SUN-909

The MEN1 gene is positioned on the long arm of chromosome 11 (11q13) and results in the production of menin. A classical tumour suppressor gene; the spectrum of reported germline MEN1 mutations occur throughout the gene with no strong genotype/phenotype relationship. Mosaicism is extremely rare, a recent report citing only 2 mosaic cases by next generation sequencing[1]. We describe a 43-year-old female with MEN1 mosaicism associated with parathyroid adenoma and probable gastrinoma.

Our patient initially presented with nephrolithiasis and nephrocalcinosis alongside biochemistry of primary hyperparathyroidism. Imaging confirmed a right lower pole parathyroid adenoma and the lesion was removed, pathology confirming the diagnosis (July 2018). Post operatively she remained hypercalcaemic. Repeat imaging suggested a further right sided culprit lesion.

One year previously (August 2017) she was admitted with a perforated duodenal ulcer within the first part of the duodenum (D1), ascribed to ibuprofen use, requiring surgical repair. Whilst awaiting repeat parathyroid surgery she represented with a further duodenal ulcer and perforation (February 2019) this time in the second part of the duodenum(D2). A second parathyroidectomy was performed and genetic investigations were instigated, given the presence of classical MEN1 phenotype. Again, pathology was consistent with a parathyroid adenoma (March 2019).

DNA was extracted for next generation sequencing which revealed mosaicism with a c.124 G>A variant detected in the MEN1 gene at a level of approximately 15%.

Further investigations have shown normal serum prolactin and pituitary and pancreatic MRI imaging. With no other family members testing positive (parents and 2/3 children) this mutation appears to be a *de novo* index case. Adjusted Calcium is normal 2.53 mmol/L (2.2-2.6 mmol/L) but serum Chromogranin A is elevated (2620 μg/L (ref range <95 μg/L)).

The c.124 G>A variant predicts an amino acid substitution p.(Gly42Ser) in menin structure, an amino acid change previously associated with MEN1[2]. Given the paucity of MEN1 mosaicism reported within the literature with the presence of the two cell lines and only 15% mosaicism close monitoring will be crucial to determine the genotype/phenotype relationship in our patient.

[1] Choppin et al 2019 Eur J Endocrinol 1; 180(2):L1-L3
[2] Itoh et al 2017 Clin Pediatr Endocrinol 26;25-28

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS II

Protective Effects of Smoking? Improved In-Hospital Mortality in Smokers Admitted for Diabetic Ketoacidosis

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MON-700

PURPOSE: To determine the relationship between tobacco smokers and the rate of hospital readmission within 30 days, mortality, morbidity, and health care resource utilization in patients admitted to the hospital in the United States with diabetic ketoacidosis (DKA). **METHOD**: A retrospective study was conducted using the AHRQ-HCUP National Inpatient Sample for the year 2014. Adults (≥ 18 years) with a principal diagnosis of DKA and a secondary diagnosis of tobacco dependence or active smokers were identified using ICD-9 codes as described in the literature (1). The primary outcome was in-hospital mortality. Secondary outcomes include readmission rate, length of hospital stay (LOS), total hospitalization costs. Propensity score (PS) using the next neighbor method without replacement with 1:1 matching was utilized to adjust for confounders (2). Independent risk factors for readmission were identified using multivariate logistic regression model (3). **RESULTS**: In total, 186,824 hospital admissions with a primary diagnosis of DKA were identified, of which 32.44% (47,382) had TD. In-hospital morality among the smoking cohort (0.39%, SD 0.03) was lower than the non-smoking cohort (0.32%, SD 0.04) during the first hospitalization. Similar effects were observed after propensity match - 0.33% (SD 0.18) vs 0.27% (SD 0.03). The mortality rate during next hospitalization was also lower in the smoking cohort (0.72%, SD 0.03) in comparison to their counterpart (1.16%, SD 0.01). Smokers had a higher readmission rate of 17.6% (SD 0.57) than non-smokers (9.6%, SD 0.25). The length of stay among smokers and non-smokers were similar after propensity match - 3.12 days (SD 0.03) vs 3.06 days (SD 0.09), p=0.42, respectively. Total hospital cost was also similar between the two groups, $6,898 (SD $82) vs $7,100 (SD $203), p=0.32, respectively. Based on multivariate logistic regression, female and high Charlson comorbidity index were associated with higher 30-day readmission rate; whereas private insurance and high household income were associated with reduced readmission rate. **CONCLUSION**: Smoking has been associated with improved survival in patients with DKA (4). Previous studies have shown that glucose concentration were significantly lower at fasting and 120 min in current smokers than non-smokers. However, the effects of cigarette smoking on glucose metabolism and insulin resistance are still disputed.

