Conclusion:
Elevated ALT can be associated with NAFLD related risk factors. Type 1 diabetics with elevated ALT should be evaluated. And patients with type 1 DM should undergo screening for other autoimmune disease.

Adrenal

ADRENAL PHYSIOLOGY AND DISEASE

Investigating the Role of the Liver X Receptor in Potentiating Mitotane Therapy in Adrenocortical Carcinoma

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SUN-216

Introduction: Adrenocortical Carcinoma is a rare aggressive cancer which carries a poor prognosis. Adjuvant mitotane improves survival but is limited by a narrow therapeutic window and severe adverse effects. Liver X receptors (LXRs), part of the nuclear receptor superfamily are highly expressed in adrenal tissue and mediate transcellular and intracellular cholesterol homeostasis. We hypothesise that LXRα inhibition increases toxic lipid accumulation in adrenocortical cancer cells and potentiates the adrenolytic effect of mitotane. Methodology: ATCC-H295R and MUC1 ACC cells and were pre-treated with the LXRα inverse agonist SR9243 5µM and antagonist GSK2033 5µM followed by mitotane treatment (20, 40, 50µM) for 6 hours. Cholesterol-methyl-β-cyclodextrin treatment was carried out 1hr prior to mitotane. H295R cells were transfected with a LXRα dominant negative construct using lipofectamine. Cell death was assessed using annexin/PI staining and proliferation using MTT assay. Free cholesterol (FC) levels were assayed using filipin staining and lipid droplets via BODIPY® and analysed on the Amnis ImageStream® imaging cytometer. Downstream targets ABCA1 and ABCG1 were evaluated by qRT-PCR. Lipid droplet associated proteins PLIN1-4 and hormone sensitive lipase (HSL) expression were evaluated using western blotting. Results: Downstream reduction of ABCA1 and ABCG1 expression confirmed LXRα blockade. Mitotane effectively induced dose-dependent H295R apoptotic cell death which was potentiated pharmacologically and genetically by LXRα inhibition. In line with these findings, cholesterol-methyl-β-cyclodextrin treatment increased cell death in H295R and MUC1 cells. In addition to inducing cell death, LXRα inhibition decreased proliferation of both cell lines. An increase in FC and a decrease in cholesterol esters was observed following mitotane treatment in H295R cells. This was accompanied by decreased lipid droplet numbers confirmed by lower expression of lipid droplet associated proteins, PLIN1-3. These effects were potentiated when mitotane was combined with LXRα inhibition. We demonstrate increased HSL activity, which was associated with higher SOAT-1 expression and increasing toxic FC accumulation. Investigation of lipid droplet content BODIPY® of both cell lines showed H295R cells preferentially store cholesterol esters and MUC1 cells store triacylglycerides. Conclusion: We propose a mechanism for enhancing mitotane’s efficacy as an adrenolytic through increased free cholesterol via LXRα inhibition. Targeting the LXRα, its putative ligands, or associated lipid mediators may present a novel therapeutic approach in the setting of primary and metastatic ACC.

Adrenal

ADRENAL - HYPERTENSION

Developing a Research Database About Primary Aldosteronism: Rationale and Baseline Characteristics

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MON-197

Introduction There were limited evidence supporting the management of PA, primarily due to lack of high quality of data. Developing a research database through integrate both retrospective and prospective collected data regarding clinical care and outcomes of patients with PA may provide valuable evidence on management of PA. Methods The establishment of PA research database involved two steps. Firstly, patients with confirmation of PA between 1 Jan 2009 to 31 Aug 2019 were identified and data were extracted from EMR. Secondly, patients who have positive confirmatory testing for PA and agree to participant a prospective cohort will be enrolled. Data regarding clinical care and long-term outcomes will be prospectively collected based on the case report forms since 1 Sep 2019. We evaluated the quality of research database through assessment of quality of key variables. Results Totally, 904 patients diagnosed as PA in WCH were identified, of which 507 patients had positive confirmatory testing for PA were finally included into the retrospective database. Among included patients, the mean age was 49.2 years old, and the mean BMI was 24.72 kg/m². There were 37 (3.7%) patients diagnosed as chronic kidney disease (CKD), 13 (2.6%) as coronary artery disease (CAD), 95 (18.7%) as diabetes mellitus (DM) and 77 (15.2%) as obstructive sleep apnea-hypopnea syndrome (OSA). The mean systolic blood pressure (SBP) was 155.8 mmHg, and the mean diastolic blood pressure (DBP) was 96.2 mmHg. Among included patients, the lowest serum potassium during admission was 2.96 mmol/L, and the mean serum aldosterone was 26.4 ng/dL. Validation of data extracting and linking showed the accuracy were 100%. Evaluation of missing data showed that the completeness of BMI (95.9%), SBP (1%) and DBP (1%) were high. Conclusion Through retrospective and prospective cohort of PA, a research database about PA with high quality and comprehensive data will be established. We anticipate that the research
database will provide a high level of feasibility for management of PA in China.

