0.02, 95%CI: -0.27, 0.22), verbal processing (SMD: -0.38, 95%CI: -0.93, 0.17). Regarding behavioral problems, no significant differences in the domains of internalizing problems (SMD: 0.16, 95%CI: -0.49, 0.81), externalizing problems (SMD: 0.07, 95%CI: -0.30, 0.43), total problems (SMD: 0.14, 95%CI: -0.23, 0.51). With respect to temperament, no significant differences in the domains of emotionality (SMD: 0.13, 95%CI: -0.79, 1.05), activity (SMD: 0.04, 95%CI: -0.32, 0.39), shyness (SMD: 0.25, 95%CI: -0.70, 1.20), sociability (SMD: -0.23, 95%CI: -0.90, 0.44).

Conclusions: Prenatal DEX treatment reduced virilization with no significant differences in newborn physical outcomes, cognitive functions, behavioral problems, temperament. The results need to be interpreted cautiously due to the existence of limitations.

Diabetes Mellitus and Glucose Metabolism

TYPE 1 DIABETES MELLITUS

Diabetes Mellitus Induced by Programmed Cell Death-1 (PD-1) Inhibitors: A Case Report
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SAT-680
Introduction: Immune checkpoint blockade has revealed a remarkable success in the treatment of a range of cancer types. Immune-related adverse events on the endocrine system may be permanent and carry high morbidity and mortality. Case: A 35-year-old black male presented to the ED with acute onset diffuse abdominal pain, along with nausea and vomiting. Review of systems was positive for polyuria and polydipsia. The examination was unremarkable apart from a sizeable fungating lesion of the left lower extremity by the ankle measuring 12 x 8 cm. Investigations indicated blood sugars around 600, serum bicarbonate of 19 mEq/L, an anion gap of 19 mEq/L, serum BHB was elevated, and lactate within normal. The patient was diagnosed with DKA, started on an insulin drip, and admitted to the ICU. Our patient had no known personal or family history of diabetes. A few years ago, he had suffered from a non-healing chronic ulcer in his left ankle secondary to a motor vehicle accident. Three months ago, he had been diagnosed with a well-differentiated squamous cell carcinoma, arising from his chronic non-healing ulcer. One month ago, He had started Pembrolizumab 200mg Intravenously, and he had received a total of two cycles, the last cycle was one week ago. Shortly after he presented to the ED with the above chief complaint. He made a complete recovery and further investigations revealed HbA1c of 7.2%, C-peptide levels of <0.1 ng/mL, which supports the diagnosis of T1-DM. He was discharged home, and Pembrolizumab was continued.

Conclusion: Autoimmune T1-DM has been reported after receiving anti-PD-1 therapy. In a recent study included 27 patients with a variety of solid-organ cancers, and all had received anti-PD-1 antibodies treatment, autoimmune, T1-DM diabetes occurred in close to 1% of patients (1). A systematic review and meta-analysis were conducted recently showed that people developed T1-DM within three months of the initial PD-1 inhibitor exposure. Since patients treated with anti-PD-1 antibodies can present with life-threatening DKA, a high index of suspicion is crucial as early detection is the key to successful treatment and prevention of morbidity and mortality. It remains unclear if it is safe to restart the checkpoint inhibitor after an immune-related adverse event, and further studies are necessary in order to resolve this dilemma. A recent retrospective study included patients with melanoma showed that anti–PD-1 therapy could be safely resumed after severe adverse event requiring immunosuppression (2).

References:
1. Stamatouli, A. M. et al. Collateral Damage: Insulin-Dependent Diabetes Induced With Checkpoint Inhibitors. Diabetes 67, 1471–1480 (2018).
2. Menzies, A. M. et al. Anti-PD-1 therapy in patients with advanced melanoma and preexisting autoimmune disorders or major toxicity with ipilimumab. Ann. Oncol. 28, 368–376 (2017).

