the transgenerational metabolic benefits of maternal exercise, which provides some novel evidence and targets for combating the metabolic diseases.

Reproductive Endocrinology

SEX DETERMINATION AND REPRODUCTIVE AXIS DEVELOPMENT

Social and Psychological Aspects of Partial Androgen Insensitivity Syndrome, Therapeutic Challenges.

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SUN-038

Social and Psychological Aspects of partial Androgen Insensitivity Syndrome, Therapeutic Challenges

Background: Partial Androgen Insensitivity Syndrome (PAIS) is a rare congenital condition with incongruence of chromosomal, gonadal and phenotypic sex and classified as differences of sex development. Distinct from complete Androgen Insensitivity by the presence of ambiguous genitals in a 46, XY individual with normal testis development and partial responsiveness to androgens.

Clinical Case: 18 years phenotypic female presented with primary amenorrhea and ambiguous genitalia with poor secondary sexual characteristics after puberty. Born out of a consanguineous marriage, normal vaginal delivery conducted by midwife at home in a small village, who informed a female with ambiguous genital though. Since childhood she uses to dress up in female attire. She has 5 siblings, two brothers and three sisters, one year back she got engaged to her distant cousin and was about to get married when one of her younger sister now 8 years having similar problem alarmed family to report before the wedlock.Vitals:Weight 55kg,Height 167cm,Physical, biochemical, chromosomal testing and imaging revealed:micropenis 3cm(N=8cm) with hypospadias, a small blind vaginal orifice, hormones within normal male ranges, Karyotype: XY, MRI revealed no female internal organs or prostate gland, left testis seen in partly formed scrotal sac (4.6x2.5cm) right in superficial inguinal region (2.7x1.9cm),normal testes size(4x3cm), bilateral cavernous tissue,respectively. Findings suggested phenotypic female with PAIS. Further investigations could not be carried out due to poor affordability and non-availability of Genetic testing facility. Management: Male gender was preferred (after discussion with urologist and consent of the patient and the family) Assigning the gender, health-related quality of life (QoL), social and psychological well-being, and affective disorders, like fertility and sexual functions in PAIS were discussed. Psychometric data was obtained through psychological questionnaires: Beck Depression Inventory & Hospital Anxiety and Depression Scale revealed moderate depression. An important pre-decision analysis regarding the potential impact of clinical decisions such as the type and timing of genital surgeries on patient's life is missing due to absence of a multidisciplinary team for counseling and decision making.

Conclusion: After spending 18.yrs as a phenotypic female the patient and her family experienced considerable emotional distress. In our culture and society these types of cases are seldom reported. We as medical professionals need to be sensitive to the social and psychological wellbeing of patients so that they can be settled and acceptable in their part of the world.

Tumor Biology

TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS

Determining the Undetermined: The Role of Tumor Tissue Staining for Interpretation of Inconclusive Genetic Testing Results in Patients with Pheochromocytomas and Paragangliomas.

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SAT-140

Background:

Paragangliomas and pheochromocytomas are neuroendocrine tumors that can occur in several hereditary tumor syndromes. While these are generally rare, individuals with germline loss of function mutations in the succinate dehydrogenase (SDH) genes are at high risk of developing these tumours, with a penetrance of 70% by age 50. Functional SDHB acts as a tumor suppressor. Consequently, pathogenic mutations in the *SDHB* gene predispose to familial paraganglioma syndrome type 4, with high incidence of extra adrenal paragangliomas and high rates of metastasis. *SDHB* mutation carriers are also predisposed to developing tumors in other sites such as renal cell cancer, gastrointestinal stromal tumors and pituitary adenomas. Genetic testing for hereditary syndromes is recommended in patients who present with paragangliomas and pheochromocytomas, especially in those with aggressive tumours or who present at a young age. It is recommended that mutation carriers are monitored with routine clinical and imaging surveillance, and effort is made to identify and screen at-risk family members. In some cases, genetic testing can identify variants that are not clearly pathogenic or benign. In such "variants of undetermined significance", immunohistochemistry or family history can be a helpful tool in discriminating between SDHB related and non-SDH-related pheochromocytomas and paragangliomas.

Clinical case:

We report on three families who presented with manifestations of paraganglioma syndrome and were found to have Variants of Uncertain Significance (VUSs) in the SDHB gene. Absence of SDHB staining was seen on tumour histopathology in two of the families; staining was not performed in the third. The proband in the third case initially presented at the age of 22 with a cardiac pheochromocytoma. Subsequently, her son was diagnosed with metastatic renal cancer at the age of 37. Genetic test results from both these patients identified a heterozygous VUS in SDHB. The son passed away from complications of his aggressive cancer shortly after diagnosis. Had familial screening and surveillance been initiated sooner in this family, this poor outcome may have been prevented.

