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SUN-027

Background: Testicular regression syndrome (TRS), also known as vanishing testes syndrome, is a condition of 46, XY males presenting with male phenotypic genitalia and testicular absence. Normal testes are thought to have once existed in fetal life and subsequently atrophied following a catastrophic event. It may present as partial or complete absence of testicular tissue. Fibrotic remnants are commonly found upon surgical exploration.

Case: This is the case of a 20-year-old male with a birth-diagnosis of primary hypogonadism. The patient was born prematurely at 5 months following a motor vehicle accident that resulted in his mother's death. Neonatal evaluation for cryptorchidism revealed no radiological evidence of intra-abdominal testicular mass. Referral to a pediatric-endocrinologist was done at early childhood. Testosterone replacement was started at 12 years of age and pubarche was adequate. After surgical exploration, a testicular remnant was surgically removed. Pathology report revealed fibrotic tissue, yet no histological testicular tissue was found. Due to lack of testes in the scrotum, testicular prosthesis was implanted at age 14, but the etiology of the hypogonadism was never elucidated. The patient was initially seen in our adult-endocrinology clinics at age 21. Upon evaluation, secondary sex characteristics were adequate for age. Penile length was of 3.5 inches. Bilateral testicular prostheses were palpable, and no gynecomastia was present. Despite testosterone replacement, total testosterone was 3.38 ng/ml (n; 2.41-8.27 ng/ml), FSH was 106 mIU/ml (n; 1.4-18.1 mIU/ml) and LH was 34.7 mIU/ml ml (n; 1.5-9.3 miu/ml). Based on history, laboratory workup and surgical pathology, TRS was presumed as the etiology of this patient's hypogonadism. Testosterone therapy was adjusted to reach physiological expected levels.

Conclusion: TRS is an underdiagnosed cause of hypergonadotropic hypogonadism. It is supposed that the initial embryologic development was normal, followed by a vascular accident. There is no clear recommended approach for evaluating a patient once the diagnosis of TRS is suspected. Diagnostic methods may include hormonal and karyotype testing, imaging, and surgical exploration. Furthermore, although clinical recommendations have been published for other disorders of sex development, TRS management has been understudied. Testosterone replacement therapy at the typical time of puberty ensures the development of secondary sexual characteristics, bone health and pubertal growth. Unlike Klinefelter syndrome and cryptorchidism, TRS has not been associated with increased risk of cancer. Thus, it is important to establish the etiology to avoid invasive and unnecessary workup, which will result in psychological distress and excessive healthcare costs.

Pediatric Endocrinology

SEXUAL AND GENDER DEVELOPMENT IN THE PEDIATRIC POPULATION

Central Precocious Puberty without Central Nervous System Lesions: Is It Really Idiopathic?

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OR15-04

Background: The etiological diagnosis of central precocious puberty (CPP) has been classically divided into causes with or without central nervous system (CNS) lesions. Among the cases without CNS lesions, most of them are classified as idiopathic. In clinical practice, about 90% of girls and 40% of boys with CPP are considered having the idiopathic form. In the last two decades, pioneering studies have revealed underlying genetic causes in patients with apparently idiopathic CPP.

Objective: To describe the frequency of genetic causes identified in a large cohort of patients with CPP followed in a single research center and to evaluate its role in the distribution of the etiology of CPP.

Patients and methods: A retrospective evaluation was performed analyzing the etiological diagnosis of 276 patients (246 girls, 30 boys) with CPP followed in a single university hospital outpatient clinic from 2006 to 2019. The great majority (230 patients) presented without CNS lesions, being classified as idiopathic CPP group. Among the idiopathic CPP group, 170 of them had DNA samples available and were included for genetic analysis. Patients included for genetic analysis were systematically investigated for genetic causes of CPP using standard methodologies of genetic-molecular analysis. Briefly, they were studied as follows: 120 by Sanger sequencing; 18 by target panel sequencing; 27 by whole-exome sequencing; 5 by whole-genome sequencing; 113 by specific DNA methylation analysis; and 38 by genomic microarray.

Results: Among the 276 patients with CPP, 46 (16.7%) had pathological CNS lesions: 19 boys and 27 girls, indicating the prevalence of CPP with CNS lesions (organic) of 63.3% in boys and 11% in girls. The most common cause of organic CPP was hypothalamic hamartoma (20 cases). Meanwhile 230 patients (83.3%) encompassed the apparently idiopathic CPP group. Main characteristics of this idiopathic CPP group were: 219 girls and 11 boys; 158 sporadic (69%), 68 familial (29.5%) and 4 adopted (1.5%). In the subset of patients with DNA available (162 girls, 8 boys), the frequency of genetic causes was 11.8% (20 cases: 18 girls and 2 boys). Analyzing by sex, the frequency of genetic causes was higher in boys (25%) than in girls (11.1%). The identified genetic defects were the following: 9 cases with inactivating *MKRN3* mutations (8 families), 6 cases with inactivating *DLK1* mutations (2 families), 1 case with activating *KISS1R* mutation, 1 case with activating *KISS1* mutation, 2 sporadic cases with maternal uniparental disomy

of chromosome 14, and 1 sporadic case with epimutation at *DLK1* locus.
Conclusion: Pathogenic genetic defects were identified in 11.8% of patients with apparently idiopathic CPP involving four distinct genes. Altogether, these genetic findings indicate a context of changing in the distribution of the etiological diagnosis of CPP in both sexes, highlighting the genetic causes.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS II

