

Results: SOAT1 protein expression was heterogenous in this cohort; 38% of ACCs demonstrated strong SOAT1 protein expression while 62% demonstrated weak or absent SOAT1 protein expression. Strong SOAT1 protein expression correlates with known features of high aggressiveness in ACC, such as excessive tumor cortisol secretion ($p=0.007$), advanced disease stage [ENSAT 3 and ENSAT 4 ($p=0.009$)] and high Ki67 index (0.008). On multivariate analysis, strong SOAT1 protein expression was an independent predictor of lower overall survival (HR 1.71, CI 95% 1.05-2.92; $p=0.04$) when considering all cases ($n=107$) and of lower progression free survival (HR 3.05, CI 95% 1.05-8.85; $p=0.04$) in patients with metastatic disease at diagnosis ($n=22$).

Conclusions: Our findings demonstrated that SOAT1 protein expression has prognostic value in ACC and reinforce the importance of investigating SOAT1 as a possible therapeutic target for patients with ACC. Multicentric prospective studies including a larger number of patients are needed in order to validate and consolidate the results found in this cohort.

References:

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Bone and Mineral Metabolism

PARATHYROID HORMONE TRANSLATIONAL AND CLINICAL ASPECTS

Characteristics and Outcomes of Severe Hypercalcemia Related Admissions - a Single Centre 5 Years' Experience

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SAT-397

Introduction: Severe hypercalcemia (corrected calcium ≥ 3.5 mmol/L) is typically associated with multi-organ dysfunction and increased mortality. We audited 47 consecutive patients who were admitted to a single tertiary referral center over 5 years period (2014-2019) with severe hypercalcemia. **Results:** The median age 69 years (10-97yrs); 55% females, and median length of stay was 9 days (1-120). Most patients (30%) were admitted under general medicine and 53% received endocrinology consultation. Renal dysfunction (91%) dominated the clinical presentation, but gastrointestinal abnormalities (70%), neuropsychiatric manifestations (53%), and musculoskeletal involvement (45%) were also very common. PTH was measured in 43/47 patients with 37 PTH independent (calcium level 3.82 mmol/L) and 6 PTH dependent (calcium level 3.70mmol/L) hypercalcemia. Recurrence of the condition within five years was recorded for 5 patients (11%), ten (21%) patients died during the admission, and 4 patients (9%) required ICU admission in PTH independent severe hypercalcaemia, majority are due to malignancy;

while none of these outcomes were observed in PTH dependent severe hypercalcaemia. The length of hospital stay is longer in PTH independent (15.5 days) as compared to PTH dependent severe hypercalcaemia (12 days). The most common cause of severe hypercalcemia was malignancy (47%) with multiple myeloma as the most common in 32% followed by lung cancer at 27%. The other non-malignancy causes are calcium supplementation, vitamin D toxicity, and hyperparathyroidism implicated in 13% each. Twenty eight patients (65%) were managed by fluid and antiresorptive agent with 26 patients able to decrease calcium level to <3 mmol/L (93%). Eight patients (19%) were managed by fluid alone (not effective in 37%), 9% by antiresorptive agent alone (not effective in 25%), and 16% did not receive any fluid nor antiresorptive agent (not effective in 43%). **Conclusion:** Similar to previous studies, severe hypercalcaemia is commonly seen in patients with malignancy and associated with significant symptoms, recurrence in 5 years, ICU admission and mortality. Calcium and vitamin D supplementation and hyperparathyroidism are also found to commonly cause severe hypercalcemia. The most effective management is combination of fluid resuscitation and antiresorptive agent to decrease the calcium level to <3 mmol/L.

Neuroendocrinology and Pituitary

NEUROENDOCRINOLOGY AND PITUITARY

Peak Stimulated Growth Hormone Is Lower in Subjects with Nonalcoholic Fatty Liver Disease Than Controls of Similar Sex, Age and BMI

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MON-286

Background: Nonalcoholic fatty liver disease (NAFLD), fatty infiltration of the liver in the absence of alcohol use, is a prevalent and serious complication of obesity. Obesity is a state of relative growth hormone (GH) deficiency, and GH has been identified as a candidate disease-modifying target in NAFLD because of its lipolytic and anti-inflammatory properties. However, it is not known whether individuals with NAFLD phenotyped by proton magnetic resonance spectroscopy (1H-MRS), the gold standard imaging modality for assessment of intrahepatic lipid (IHL) content, have lower peak stimulated GH levels as compared to those of similar age, sex and BMI without NAFLD.

Methods: We studied 99 generally healthy adults without diabetes or significant alcohol use, ages 19-67 y and BMI >25 kg/m². All subjects underwent 1H-MRS for assessment of IHL content. Using a cutoff of $>5.5\%$, 65 subjects had NAFLD and 34 did not (controls). GHRH-arginine

stimulation testing was performed. GH was measured by immunoassay and IGF-1 by LC/MS/MS (Quest Diagnostics, CA, USA). Visceral and subcutaneous adipose tissue (VAT/SAT) were assessed by cross-sectional CT at L4. Results are reported as mean \pm SD.

