manifestations were also noted, such as psychological presentations and incontinence.

Adrenal

ADRENAL CASE REPORTS II

Case of Non-Classic Congenital Adrenal Hyperplasia with Compound CYP21A2 Mutations Combined with CYP11B1 Mutation

Rami Salameh, MD, Janna Prater, MD.
Einstein Medical Center, Philadelphia, PA, USA.

SUN-204

Introduction:
Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder, caused by a deficiency in one of the enzymes involved in adrenal steroid synthesis. Homozygotes usually have a severe classical CAH phenotype. Heterozygotes, carrying only one abnormal copy of the gene, are thought to be generally asymptomatic, although could be associated with hyperandrogenism, decreased fertility, adrenal incidentalomas.
21-hydroxylase deficiency (21OHD) accounts for 90% of all CAH cases, while 11 β-hydroxylase deficiency (11OHD) accounts for 4–8% of CAH cases.
The nature and mechanism of a combined enzymatic defect are unknown. The coincidental presence of gene mutation for both 21OHD and 11OHD CAH in a single individual is very unlikely to occur.
Clinical case:
A 22-year old female with no significant past medical history presented to endocrinologist for evaluation of facial hirsutism.
Patient had menarche at age 11, and menstrual cycle was regular since. No concerns for virilization of external genitalia. She was not sexually active, no pregnancies. No Family history of infertility or genetic conditions. Patient's father was Jewish, and mother was Slavic.
Physical examination revealed female phenotype, normal Blood pressure and BMI, acne on the back and upper arm, Ferriman-Gallwey hirsutism score 5.
Labs: AM cortisol, CMP, CBC and TSH were normal. Total testosterone **68** ng/dL (2–45), free testosterone **7** pg/mL (0.1 - 6.4), FSH 5.7 mIU/mL (2.5–10.2), LH 10.6 mIU/mL (1.9–12.5), Progesterone **2.1** ng/mL (<1), Estradiol 51 pg/mL (19–144), 17-OH Progesterone **6728** ng/dL (45–285), Androstenedione **710** ng/dL (35–250), DHEA **1216** ng/dL (102 - 1185), 11-Deoxycortisol **204** ng/dL (<107), Pregnenolone **661** ng/dL(22–237), DHEAS **435** ng/dL (18–391).
Elevated 11-Deoxycortisol level raised a suspicion for 11-OHD CAH, or adrenal vs ovarian hormone-producing mass.
Abdominal CT and pelvic US were negative for adrenal or ovarian masses.
3-day dexamethasone suppression test completely normalized all biochemical abnormalities the patient had.
Genetic testing showed: CYP21A2 c.844G>T (non-classic 21OHD CAH mutation), CYP21A2 c.923dupT (classic 21OHD CAH mutation), CYP11B1 c.953C>G mutation.
Thus diagnosis of non-classic 21OHD CAH, and carrier status of 11OHD CAH was made. She was started on oral Dexamethasone 0.25 mg every other day.
11-Deoxycortisol elevation could not be explained by 21OHD alone. Her carrier state of the CYP11B1 mutation also cannot cause elevated 11-Deoxycortisol level.
We hypothesize that 11-Deoxycortisol was elevated either from extra adrenal conversion of 17-hydroprogesterone to 11-Deoxycortisol, or from 11 β-hydroxylase inhibition by excess intra-adrenal androgens.
Conclusion: Our case reports a rare finding of both CYP21A2 and CYP11B1 mutations in the same individual, which has implications for relatives, family planning and partner genetic screening.

Bone and Mineral Metabolism

NEW FRONTIERS IN BONE AND MINERAL METABOLISM

Burosumab Improves Biochemical, Skeletal, and Clinical Features of Tumor-Induced Osteomalacia Syndrome

Thomas O. Carpenter, MD[1], Paul D. Miller, MD[2], Thomas J. Weber, MD[3], Munro Peacock, MD[4], Karl L. Insogna, MD[1], Rajiv Kumar, MD[5], Diana Luca, PhD[6], Tricia Cimms, MPH[6], Mary Scott Roberts, MD[6], Suzanne Jan de Beur, MD[7].
[1]Yale Univ Schl of Med, New Haven, CT, USA, [2]Colorado Center for Bone Research, Lakewood, CT, USA, [3]Duke University, Durham, NC, USA, [4]Indiana University School of Medicine, Indianapolis, IN, USA, [5]Mayo Clinic College of Medicine, Rochester, NY, USA, [6]Ultragenyx Pharmaceutical Inc., Novato, CA, USA, [7]Johns Hopkins University School of Medicine, Baltimore, MD, USA.