Presumed Parathyroid Infarction Leading to Remission of Primary Hyperparathyroidism: A Rare Clinical Occurrence

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MON-336

Background: Infarction of a parathyroid adenoma, also known as 'parathyroid auto-infarction' or 'parathyroid apoplexy,' is a rare condition that can present and lead to acute and dramatic reduction of calcium (Ca2+) and parathyroid hormone (PTH) levels and spontaneous remission of primary hyperparathyroidism (PHPT). Some patients may experience neck pain, dysphagia, hoarseness, anterior neck swelling or ecchymoses, while others are asymptomatic. Ultrasound can show the lesion getting larger due to hemorrhage, but weeks to months later, there can be a size decrease of the adenoma due to loss of blood supply and necrosis. Sestamibi scans can also show non-localization on serial exams. Few case reports have evidence of infarction on pathology.
Clinical Case: A 38 year old man with no significant past medical history presented after a pedestrian-motor vehicle accident with polytrauma, including a cervical spine injury requiring tracheostomy and immobilization of his neck. Over the first week of his hospitalization, his Ca2+ rose as high as 14.0 mg/dL (8.9-10.2 mg/dL). Concurrent PTH level was 233 pg/mL (12-88 pg/mL) and 25-OH vitamin D level was 14.8 ng/mL (20.1-50.0 ng/mL). A neck ultrasound showed a hypoechoic nodule measuring 1.4 x 1.2 x 1.6 cm posterior to the superior aspect right thyroid lobe. A sestamibi scan with SPECT-CT showed a persistent focal activity in the region of right thyroid bed. He was treated with aggressive intravenous (IV) hydration, 7 doses of intranasal calcitonin 500 units, multiple doses of furosemide 40-80 mg IV, pamidronic acid 90 mg IV, and eventually transitioned to cinacalcet 30 mg twice daily. Due to his C-spine injury, parathyroid surgery was deferred.
Four months later, the patient developed acute muscle spasms. He denied anterior neck pain, dysphagia, bruising, or swelling. Ca2+ level was checked and found to be 7.0 mg/dL. Cinacalcet was decreased, and eventually had to be discontinued. His serial Ca2+ and PTH levels normalized to 9.8 mg/dL and 55 pg/mL, respectively. A repeat 25-OH vitamin D level was replete at 31.1 ng/mL. A follow up ultrasound redemonstrated a slightly ill-defined hypoechoic nodule, now only measuring 0.9 x 0.9 x 1.4 cm along the the right thyroid. A sestamibi scan was also obtained and did not localize any lesion.
The biochemical and imaging findings were most consistent with a parathyroid infarction resulting in spontaneous remission of PHPT. Now one year following his initial presentation, he remains normocalcemic.
Clinical Lesson: The differential diagnosis for a sudden remission of PTH-dependent hypercalcemia is limited. Parathyroid infarction is a rare condition with paucity of data regarding follow up, but these patients likely need to remain under close long term clinical and biochemical surveillance as recurrence has been documented in the literature.

Adrenal

ADRENAL PHYSIOLOGY AND DISEASE

LC-MS-Based Profiling of Adrenal Steroids Reveals Metabolic Signatures of 17á-hydroxylase Deficiency

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SUN-215

LC-MS-based profiling of adrenal steroids reveals metabolic signatures of 17α-hydroxylase deficiency
The comprehensive metabolic signatures of adrenal steroids are necessary to understand their pathophysiological functions in adrenal diseases, such as Cushing's syndrome (CS) and congenital adrenal hyperplasia (CAH). The 17α-hydroxylase deficiency (17α-OHD) CAH, accounted for <1% of CAH cases, is caused by mutations of CYP17A1 gene leading to impaired production of cortisol and adrenal androgens. It may be under-diagnosed in patients in whom routine screening for the early detection of CAH subtypes. A validated liquid chromatography-mass spectrometry (LC-MS)-based quantitative profiling of 27 adrenal steroids in human serum, therefore, has been developed and employed in patients with CS (n = 7) and 17α-OHD CAH (n = 1). In a patient with 17α-OHD, adrenal androgen levels were significantly decreased, especially DHEA sulfate (~1/1,000 times), while pregnenolone sulfate was increased against both healthy (n =43) and CS subjects ($p < 0.001$). In addition, increased mineralocorticoids and decreased glucocorticoids as well as DHEA-S/Preg-S were observed in a 17α-OHD patient, which mean DHEA-S, Preg-S, and these metabolic ratios could be good biomarkers for detecting 17α-OHD CAH in part of an overall plan of medical care. The developed LC-MS method can quantitatively profile biologically active adrenal steroids and sulfate conjugates in a single run to be a comprehensive diagnostic tool in adrenal diseases.