high selectivity to MR, which became clinically available in Japan in 2019.
Clinical Case: A 57-year-old woman showed a left adrenal incidentaloma (15mm) on MRI. Serological tests confirmed a diagnosis of primary aldosteronism: baseline plasma aldosterone concentration (PAC) was elevated (47.3 ng/dL, n < 15.9 ng/dL), and plasma renin activity (PRA) below sensitivity. PAC after saline infusion was 43.2 ng/dL. Overnight 1mg dexamethasone suppression test was negative. Her blood pressure had been well-controlled with amlodipine 5mg daily. Despite of large amount of potassium supplementation (96 mmol/day orally and 50 mmol/day intravenously), the level of serum potassium remained low (3.2 mmol/L). Adrenal venous sampling (AVS) was performed successfully, showing laterality index of 45.8 on left. Segmental AVS supported aldosterone hypersecretion from the tumor. After diagnosis, esaxerenone was introduced and the patient became normokalemic without potassium supplementation after a week. No adverse effect occurred in a period of two months before surgery. She underwent laparoscopic left total adrenalectomy. The tumor was positive for CYP11B2, consistent with aldosterone producing adenoma (APA). She became normotensive and normokalemic without any medications.
Conclusion: This case illustrates the preoperative effectiveness of esaxerenone on blood pressure and hypokalemia in patients with APA.
Key words: Esaxerenone; mineralocorticoid receptor antagonist; case report; adrenal venous sampling; primary aldosteronism; aldosterone producing adenoma

Tumor Biology

TUMOR BIOLOGY: DIAGNOSTICS, THERAPIES, ENDOCRINE NEOPLASIAS, AND HORMONE DEPENDENT TUMORS

Clinico-Pathological Features, Treatment Modalities and Survival of Patients with Malignant Insulinoma: A Multicenter Study

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SUN-136

Introduction: management of malignant insulinoma is challenging due to the need to control both hypoglycemic syndrome and tumor growth. Literature data is limited to small series.
Aim of the study: to analyze clinical-pathological characteristics, treatment modalities and prognosis of patients with malignant insulinoma.
Materials and methods: Multicenter retrospective study on 31 patients (M 61.3%) diagnosed between 1988 and 2017.
Results: The mean age at diagnosis was 48 ± 15 years. In 5 cases (16.1%) the hypoglycemic syndrome occurred after 46 ± 35 months from the diagnosis of NET, in 26 (83.9%) cases it led to the diagnosis of NET, of which 11 cases (42.3%) with mean diagnostic delay of 32.7 ± 39.8 months. The majority of the NET were G2 (70.8 %) and in the pancreatic body-tail (78.6%). The mean NET diameter was 41 ± 31 mm. Metastases were widespread in 40.7%, only hepatic in 37%, only lymph nodal in 18.5%..Surgical treatment was performed in 21/31 (67.7%) with hypoglycemic control in 42.9%. Except for 2 patients with curative surgery, the others underwent further different lines of therapies including somatostatin analogues (SA), Peptide Receptor Radionuclide Therapy (PRRT), everolimus, chemotherapy, TAE/TACE/RFA, radiotherapy. PRRT was performed in 14/31 (45.1%) with complete (42.9 %) or partial (50%) syndrome control.
The median follow-up was 60 months. The 5-year survival rate was 62%. The median overall survival (OS) was 40 months. No significant difference in OS was observed according to the site of primary tumour and its dimension. A trend towards increased survival was found according to grading (5-year OS 100% for G1, 77% for G2, 33% for G3). Patients with Ki-67 ≤ 10% had a significant higher survival rate compared to patient with Ki-67 >10% (5-year OS rate 87% *vs* 43%, p: 0.03). As regards the type of treatment, patients who underwent surgery had a higher survival rate than those who did not (5-year OS 76% vs 31.7%, p= 0.006). Moreover, patients receiving PRRT as II line treatment had a better prognosis than those who underwent it in further lines, although the 5-year OS was not significantly different (80% vs 25% respectively, p=0.057).
Conclusions: Our study includes the largest series of patients with malignant insulinomas up to now reported. The hypoglycemic syndrome may occur after years in initially non-functioning NETs, or be misunderstood with delayed diagnosis of NETs. Surgical treatment and Ki67 <10% are prognostic factors associated with better survival. PPRT seems to be promising in the control of hypoglycemic syndrome.

Neuroendocrinology and Pituitary

HYPOTHALAMIC-PITUITARY DEVELOPMENT AND FUNCTION

Chronic, Excess Growth Hormone Action Alters the Development and Aging of the Microbial Community in the Mouse Gut

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SAT-281

Emerging evidence proposes that the gut microbiome has an vital role in host growth, metabolism and endocrinology.