Results: There was no difference between NAFLD vs controls in mean age (48 ± 12 vs 45 ± 14 y, $p=0.30$), BMI (33 ± 4 vs 33 ± 7 kg/m², $p=0.96$), sex (43% vs 44% female, $p=0.90$) or premenopausal status (50% vs 60%, $p=0.50$). Mean IHL was $21.8\pm 13.3\%$ (range 5.5-57.8%) and $2.9\pm 1.1\%$ (range 1.0-4.9%) in the NAFLD and control groups, respectively ($p<0.0001$). NAFLD subjects had higher ALT, total cholesterol, triglycerides, VLDL, LDL and lower HDL than controls. Fasting glucose was statistically but not clinically significantly higher in NAFLD vs controls (90 ± 9 vs 86 ± 7 mg/dL, $p=0.03$), and mean HbA1c did not differ significantly. There was a trend towards a higher mean VAT in the NAFLD vs controls (157 ± 70 vs 131 ± 67 g, $p=0.07$) but no difference in SAT. Mean peak stimulated GH was significantly lower in NAFLD vs controls (9.0 ± 6.3 vs 15.4 ± 11.2 ng/mL, $p=0.003$) which remained significant after controlled for age, BMI, sex and VAT. In a stepwise model including peak stimulated GH, VAT, age, BMI and sex, peak stimulated GH predicted 8% of the variability in IHL ($p=0.004$); no other variables were significant predictors of IHL. Mean IGF-1 (149 ± 53 vs 151 ± 49 ng/mL, $p=0.80$) and IGF-1 Z-score (-0.03 ± 0.61 vs -0.03 ± 0.68 , $p=0.90$) were not significantly different between the groups.

Conclusion: Subjects with NAFLD have lower peak stimulated GH but similar IGF-1 levels compared to non-NAFLD controls of similar age, BMI and sex. Additionally, lower peak stimulated GH was predictive of higher IHL, independent of age, BMI, sex and VAT. This suggests that the relative GH deficiency of obesity may be an independent contributor to the development of NAFLD and that the GH axis and downstream signaling pathways may be a therapeutic target for this disease where few currently exist.

Adrenal

ADRENAL CASE REPORTS I

50-Year-Old Fungus Suddenly Flourishes in Adrenal Glands: A Case of Sudden-Onset Bilateral Adrenal Masses Due to Latent Disseminated Histoplasmosis

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SAT-221

Histoplasma capsulatum is endemic to Africa, Asia, Central and South America, and within the US, to the Ohio and Mississippi River Valley. Disseminated histoplasmosis is less commonly seen in immunocompetent individuals, who usually present with asymptomatic self-limited acute pneumonitis. Time to involvement of the adrenals is unknown. Adrenal insufficiency occurs in 45% of cases involving the adrenals, and is thought to be irreversible even in patients in remission.

A 76-year-old man with no significant past medical history was incidentally found to have large bilateral adrenal masses during routine surveillance of a 7 mm pulmonary nodule on annual Chest CT, which showed normal adrenal

glands the year prior. He was asymptomatic. A lifetime non-smoker native to California, whose only significant travel history was in his 20s to Ecuador and Puerto Rico, areas endemic to *Histoplasma*.

Abdominal CT showed large bilateral adrenal masses with intermediate density and low washout values (right: 4.9 cm, HU 45, absolute washout 30%; left: 4.8 cm, HU 30, absolute washout 25%).

On exam, vital signs were stable with normal orthostatics. Labs revealed normocytic anemia, normal chemistry panel, normal cortisol after 1-mg dexamethasone overnight test 2.6 mcg/dL ($n<5$ mcg/dL), plasma metanephrine <0.10 nmol/L ($n<0.50$ nmol/L), plasma normetanephrine 0.89 nmol/L ($n<0.90$ nmol/L), aldosterone 4.0 ng/dL ($n<31$ ng/dL), PRA 2.0 ng/ml/hr (n 0.5-4 ng/ml/hr) and random free cortisol 0.38 ug/dL (n 0.022-0.254ug/dL). HIV antigen and antibody, and Histoplasma urinary antigen were negative.

Left adrenal mass biopsy revealed necrotizing granulomatous inflammation with fungal culture revealing budding yeast morphologically consistent with Histoplasmosis, with DNA probe confirming *Histoplasma capsulatum*.

Treatment with itraconazole was initiated and the patient is tolerating the treatment well.

To our knowledge, this is the first case demonstrating rapid development of large bilateral adrenal masses within a year due to latent disseminated histoplasmosis in an asymptomatic individual, which highlights the need for appropriate testing in patients with known exposure or travel history to endemic areas, regardless of time since exposure.

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Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS II

A Neuro-Radiological Stroke Mimicker: Non-Ketotic Hyperglycemia Induced Occipital Lobe Hyperdensity Presenting with Seizures.

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Background: Acute hyperglycemia in absence of DKA or HHS is a common cause for hospitalization and is termed as Non-Ketotic Hyperglycemia (NKH). NKH-related occipital lobe seizure activity is a rare entity and it's neuroradiological findings can be confused for acute stroke. We describe a case of NKH-related seizure activity presenting with distinct MRI findings.

Clinical Case: 19-year-old male with DM-1 presented with complaints of burning and numbness involving the left side of face, left upper and lower extremity. These lasted for a few hours and had resolved upon arrival to the ER. At the time of presentation, vitals were stable. Physical examination was significant for flat affect with delayed response to questions without any focal deficits. History obtained from his father revealed that he has had similar episodes of decreased responsiveness during periods of