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Tumor-induced Osteomalacia (TIO) is a rare condition in which excess FGF23 produced by a tumor leads to renal phosphate wasting, impaired $1,25(OH)_2D$ synthesis, osteomalacia, fractures, weakness, fatigue, and decreased mobility. In an ongoing open-label Phase 2 study (NCT02304367), 17 adults with TIO or cutaneous skeletal hypophosphatemia syndrome (CSHS) were enrolled and received burosumab, a fully human monoclonal antibody against FGF23. Key endpoints were changes in serum phosphorus and osteomalacia as assessed from trans-iliac crest bone biopsies. This report excludes 3/17 subjects who did not have TIO: 2 subjects diagnosed with X-linked hypophosphatemia post-enrollment and 1 subject with CSHS. Serum phosphorus increased from baseline (BL; 1.60 mg/dL) and was maintained after titration, from Week (W) 22 (2.85 mg/dL, dosing cycle midpoint) to W144 (2.56 mg/dL, dosing cycle endpoint, $p<0.0001$). Serum TmP/GFR and $1,25(OH)_2D$ also increased with burosumab. Eleven subjects underwent paired bone biopsies at BL and W48. Osteoid volume/bone volume decreased from a mean ± SE of 17.6% ± 5.9% at BL to 12.1% ± 4.7% at W48 ($p=0.086$). Mean ± SE osteoid thickness decreased from 16.5 ± 3.6 μm to 11.3 ± 2.8 μm ($p<0.05$). Using imputation (Dempster et al. 2012), mineralization lag time decreased from a mean ± SE of 1598 ± 420 days to 1032 ± 712 days ($p=0.41$). Osteoid surface/bone surface showed no change from BL (mean ± SE BL: 57% ± 9%, W48: 57% ± 7%). Of 249 areas identified with increased uptake on bone scan at BL, 68 (27%) and 81 (33%) were fully healed at W96 and W144, respectively; 56 (23%) and 32 (13%) were partially healed at W96 and W144, respectively. Mean (SD)

Global Fatigue Score decreased from 5.6 (2.5) at BL to 3.5 (3.0) at W48, and to 3.8 (2.2) at W144 (both p<0.01). All 3 domains of the Brief Pain Inventory decreased with burosumab (W144 Pain Severity and Pain Interference p<0.05), indicating reduced pain. The SF-36 mean (SD) physical component summary score increased from 33 (10) at BL to 39 (10) at W48 (p<0.05) and to 41 (12) at W144 (p<0.01), indicating improved physical functioning. The mean (SD) number of sit-to-stand repetitions, an assessment of proximal muscle function, increased from 6.7 (4.2) at BL to 8.5 (4.2) at W48 (n=10; p<0.01). All subjects had ≥1 adverse event (AE). Two subjects discontinued: 1 to undergo chemotherapy to treat an AE of neoplasm progression and 1 failed to meet serum phosphorus dosing criteria and therefore received minimal burosumab dosing. There were 16 serious AEs in 7 subjects, all unrelated to drug. Of the 6 subjects with a serious AE of tumor progression/compression, 5 had a history of tumor progression prior to enrollment. There was 1 death, considered unrelated to treatment. In adults with TIO Syndrome, burosumab was associated with improvements in phosphate metabolism, osteomalacia, skeletal metabolism/fracture healing, physical functioning, fatigue, pain, and quality of life.

Cardiovascular Endocrinology

PATHOPHYSIOLOGY OF CARDIOMETABOLIC DISEASE

Elevation of Serum Kisspeptin in Hypertensive Women

Yanint Raksadawan, MD.[1], Chantacha Sitticharoon, MD., PhD[1], Peerada Boonpuan, Msc[2], Pailin Maikaew, Bsc[1], Issarawan Keadkraichaiwat, Bsc[1].

[1]Mahidol University, Faculty of Medicine, Siriraj Hospital, Bangkok, Thailand, [2]Faculty of Pharmaceutical Sciences, Burapha University, Chonburi, Thailand.