Conclusion:

Our case highlights the important diagnostic dilemma that can arise in patients with VUSs in risk genes for hereditary pheochromocytomas and paragangliomas. While

universally treating these VUSs as pathogenic would be costly, low-yield and potentially harmful, the incorporation of family history and tumour tissue staining for SDHB should be considered in all individuals with pheochromocytomas and paragangliomas to help guide interpretation of inconclusive genetic testing results, inform subsequent management and help predict risk for inheritance and recurrence.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS I

Hyperparathyroid Crisis Precipitated by Rapid Correction of Symptomatic Hypercalcemia in an Occult Ectopic Parathyroid Adenoma

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SAT-341

Background: Parathyroid adenomas (PA) are typically benign, slow-growing tumors causing gradual increase in parathyroid hormone (PTH) and serum calcium (s.Ca) levels. Hyperparathyroid crisis is a rare and potentially fatal syndrome, which occurs due to rapid elevation of PTH and s.Ca levels (s.Ca >15mg/dL). This can potentiate severe metabolic derangements, manifesting as altered mental status (AMS), renal insufficiency and cardiac arrhythmias. We present a case of hyperparathyroid crisis in the setting of an occult ectopic parathyroid adenoma.

Case: 75 year old female with a medical history of osteoporosis, hypertension and Parkinson's disease, presented to our hospital with AMS and one week history of diarrhea. She was recently hospitalized for pneumonia and treated with antibiotics. Biochemical analysis revealed corrected s.Ca 15.4mg/dL (8.2- 9.6mg/dL; 7 days prior s.Ca was 9.7mg/dL), renal insufficiency (Cr 2.26mg/dL; baseline 1.2) with normal serum phosphorus, magnesium, 25-hydroxyvitamin D and alkaline phosphatase. PTH was found to be elevated at 75pg/mL (15-65pg/mL). She was treated with aggressive intravenous hydration and calcitonin 200mg BID for 3 days. Her s.Ca appropriately trended down. However, her PTH level continued to rise: 319pg/mL 12 hours later, 591pg/mL on day 2 and peaked to 1,242pg/mL on day 3. CT angiography neck showed an incidental finding of a heterogeneous, possibly necrotic, soft tissue nodule in the left paraesophageal region. Additional work-up with technetium 99 Sestamibi scan revealed persistent activity in the upper tracheoesophageal groove consistent with an ectopic PA. She underwent parathyroid exploration with excision of an enlarged ectopic left superior parathyroid adenoma, confirmed on histopathological analysis. The remaining parathyroid glands were normal. PTH declined to 34pg/mL postoperatively. Her mental status improved significantly returning to baseline within a few days with normal PTH and s.Ca levels.

Discussion: Secretion of PTH is mediated by s.Ca via the calcium sensing receptors (CaSR). Studies have shown that patients with PA
have decreased expression of the CaSR leading to an autonomous rise in PTH secretion and a higher PTH-calcium set point. In our case, the patient initially presented with a mildly elevated PTH level and symptomatic hypercalcemia. The rapid correction of s.Ca levels precipitated a remarkable rise in PTH levels. We postulate that this was caused by a possible upregulation mechanism in calcium sensing by adenomatous parathyroid tissue that is responsive to acute lowering of s.Ca levels, triggering a hyperparathyroid crisis.

Reference: (1) Corbetta S., et al. Calcium-sensing receptor expression and signaling in human parathyroid adenomas and primary hyperplasia. Clinical Endocrinology. 2000; 52(3):339-48.

Bone and Mineral Metabolism

OSTEOPOROSIS: DIAGNOSIS AND CLINICAL ASPECTS

Unilateral Primary Aldosteronism as an Independent Risk Factor for Vertebral Fracture

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SUN-378

Unilateral Primary Aldosteronism as an Independent Risk Factor for Vertebral Fracture

Summary

Context: Primary aldosteronism (PA) is known to increase vertebral fracture (VF), although the detailed mechanism remains to be elucidated. PA consists of two subtypes: the unilateral and bilateral subtype. Patients with unilateral PA, who usually have a higher plasma aldosterone concentration than those with bilateral PA, exhibit a more severe clinical phenotype. We hypothesized that PA subtype affects the prevalence of VF.

Objective: To evaluate whether unilateral PA is associated with the prevalence of VF.

Design: Cross-sectional study in a single referral center.

Patients: We identified 210 hypertensive patients whose clinical data were available for case-detection results. One hundred and fifty-two patients were diagnosed with PA using captopril challenge tests.

Measurements: The prevalence of VF according to PA subtype.

Results: We included 113 patients with PA who were subtype classified according to adrenal vein sampling, of whom 37 patients had unilateral PA and 76 patients had bilateral PA, whereas 58 patients had non-PA. We excluded 39 patients with PA who were not subtype classified. Patients with PA had a higher prevalence of VF (28% [32/113]) than those with non-PA (12% [7/58]; $p = 0.020$). Moreover, unilateral PA had a higher prevalence of VF (46% [17/37]) than bilateral PA (20% [15/76]; $p = 0.021$). There was no significant difference between bilateral PA and non-PA. Unilateral PA was an independent risk factor for VF after adjusting for age and sex (odds ratio, 3.16; 95% confidence interval, 1.12-8.92; $p = 0.017$). Among patients with unilateral PA, serum cortisol concentrations after 1 mg dexamethasone suppression test were higher in those with VF (1.32 ± 0.67 g/dl) than those without (0.96 ± 0.33 g/dl; $p = 0.048$).

Conclusions: Unilateral PA is an independent risk factor for VF, which is associated with autonomous