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS I

Reversible Suppression of Serum 1,25-Dihydroxyvitamin D in Williams Syndrome
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SAT-356
Background: Hypercalcemia has been reported in 5% to 50% of patients with Williams syndrome; however, observations about the role of 1,25-dihydroxyvitamin D in hypercalcemia related to Williams syndrome have been contradictory. Objective: The objective was to investigate the mineral metabolism in an 11-month-old patient with Williams-Beuren syndrome who had hypercalcemia, hypercalciuria and nephrocalcinosis. Methods: We reviewed test results in an 11-month-old infant with Williams syndrome who developed hypercalcemia following excessive dietary calcium intake that was two to three times higher than recommended for age because he continued receiving a premature formula with high calcium content from birth. Results: Our patient presented with feeding difficulties, daily vomiting, weight loss, and constipation. He had serum total calcium 14.8 mg/dL, phosphorus 4.0 mg/dL, PTH <4 pg/mL, 1,25-dihydroxyvitamin D <8 pg/mL, 25-hydroxyvitamin D 29 ng/mL, PTH-related peptide 3.7 pmol/L (expected <4.2), alkaline phosphatase 118 U/L, beta-crosslaps 1257 pg/mL, and urinary calcium/creatinine ratio 1.19. XR Skeletal Survey revealed increased bone density in the metaphyseal regions, in particular, above the knee, distal radius and ulna that may result from hypercalcemia; no evidence of rickets, osteoporosis or congenital osteodystrophy was seen. Renal ultrasound revealed increased echogenicity of the renal medullary pyramids consistent with medullary nephrocalcinosis. Hypercalcemia and hypercalciuria were initially treated with IV fluids and Furosemide IV, and resolved only after Pamidronate 0.5 mg/kg/dose IV x 2 doses. After serum calcium normalized, the patient’s symptoms resolved, PTH recovered to 18 pg/mL (expected 10 - 65), and 1,25-dihydroxyvitamin D increased to 27 pg/mL (expected 24 - 86). Chromosomal micro-array analysis showed a 1.9 megabase deletion at 7q11.23 that overlapped the Williams syndrome critical region including the ELN gene, consistent with diagnosis of Williams syndrome. Serum calcium remained normal with dietary calcium restriction using a low-calcium formula and complementary foods. Conclusions: PTH-independent hypercalcemia in our patient with Williams syndrome was due to calcium overload resulting from dietary calcium excess in addition to possibly enhanced intestinal calcium absorption. Serum 1,25-dihydroxyvitamin D was undetectable and returned to normal only with resumption of PTH secretion required for its synthesis after hypercalcemia resolved. The balance between bone formation and resorption was shifted to resorption possibly to remove skeletal calcium excess, based on normal alkaline phosphatase (marker of osteoblast activity) and high collagen beta-crosslaps (marker of osteoclast activity). A premature formula with high calcium content should be switched to a full-term formula when risk for rickets of prematurity clears.

Reproductive Endocrinology
CLINICAL STUDIES IN FEMALE REPRODUCTION II
Hormonal Profile of Ovarian Sertoli-Leydig Cell Tumor
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SUN-002
Background: Sertoli-Leydig cell tumors account for less than 1% of ovarian tumors, and information about their biochemical markers has been lacking. Objective: The objective was to characterize the hormonal profile of Sertoli-Leydig cell tumor, which should be helpful in recognizing this rare condition in the future. Methods: We reviewed test results including serum total and free testosterone, steroid hormone precursors, and inhibit B levels in a 17-year-old adolescent girl with ovarian Sertoli-Leydig cell tumor who developed secondary amenorrhea for 6 months, deepening of the voice, acne, and severe hirsutism. Results: Our patient had serum testosterone 641 ng/dL (expected 20 - 38), dihydrotestosterone 42.5 ng/dL (expected 3 - 18), 17-OH progesterone 659 ng/dL (expected 20 - 265), androstenedione 869 ng/dL (expected 50 - 224), 17-OH pregnenolone 760 ng/dL (expected 53 - 357), DHEA 1250 ng/dL (expected 4 - 491), and DHEA-S of 366 mcg/dL (expected 44 - 248). Inhibit B level was 321 pg/mL (expected <136); inhibit A was normal. Anti-mullerian hormone, a-fetoprotein, carcinoembryonic antigen, and CA-125 tumor markers were not elevated. Karyotype was female 46,XX. Dexamethasone 0.5 mg QID PO for 4 days resulted in plasma ACTH <5.0 pg/mL and serum cortisol <1.0 mcg/dL, total testosterone 611 ng/dL, free testosterone 25.1 ng/dL (expected <0.04 - 1.09 ng/dL), and 17-OH progesterone 887 ng/dL. Abdomen and pelvis MRI demonstrated a right ovarian mass primarily solid with high cellularity, measured 4.4 x 3.9 cm; there was at least moderate diffuse enhancement of the mass after contrast administration; adrenal glands were normal. Surgical pathology of the resected right ovary revealed moderately to poorly differentiated Sertoli-Leydig cell tumor. Single antibody immunostain procedures with appropriate controls showed a staining pattern supportive of this rare diagnosis: WT-1 showed moderate nuclear staining, calretinin showed a strong positive stain, and CK showed a patchy moderate staining pattern; immunostains for myogenin, desmin, and EMA were negative. Genetic testing revealed a germline heterozygous mutation in DICER1 gene, c3737del, p.Asn1246Metfs*12, establishing the diagnosis of DICER1 syndrome, an autosomal dominant disorder predisposing to cancer. Menses resumed one month after tumor resection. Conclusions: High serum 17-OH progesterone, androstenedione, 17-OH pregnenolone, and DHEA levels used as indicators of adrenocortical function could be markers of an ovarian tumor. If serum 17-OH progesterone and testosterone remain high when cortisol and plasma ACTH are suppressed on Dexamethasone test, a source of 17-OH progesterone and testosterone is other than ACTH-dependent adrenal one. High serum inhibit B level may be sign of an ovarian tumor. Patients with Sertoli-Leydig cell tumor should be screened for DICER1 gene syndrome to assess risk for other rare neoplasms.

Pediatric Endocrinology
PEDIATRIC ENDOCRINE CASE REPORTS II
Prevention of 6-Mercaptopurine-Induced Hypoglycemia by Levocarnitine Replacement
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