That is, gut microbes impact growth by potentially altering the growth hormone (GH)/insulin-like growth factor-1 axis. Our previous research has also shown that GH - in states of absence and excess - is associated with altered gut microbial composition, maturity and predictive metabolic function in mice. Moreover, both GH and the gut microbiome are implicated in development and aging. Yet, it is unknown how GH impacts the longitudinal microbiome. This study thus aimed to characterize the longitudinal changes in the gut microbial profile of bovine GH transgenic mice (a model of chronic, excess GH action and accelerated aging). Microbial composition was quantified from fecal pellets of the same bGH and control mice at 3, 6 and 12 months of age through 16S rRNA gene sequencing and QIIME 2. Additional bioinformatic analyses assessed the unique signature and predictive metabolic function of the microbiome. The bGH mice had a distinct microbial profile compared to controls longitudinally. At 3 months, bGH mice had increased Firmicutes and Actinobacteria, decreased Bacteroidetes, Proteobacteria and Campylobacterota, and a significant reduction in microbial richness and evenness. By 6 months, all of the aforesaid phyla were increased with the exception of Firmicutes. By 12 months, bGH mice exhibited dysbiosis with increased Firmicutes and Proteobacteria and reduced Bacteroidetes, microbial richness and evenness. Moreover, abundance in Firmicutes, Bacteroidetes and Campylobacterota were significantly explained by the combined effect of genotype and age ($p = 0.006$, 0.005 and 0.02, respectively). Across all timepoints, bGH mice had a significantly different microbiome compared to controls ($p = 0.002$), and the development of microbial richness and evenness were also significantly different in bGH mice ($p = 0.034$ and 0.023). Bacterial genera *Lactobacillus*, *Ruminococcaceae* and *Lachnospiraceae* were identified as a unique candidates in bGH mice across all timepoints. Likewise, metabolic pathways involved in biosynthesis of heme b, menaquinol, acetate and butyrate differentiated the longitudinal bGH microbiome. Collectively, these results show that chronic, excess GH impacts the development and aging of the gut microbiome. Notably, several of the stated bacterial genera and metabolic pathways were associated with GH in our previous study, suggesting that GH may influence the longitudinal presence of certain gut microbes and metabolic functions. Additional studies will be performed to further explore the GH-associated gut microbiome and its impact on host health. *Research was partially funded by the John J. Kopchick MCB/TBS Fellowship, a fellowship from the Osteopathic Heritage Foundation and the MMPC at UC, Davis (NIH grant U240DK092993).*

Reproductive Endocrinology

FEMALE REPRODUCTION: BASIC MECHANISMS

Peripartum Sertraline (Zoloft®) Increases Pup Mortality Immediately Postpartum

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MON-001

Peripartum and postpartum depression can be detrimental to both the mother and the developing child. Use of antidepressants, such as selective serotonin reuptake inhibitors (SSRIs), is common during the peripartal period and SSRIs have been the leading prescribed antidepressant to treat maternal depression. One of the most commonly prescribed SSRIs is sertraline (Zoloft®) because of the limited fetal teratogenic effects observed, unlike maternal paroxetine (Paxil®) usage which can manifest in fetal cardiovascular defects. Fluoxetine (Prozac®), like sertraline, has previously been shown to have limited teratogenic effects, however, we have shown treatment with fluoxetine for the entire period of pregnancy and lactation in mice compromises pup bones at weaning resulting in decreased long bone length and head circumference. Furthermore, maternal fluoxetine usage results in a sustained reduction in maternal bone mineral density post weaning, which may lead to long-term osteopenia, putting the mother at risk for bone-related disorders later in life. We hypothesized sertraline, like fluoxetine, will compromise maternal bone postpartum and fetal bone development at weaning. Treatment with sertraline in C57BL/6 dams throughout pregnancy and lactation reduced litter size (5.4 pups/dam) and increased pup mortality during the first 24 hours postpartum (20% dead pups/litter) compared to controls (6.8 pups/dam, 5% dead pups/litter, respectively; $P < 0.018$). Maternal calcium transporters (Orai1 and Serca2) were downregulated in the mammary gland in sertraline-treated dams on day 21 of lactation ($P < 0.0032$). Together, our data suggests *in utero* pharmacological exposure to sertraline may induce a failure to thrive in the pups and alters calcium metabolism in the dam. SSRI exposure during pregnancy and lactation may adversely affect the developing neonate(s) as well as have lasting impacts on the mother.

Cardiovascular Endocrinology

PATHOPHYSIOLOGY OF CARDIOMETABOLIC DISEASE

Long-Term Mental Stress Implications to Cardiovascular Disease in an Aged Mouse Model

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SUN-562

While clinical evidence indicates that exposure to mental stress is a linked to a two-fold increased risk for coronary heart disease, even independently from traditional risk factors, the underlying direct mechanisms between psychological stress and cardiovascular health status has not been determined. A growing aging population of adults 65 and older represents a particular patient population vulnerable to chronic mental stressors due to a decline in normal physiologic functions. The decrease in function of the cardiovascular system that occurs during aging leads to the activation of pathological processes associated with