

Reproductive Endocrinology

CLINICAL STUDIES IN FEMALE REPRODUCTION I

Elevated Testosterone Secondary to Leydig Cell Hyperplasia in Bilateral Ovaries

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SAT-LB2

Elevated testosterone secondary to Leydig cell hyperplasia in bilateral ovaries

Background: Postmenopausal hyperandrogenism can be caused by androgen use, ovarian hyperthecosis, ovarian neoplasms, and adrenal neoplasms. **Clinical case:** A 64 year old postmenopausal woman presented for evaluation of hirsutism. She had developed generalized hair loss, terminal hairs on face and chest, and new onset acne after discontinuing hormone replacement therapy. During workup for hirsutism, she was found to have elevated testosterone at 119 ng/dL (reference range: 2-45 ng/dL). Other hormonal evaluation came back within normal limits, with DHEA sulfate <15 mcg/dL (reference range <186 mcg/dL), estradiol 25 pg/ml (reference range <12-32 pg/ml), FSH 34.9 mIU/ml (reference range 23-116.3 mIU/ml), and LH 30.1 mIU/ml (reference range 15.9-54 mIU/ml). Transvaginal ultrasound did not reveal any abnormal adnexal masses. CT abdomen showed a 1.0 cm nodule in the left adrenal gland consistent with a lipid rich adenoma. Further work up showed a normal 24 hour urine free cortisol at 25 ug/24h (reference range: 4-50 ug/24h), normal 24 hour urine metanephrines at 709 ug/24h (reference range: 224-832 uh/24h), normal aldosterone at 13 ng/dL (reference range <21 ng/dl) and renin at 0.37 ng/mL/h (reference range 0.25-5.82 ng/mL/h). MRI of the adrenal glands showed a slightly lobular left adrenal gland and no discrete adrenal mass. MRI of the pelvis showed mildly prominent ovaries bilaterally, but no adnexal or ovarian masses. After repeat laboratory testing showed consistently elevated testosterone levels up to 170 ng/dl and symptoms of hyperandrogenism persisted, the patient underwent bilateral salpingo-oophorectomy. Testosterone level post-operatively dropped to 18 ng/dl and remained within normal limits on repeated measurements. Her symptoms of hyperandrogenism resolved over the next several months. Surgical pathology showed endosalpingiosis, benign paratubal cysts, and confluent aggregates of Leydig cell hyperplasia in bilateral ovaries. **Conclusion:** Leydig cell hyperplasia is a rare cause of hypertestosteronemia that may be considered in patients with negative work up for alternative etiologies for post-menopausal hirsutism.

Diabetes Mellitus and Glucose Metabolism

METABOLIC INTERACTIONS IN DIABETES

Nifedipine Worsens Glucose Tolerance in C57BL/6J Mice Exposed to Intermittent Hypoxia

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SUN-LB121

Background: Intermittent hypoxemia (IH), a pathogenic component of obstructive sleep apnea (OSA), has been independently associated with development of glucose intolerance, insulin resistance, and type 2 diabetes. L-type calcium channel blockers (CCB) influence glucose homeostasis including insulin sensitivity and secretion. To date, the potential impact of the combined effects of L-type CCB and IH on fasting glycemia and glucose tolerance have not been examined. The objective of this study was to determine whether CCB alters glucose metabolism in a murine model of IH. **Methods:** Adult male C57BL6/J mice (age 19-week-old) were exposed to IH using an automated system with specially-modified cages that oscillated FiO₂ from 21% to 5.5% at a target rate of 60 events/h during a 12 h (7am – 7pm) light cycle to simulate severe OSA for 5 days. The L-type CCB, nifedipine, or vehicle (polyethyleneglycol-400) were administered at a dose of 20mg/kg/day via subcutaneous osmotic pumps (Alzet model 2001). Mice were exposed to IH or intermittent air (IA) with four resulting groups: IA-vehicle (n=12), IH-vehicle (n=16), IA-nifedipine (n=10), and IH-nifedipine (n=13). Fasting glucose, intraperitoneal glucose tolerance test, and insulin levels were obtained after exposures. **Results:** In the absence of a L-type CCB, IH increased fasting (105.1 vs. 71.2 mg/dL; p<0.001) and 2-hour glucose levels (104.8 vs. 82.0 mg/dL; p=0.003). The area under the glucose tolerance curve (AUC) was also higher with IH than IA in mice treated with vehicle (17896.3 vs.13965.8 mg-min/dL; p<0.001). Although the effects of IH on fasting glucose levels were comparable with and without L-type CCB treatment, the 2-hour glucose levels and the AUCs were substantially different. A statistically significant interaction was noted for the 2-hr glucose levels between IH and treatment with a L-type CCB (IH-CCB: 193.7; IH-V: 122.6; IA-CCB: 103.5; and IA-V: 82.0 mg/dL; p<0.05 for interaction between IH and CCB). Finally, the AUC for IH-CCB treated mice was significantly higher than the AUC for IH-V treated mice (IH-CCB: 30223.1; IH-V: 17896.3. mg-min/dL; p=0.0001) **Conclusions:** In a murine model of IH, treatment with an L-type CCB exacerbates the deleterious effects of IH on glucose tolerance. Thus, use of CCB in patients with OSA should take into consideration these unfavorable effects particularly in those who are metabolically compromised.