**Neuroendocrinology and Pituitary ADVANCES IN NEUROENDOCRINOLOGY**

**Rescue of Function of Inactivating Mutations in Human GPCRs in the Reproductive Hypothalamic-Pituitary-Gonadal Axis**

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**SUN-252**

Inactivating mutations have been described for human GPCRs at all levels of the reproductive hypothalamic-pituitary-gonadal (HPG) axis which results in reproductive incompetence. The majority of the mutations in GPCRs give rise to misfolding and a failure to traffic to the cell surface. We have interrogated data bases for cell-permeant small molecules which bind to and stabilise the GPCR as it emerges from the endoplasmic reticulum and hence facilitate trafficking of the mutant GPCR to the cell membrane and restoration of function. In this way we have successfully ‘rescued’ function of mutant Neurokinin B, GnRH, LH and FSH receptors using small molecule antagonists which bind orthosterically or agonists which bind allosterically. These discoveries represent an advance towards novel personalized medicine for GPCR deficiencies in the human HPG axis.

**Tumor Biology**

**TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS**

**Ectopic ACTH Secretion Has Varied Presentation and Requires Individualized Treatment - One Size Does Not Fit All**

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**SAT-148**

Ectopic ACTH secretion (EAS) presents in myriad ways. We present five cases of EAS to highlight similarities and differences in presentation and treatment. The first woman with known metastatic lung neuroendocrine tumour (NET) for two years presented with facial fullness, proximal weakness, worsening hypertension and hypokalaemia. Random cortisol of 2742nmol/L (99.39mcg/dL), with adrenocorticotrophic hormone (ACTH) of 201ng/L, was in keeping with EAS. She received medical treatment followed by bilateral adrenalectomy with EAS resolution and development of adrenal insufficiency. She is doing well. The second woman with proximal weakness, worsening hypertension and severe hypokalaemia. Morning cortisol of 188ng/L. He was commenced on medical treatment but declined rapidly and died. The third woman with significant smoking history presented with haemoptysis and breathlessness. A right lung mass was suspected on chest X-ray and confirmed with CT. Endobronchial ultrasound-guided biopsy revealed small cell lung cancer (SCLC). She developed generalised weakness and severe hypokalaemia. Random cortisol of 1645nmol/L (59.63mcg/dL) with ACTH of 282ng/L suggested EAS. Despite medical treatment, she died within two weeks. The fourth woman presented with confusion, hypertension and severe hypokalaemia. Morning cortisol of 8557nmol/L (310.19mcg/dL) and random ACTH of 73ng/L were suggestive of EAS. CT demonstrated left lung mass with widespread metastases. She deteriorated and died within 2 weeks. Our only man had incidentally discovered metastatic liver lesions on ultrasound. Further imaging revealed prostatic mass and biopsy showed small cell neuroendocrine cancer. He presented with severe hypokalaemia. Random cortisol was 1065nmol/L (38.61mcg/dL) and ACTH was 188ng/L. He was commenced on medical treatment but declined rapidly and died.

All our patients had profound hypokalaemia and metastatic disease at presentation. Many patients do not exhibit classical cushingoid features as EAS tends to develop acutely and underlying malignancy drives weight loss. A high index of suspicion is required to make a diagnosis. EAS should be considered in patients with proximal myopathy, pigmentation, resistant or severe hypokalaemia or hypertension and known or suspected malignancy. Early and quick control of cortisol excess is essential to minimise cardiometabolic abnormalities, severe infections and thromboembolic complications. Prognosis depends upon age, frailty, comorbidity, nature of neoplasm and extent of hypercortisolism. Adrenolytics with or without bilateral adrenalectomy, reduction in tumour burden and management of complications are the mainstay of treatment.

**Diabetes Mellitus and Glucose Metabolism**

**DIABETES COMPLICATIONS II**

**Necrotising Fasciitis- Importance of Glycemic Control**

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**MON-697**

Necrotising fasciitis- Importance of glycemic control

Introduction:

Necrotising fasciitis is an infection of the deep soft tissues characterised by fulminant tissue destruction, systemic toxicity and high mortality. We report a case where accurate diagnosis, timely surgical intervention and antibiotic therapy along with strict glycemic control resulted in a favourable outcome.

Case:

A 74 year old woman with a history of type 2 diabetes mellitus, hypertension and end stage renal disease(ESRD) on peritoneal dialysis(PD) presented to the emergency department with the complaint of pain in the right lower quadrant of abdomen, right pelvis and right groin since 4 days which acutely worsened overnight. Of note the patient has Peritoneal catheter for dialysis and was last dialysed last...