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Kisspeptin and leptin have been shown to have an effect on the cardiovascular system. This study aimed to compare serum kisspeptin and leptin levels between the non-hypertensive (non-HT) and the hypertensive (HT) groups with or without body mass index matching, and determine correlations between systolic blood pressure or diastolic blood pressure with serum kisspeptin and leptin levels as well as clinical and adipocyte parameters. 30 female patients who underwent abdominal surgery were recruited. Blood samples, anthropometric data, and tissue samples of visceral and subcutaneous fat were obtained. Serum kisspeptin levels (ng/ml) (non-HT=1.01±0.1 vs. HT=1.53±0.19), body weight (kg) (non-HT=55.45±3.37 vs. HT=63.69±2.42), waist circumference (cm) (non-HT=78.01±2.49 vs. HT=84.89±2.40), hip circumference (cm) (non-HT=92.94±2.18 vs. HT=99.43±1.85), plasma glucose (mg/ml) (non-HT=55.45±3.37 vs. HT=63.69±2.42), plasma insulin (μM/ml) (non-HT=4.64±0.92 vs. HT=7.13±0.85), the homeostatic model assessment for insulin resistance (HOMA-IR) (non-HT=0.94±0.20 vs. HT=1.72±0.22), and height of visceral adipocytes (μm) (non-HT=72.64±6.75 vs. HT=90.25±4.52) were significantly higher but the quantitative insulin sensitivity check index (QUICKI) (non-HT=0.41±0.01 vs. HT=0.36±0.01) was significantly lower in hypertensive compared to non-hypertensive subjects (p<0.05 all). Systolic blood pressure had significantly positive correlations with diastolic blood pressure
(R=0.568), glucose (R=0.526), the HOMA-IR (R=0.387), and serum kisspeptin (R=0.569), but has a significantly negative correlation with the QUICKI (R=-0.414). Diastolic blood pressure had positive correlations with body weight (R=0.477), waist circumference (R=0.517), hip circumference (R=0.578), glucose (R=0.533), the HOMA-IR (R=0.415), and width (R=0.436) and height (R=0.439) of visceral adipocytes, but has a negative correlation with the QUICKI (R= -0.464). In conclusion, kisspeptin, obesity especially visceral adiposity, and insulin resistance might contribute to increased blood pressure in hypertensive subjects.

Thyroid

THYROID DISORDERS CASE REPORTS I

A Case of T3 Thyrotoxicosis

Isabelle Daneault Peloquin, Resident Doctor[1], Matthieu St-Jean, MD[2].

[1]Université de Sherbrooke, Rosemre, QC, Canada, [2]Université de Sherbrooke, Sherbrooke, QC, Canada.

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Clinical vignette ENDOCRINE SOCIETY 2020
Title: A case of T3 thyrotoxicosis induced by a dietary supplement.
A 24 yo man consulted for a 2 weeks history of diaphoresis, fatigue, insomnia, palpitations and headache associated with a 20 pounds lost. The patient didn't have a goiter or any signs of orbitopathy.
The results revealed a free T3 level of 45.8 pmol/L upon arrival (normal (N) 3.4- 6.8 pmol/L), free T4 level of 6.4 pmol/L (N 11.0–22.0 pmol/L) and TSH level less than 0.005 mUI/L (N: 0.35 to 3.50 mUI/L). Facing those results, a complete review of the patient medication and natural product consumption was done. The patient revealed that he was using, since a month, a vegetable extracts nutritional supplement that didn't included iodine. He was asked to stop the nutritional supplement and propranolol 10 mg twice daily was prescribed. Thyroid function tests were done 3 days after. The results demonstrate a fT3 level of 4.6 pmol/L, a fT4 level of 5.6 pmol/L and a TSH that still suppressed. A thyroid scintigraphy was performed 7 days later and showed a homogeneous uptake of 18.5% (N 7.0% – 35.0%). We saw the patient 2 weeks later and we ordered another thyroid function test with TSH receptor antibodies, TPO antibodies and thyroglobulin. The results were the following: fT3 of 5.1 pmol/L, fT4 of 12.1 pmol/L, TSH of 2.31 mUI/L, thyroglobulin of 19.8 ug/L (N: 1.4 – 78) and normal levels of antibodies against TPO and TSH receptors. To confirm the contamination of the nutritional supplement by fT3 we used a plasma pool of normal patients in which we measured thyroid function tests at baseline and after we have added the nutritional supplement powder to reflect the dose suggested by the manufacturer. The results showed that fT3 level increased by 36.5%, fT4 by 11.2% and TSH didn't changed. The powder was then analyzed by an external laboratory that wasn't able to demonstrate the presence of fT3 nor fT4. The two diagnostic possibility facing those results were that the powder induced an interference