Thyroid

THYROID NEOPLASIA AND CANCER

Recombinant Human TSH vs Thyroid Hormone Withdrawal Preparation for Radioiodine Ablation in Pediatric Differentiated Thyroid Cancer

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MON-LB87

Introduction: Recombinant human TSH (rhTSH) is commonly used to prepare patients with differentiated thyroid cancer (DTC) for radioiodine (I-131) ablation after total thyroidectomy (TT). In adults, rhTSH is associated with equivalent oncologic efficacy and improved health-related quality of life in comparison to thyroid hormone withdrawal (THW). In this study, we aimed to measure disease-free survival after rhTSH stimulation vs. THW in pediatric patients with DTC. **Methods:** A prospective database was analyzed for pediatric patients under the age of 21 with DTC who underwent TT and I-131 ablation with rhTSH preparation at a single tertiary institution from 2012 through 2018. These patients were compared against historical controls prepared with THW. Tumor stage, I-131 treatment details, disease-free survival, structural recurrence, biochemical recurrence (defined as serum Tg > 2 at one year), and postoperative serum TSH, thyroglobulin (Tg) and Tg antibody levels were recorded. The log-rank test was used to compare groups, and time to recurrence was estimated by Kaplan-Meier analysis. **Results:** Seventeen patients who received rhTSH (mean age, 16.6±3.2 [SD] years) were compared to 28 historical controls prepared with THW. No differences were observed in RAI dose (mean 2.3±0.7 mCi/kg), tumor stage, or follow-up time (median [IQR] 2.6 [1.1-3.1] years) between groups. The THW group exhibited a nonsignificantly greater recurrence rate (14 [50%], 7 with biochemical recurrence and 7 with structural recurrence) than the rhTSH group (three [18%], 2 with biochemical recurrence and 1 with structural recurrence, p=0.2). A trend toward improved disease-free survival was identified in those treated with rhTSH compared to THW. **Conclusion:** In this cohort of pediatric patients with DTC, we observed a trend toward improved disease-free survival among those prepared with rhTSH compared to historical controls prepared with THW. Long-term follow up is needed to better characterize outcomes associated with rhTSH stimulation prior to I-131 ablation in the pediatric population.

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS II

Pulmonary Embolism in the Setting of Diabetic Ketoacidosis, an Under-Recognized Complication.

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MON-LB127

The relation between Diabetic Ketoacidosis and Venous Thromboembolism is important to appreciate for early recognition and management. 90 year old female with Type 2 DM was brought to the ER after a syncopal episode. Family reported the patient to be lethargic with a decreased appetite for one week. On arrival, patient had a blood pressure

of 84/44 mmHg. Oxygen saturation was 89% at room air and improved to 93% on supplemental O₂. Patient was afebrile with a respiratory rate of 16 and heart rate 89/minute. On exam, she was dehydrated with decreased skin turgor, dry oral mucosa. Labs revealed blood glucose of 621 mg/dL, Bicarbonate 16 mmol/L, B-Hydroxybutyrate 5.00 mmol/L, Anion Gap 21, pH of 7.26 on ABG. Urinalysis was suggestive of a urinary tract infection. After initiation of IV antibiotics and insulin, she was transferred to the intensive care unit. In the ICU, her blood pressure failed to improve with fluid resuscitation, ultimately requiring vasopressors. Due to hypotension with hypoxia, CT Chest was performed which revealed extensive bilateral PE. She was started on IV heparin infusion. Pro-Brain Natriuretic Peptide was elevated at 4,716 pg/mL. Echocardiogram confirmed right heart strain with severely dilated right ventricle, positive McConnell's sign, systolic and diastolic septal flattening and an estimated RSV 67mmHg consistent with moderately severe pulmonary hypertension. Tissue plasminogen activator was recommended however given the patient's age and functional status; family decided against systemic thrombolysis. Duplex ultrasound of her lower extremities also showed bilateral acute deep venous thrombosis. She was continued on intravenous anticoagulation and eventually was able to come off vasopressors. As the patient's blood glucose levels improved and her anion gap closed, she was transitioned to basal/bolus insulin and transferred to the general medical floor. She was started on Apixaban and discharged home per family's request after her code status was changed to DNR-Comfort Care Arrest. Pulmonary embolism is a serious venous thromboembolic event that is rarely reported in association with DKA. Proposed mechanisms include some of the same mechanisms implicated in arterial thrombosis, namely abnormalities in coagulation factors, increased platelet aggregation, impaired fibrinolysis and endothelial injury due to hypertonicity. Also, severe dehydration associated with DKA may contribute by virtue of increased red blood cell rigidity and increased blood viscosity establishing DKA as an underlying cause or contributing factor of pulmonary thromboembolism².¹ Langevin C et al Presumed paradoxical embolus in a patient with diabetic ketoacidosis Int J Gen Med 2015;8:297–301 2015 Sep 18

² Scordi Bello I et al Fatal Pulmonary Thromboembolism in Patients with Diabetic Ketoacidosis A Seven-Case Series and Review of the Literature Acad Forensic Pathol 2016;6(2):198–205

Bone and Mineral Metabolism

PARATHYROID HORMONE TRANSLATIONAL AND CLINICAL ASPECTS

Design of the PaTH Forward Phase 2 Trial of TransCon PTH, a Long-Acting PTH, in Patients With Hypoparathyroidism

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