Thyroid

HPT-AXIS AND THYROID HORMONE ACTION

A Novel Role of Thyroid Hormone Receptor in Synaptic Plasticity in Cerebellar Purkinje Cells

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SAT-454

Thyroid hormone (TH) is essential for the development and the maintenance of the brain function. TH action is mediated by TH receptor (TR). TR binds to a specific DNA sequence on TH-target genes and thus functions as a ligand-dependent transcription factor. In thyroid diseases such as congenital hypothyroidism or resistance to TH (RTH), TH-TR binding is dominantly disrupted, leading to the various symptoms such as motor deficits. However, in such cases, all the cells that express TR get affected by the

disrupted TR signaling; thus, the specific mechanism has not been cleared. It has been well known that proper motor coordination is deeply related to long term depression (LTD) of synaptic transmission from parallel fiber (PF) to Purkinje cell (PC) in the cerebellum (Ito, 1989). Therefore, we examined the involvement of TR in synaptic plasticity at PF-PC synapses by using transgenic mice (Mf-1 mice) which express dominant-negative TR specifically in PCs. Since Mf-1 display the impairment of motor coordination and motor learning, a decrease in TR signaling in PCs may alter synaptic plasticity and contribute to motor incoordination. A whole-cell patch clamp recording of Mf-1 PCs revealed the inhibition of LTD but instead the induction of long term potentiation (LTP) of the synaptic transmission at PF-PC synapses. This indicates that the intracellular calcium dynamics may be disrupted in Mf-1 PCs since LTD requires a higher elevation of the intracellular calcium concentration in PCs than LTP does. Indeed, single-PC qPCR showed that the mRNA levels of some important molecules for the intracellular calcium dynamics in PCs (SERCA2, IP_3R, and P/Q-type calcium channel) are downregulated in Mf-1 PCs. This result suggests those genes as possible TH-target genes. Taken together, the present study suggested a novel possible role of TR in synaptic plasticity at PF-PC synapses by regulating the expression of some important genes for LTD occurrence in the cerebellum. This finding could give a new insight into the mechanism of motor deficits in thyroid diseases.

Neuroendocrinology and Pituitary

CASE REPORTS IN SECRETORY PITUITARY PATHOLOGIES, THEIR TREATMENTS AND OUTCOMES

Crooke's Cell Adenoma- an Aggressive Form of Cushing's Disease

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SAT-279

Introduction: Cushing's disease is a condition of cortisol overproduction caused by an ACTH-producing tumor. Corticotroph cells surrounding an ACTH-producing tumor usually undergo Crooke's hyaline change, where cytokeratin filaments accumulate in the cytoplasm in response to glucocorticoid excess. These changes are thought to be a mechanism of feedback inhibition and thus facilitate a suppression of ACTH. However, in a subtype of ACTH-secreting tumors known as Crooke's cell adenomas (CCA), the ACTH-producing cells also undergo these hyaline changes. This would be expected to suppress hormone secretion but these cells are still able to release significant amounts of ACTH.

Case presentation: A 32-year-old woman presented to the hospital after an episode of syncope. On head MRI, she was found to have a 2 cm sellar mass with optic chiasm compression. Labs showed low TSH, free FT4, T3, FSH, and LH. She was also pre-diabetic with an HgbA1c of 6.2%. Her baseline cortisol of 20.6 μg/dL did not suppress after 1 mg of dexamethasone. After receiving 4 mg of dexamethasone, her cortisol suppressed to 5.2 μg/dL. She was diagnosed with hypopituitarism except for cortisol and a likely ACTH-producing pituitary macroadenoma. She completed a transsphenoidal pituitary resection and pathology revealed Crooke's hyaline changes with immunohistochemical stains positive for ACTH. The immunostain for the proliferation marker Ki67 showed a relatively low proliferation index. Her course was complicated by diabetes insipidus. She was ultimately discharged on 20 mg hydrocortisone each morning, 10 mg hydrocortisone each afternoon, desmopressin 0.05 μg daily, and levothyroxine 125 μg daily. Two weeks later, the patient was sent to the emergency room by her endocrinologist for hyperglycemia up to 288 mg/dL. She was also found to be newly diabetic with an HgbA1c of 6.5%. A fasting morning cortisol was collected during her admission and showed a cortisol level of <1.0 μg/dL, proving she was cured of Cushing's disease. However, she will need close endocrinology follow up and MRI imaging of her pituitary for this aggressive type of pituitary adenoma.

Discussion: We have come across an interesting case of a young woman who presented for syncope and was found to have a pituitary macroadenoma with pathology consistent with CCA. This type of ACTH-producing tumor is known for aggressive patterns including high rates of recurrence with rates of up to 60% reported in literature, persistent disease after surgery, malignant transformation, and metastases. Despite presentation and symptoms similar to those of other ACTH-producing adenomas, the dangerous pattern of Crooke's cell adenomas necessitate long-term follow-up in affected patients.

Diabetes Mellitus and Glucose Metabolism

DIABETES TECHNOLOGY AND ADVANCES IN CLINICAL TRIALS

Real-World Minimed™ 670G System Use and Glycemic Outcomes of Pediatric and Adult Individuals Living with Type 1 Diabetes (T1D) in the United States

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OR30-01

Introduction: The MiniMed™ 670G system was FDA-approved in 2016 for adults and adolescents ≥14yrs, and in 2018 for children ages 7-13yrs with T1D. Since then, use of the system has grown to over 180,000 people in the U.S. The glycemic control benefits of real-world MiniMed™ 670G system Auto Mode use in the U.S. were assessed.
Methods: System data (aggregated five-minute instances of sensor glucose [SG]) uploaded from March 2017 to July 2019 by individuals (N=118,737) with T1D and ≥7yrs of age who enabled Auto Mode were analyzed to determine the mean % of overall time spent <54mg/dL/<70mg/dL (TBR); between 70-180mg/dL (TIR); and >180mg/dL/>250mg/dL (TAR). The impact of Auto Mode was further assessed in a sub-group of individuals (N=51,254) with, at least, 7 days