warfarin to rivaroxaban for anticoagulation, who presented to the ED after a syncopal episode following a prior episode of abdominal pain with an unremarkable work-up. He subsequently developed severe fatigue, dizziness, headaches, nausea and 15 lbs weight loss. On presentation, the patient was hypotensive(72/45 mmHg) and tachycardic. Intravenous hydration was started with minimal response. Initial laboratory testing showed serum sodium of 121mmol/L, potassium of 5.5mmol/L and random cortisol of 0.8mcg/dL. The patient was admitted to the intensive care unit where he was started on vasopressors and hydrocortisone 50 mg IV every 8 hours. A non-contrast CT of the abdomen and pelvis showed thickening of the adrenal glands with decreased attenuation. MRI of the abdomen showed hyper-intensity of the adrenal glands bilaterally (T1 images), without post-contrast enhancement suggestive of bilateral adrenal hemorrhage. His electrolytes normalized, and he was successfully discharged home on hydrocortisone and fludrocortisone replacement with outpatient follow-up.
Discussion: Atraumatic bilateral adrenal hemorrhage is rare, but remains one of the most common endocrine-related complications of antiphospholipid syndrome (APLS). The venous anatomical configuration of the adrenal gland increases risk of thrombotic hemorrhagic infarction[1]. Patients with APLS are commonly anticoagulated to prevent thrombosis. The ideal anticoagulation regimen remains controversial. Only three other cases of spontaneous bilateral adrenal hemorrhage on patients with APLS using new oral anticoagulants (NOACs) were reported. The use of NOACs seem to increase the already-elevated risk of adrenal hemorrhage seen in patients with APLS.
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Thyroid

THYROID NEOPLASIA AND CANCER

Impact of Nodule Size on the Probability of Hurthle Cell Carcinoma and Other Cancers in Thyroid Nodules with Multiple Chromosomal Copy Number Alterations

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OR21-02

Fine-needle aspiration (FNA) of thyroid nodules yields indeterminate cytological diagnosis in ~20% of cases, confounding patient management. This includes Hurthle cell nodules, which typically yield Bethesda IV and III cytology. Chromosomal copy number alterations (CNA) are known to occur in thyroid tumors, particularly in Hurthle cell carcinomas (HCC) as well as in other typically follicular-patterned tumors including papillary thyroid carcinomas (PTC) and poorly differentiated thyroid carcinomas (PDTC). The aim of this study was to evaluate thyroid nodules tested positive for CNA but negative for all other genomic alterations using ThyroSeq v3 NGS assay in order to establish the probability of cancer in these nodules and find whether it is influenced by the pattern of CNA and nodule size. We evaluated 111 nodules with multiple CNA detected by ThyroSeq in FNA samples and available surgical pathology outcome. Of those, 69 (62%) nodules showed CNA changes consistent with genome near-haploidization (GNH) whereas 42 (38%) nodules had multiple chromosomal losses and gains (CLG). Nodule size ranged from 0.5-10.2 cm; cytology was Bethesda III in 54%, Bethesda IV in 43%, and Bethesda V-VI in 3% of cases, with Hurthle cells mentioned in the cytology report in 64% of cases. On surgical pathology, 38 (34%) of these nodules were malignant (including 24 HCC, 8 PTC, and 5 oncocytic PDTC) and 73 (66%) were benign (including 43 Hurthle cell and 18 follicular adenomas). No significant difference was observed in probability of malignancy between the two patterns of CNA (p=0.41). However, a significant correlation between the nodule size and probability of cancer was found (p=0.006). In specific CNA groups, correlation between cancer and nodule size remained significant for nodules with GNH pattern (P=0.0002), but not with CLG pattern (p=0.449). Specifically, cancer probability in nodules with GNH pattern and <2 cm in size was 14% (all cancers minimally-invasive), 2.0-2.9 cm was 33%, 3.0-3.9 cm was 50%, 4-4.9 cm was 67%, and ≥5 cm was 80%. Among high-risk cancers (widely-invasive or angioinvasive HCC, PDTC), all 10 tumors had the GNH pattern (p=0.01) and average nodule size of 4.9 cm (range, 2.1-8.5 cm). These findings suggest that CNA of both types are frequently found in Hurthle cell tumors, and probability of cancer in nodules with CNA and no other mutations increases with larger nodule size. This may help to refine the pre-operative assessment of cancer probability and risk of more aggressive disease and offer more tailored management to these patients.

Reproductive Endocrinology

CLINICAL STUDIES IN FEMALE REPRODUCTION I

Fluoxetine Administration Influences Serotonin-Driven Bone Remodeling During Lactation and Pregnancy Outcome in Mice

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SAT-020

Selective serotonin reuptake inhibitors (SSRI) are the most commonly prescribed class of antidepressants during pregnancy and lactation. SSRI decrease bone mineral density (BMD) across all ages and sexes. Lactation is also characterized by increased bone resorption to mobilize calcium due to the demands of lactation and achieves this via a serotonin-induced hormonal cascade. This serotonin-mediated bone loss is normally restored after weaning but is persistent when an SSRI is administered during

the peripartum period. We hypothesize that the long-term BMD loss associated with fluoxetine administration during lactation will be seen in two sequential lactations and will have a more dramatic effect on maternal bone loss after the second lactation at both weaning and 3 months post-weaning. Female C57BL/6 mice were randomized to receive the SSRI fluoxetine hydrochloride (20 mg/kg) or saline daily from the beginning of pregnancy (E0), determined by the presence of a vaginal mucous plug, through the end of lactation (D21). They were then given a 3-week rest period before undergoing a second lactation with the same study design. Each group is paired to an age-matched virgin cohort to provide a non-lactating control. This created the following treatments: saline dam (S), fluoxetine dam (F), saline virgin pair (SV), and fluoxetine virgin pair (FV). Dual-energy X-ray absorptiometry (DEXA) was used to measure BMD of all groups throughout the peripartum period. At the end of gestation (E17.5), BMD was decreased in both the F and FV groups, and the BMD of the FV group remained persistently lower than the SV group across all timepoints. Both the F and S groups exhibited a dramatic decrease in BMD between E17.5 and the beginning of lactation (D2), then a slight increase between mid-lactation (D10) and at weaning (D21). There was an overall interaction between treatment and time for all groups across the peripartum period ($p<0.0001$). During the first peripartum period, the F dams that were mated had significantly increased pregnancy loss ($p=0.0041$) and pup mortality post-parturition compared to S mice. Of the dams that were inseminated, determined by the presence of a mucus plug, 63% of successfully mated S dams (n=19) resulted in a full-term pregnancy. Of those S dams (n=12), 25% lost their entire litter at the beginning of lactation, and 75% maintained their litter until weaning. In the F dams that were successfully mated (n=37), only 35% resulted in a full-term pregnancy. We conclude that fluoxetine administration during the peripartum period decreases long-term maternal BMD and that fluoxetine exhibits a drug-specific effect on the dam resulting in a notably decreased incidence of a successful pregnancy.

Adrenal

ADRENAL - CORTISOL EXCESS AND DEFICIENCIES

Prevalence and Assessment of Overnight Dexamethasone Suppression Tests for Screening Endogenous Hypercortisolism When Serum Dexamethasone Is Below Threshold.

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MON-187

Background: The 1mg-dexamethasone (DXA) suppression test (DST) is used to verify cortisol (F) autonomy in Cushing's syndrome (CS) and subclinical hypercortisolism (SCH) of adrenal incidentalomas (AI), based on the ability of DXA to suppress F by inhibiting the HPA axis. A post-DST serum F >1.8 µg/dL usually defines autonomy. **Aim**: 1) determine the prevalence of invalid tests in a large series of DST used to investigate hypercortisolism during a 12y period in a single institution; 2) assess the percentage of negative tests (normal F suppression) among the subpopulation of invalid DST; 3) examine for interfering substances and clinical conditions that may justify and low DXA levels. **Methods:** DXA-controlled 1mg-DST was carried out in 162 control subjects (Cont; 107F/55M; 20-75y [median 50y]), to determine a valid threshold for serum DXA, and in 768 patients (80% female; 11-91y [median 53y]), investigated from 2007-19, for F autonomy (a total of 1,300 tests, with 41% repetitions). F and DXA were determined by specific RIA. We search our laboratory data bank for "invalid" DST, tests in which post-DST serum DXA values were below the cutoff established from the control subjects. **Results**: we set a cutoff for post-DST serum DXA at 140 ng/dL, the lowest value obtained from controls in whom post-DST serum F levels were < 2.5 µg/dL. From the 1,300 DST examined, 146 (11.2%) were considered invalid (DXA <140 ng/dL), and in 36 of them (25%), DXA was undetectable. Also, 35 DST (25%) gave F results below 1.8 µg/dL. Of all 146 invalid DST, 8 (6%) did not take DXA the night before as directed and 14 (10%) admitted being on glucocorticoids (GC), most of them from the undetectable DXA subgroup. Also, 21 patients (14%) were on anticonvulsants, another 21 (14%) were using other moderate or potent CPY3A4 inducers (phenytoin, rifampicin, efavirenz), and 15 (10%) subjects had gastrointestinal abnormalities (colectomy, colostomy, erosive gastritis and disabsorptive syndromes). **Conclusions**: Test accuracy depends on the serum levels reached by DXA, after adequate ingestion and absorption. Inappropriately low values may result in false-positive test results. One-fourth of "invalid" tests, presented DXA levels below the assay limit of sensitivity, suggesting patient noncompliance. Adherence to verbal and written recommendations and use of medication are essential to interpret the test. Conditions that alter gastric pH, as well as surgical procedures in the GI tract may reduce absorption or accelerate GI transit affecting DXA absorption. DXA metabolism by cytochrome p450 enzymes, mainly CYP3A4, can be enhanced by inducing drugs, making mandatory DXA dosage to validate the test. The wide individual variability in DXA metabolism may be associated not only with environmental and health factors, but also with CYP gene polymorphisms, which can modify drug clearance.

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES

The Barnsley Diabetes Hypogonadal Questionnaire (BDHQ) - Validation for the Clinical Use to Support the Diagnosis of Testosterone Deficiency in Men with Type 2 Diabetes (T2D)

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