subjects, overt hypothyroidism (OH) in 33%, congenital hypothyroidism (CH) in 18% and overt thyrotoxicosis in 5%. Autoimmune thyroiditis constituted the major cause of hypothyroidism in the OH group with significantly higher prevalence of anti-TPO and anti-TG antibody in comparison of SCH group (61% vs 31%; 45% vs 21.9%, p<0.05) respectively. All subjects in OH group were treated whereas 76% subjects in SCH group were treated and the mean dose of L thyroxine required to treat OH was significantly higher (2.31±1.1ug/kg/day vs 1.76±1.07ug/kg/day; p<0.001) in comparison of SCH group. A major independent predictor of treatment in SCH was initial TSH which was significantly higher in the treated group (11.65±3.80 uIU/mL vs 9.24±1.31 uIU/mL; p<0.001). Subjects with congenital hypothyroidism presented at a mean age of 6 months (18 days to 2 years) with most common aetiology being thyroid hypoplasia and dyshormonogenesis (20% each). Graves’ disease was diagnosed in 11 out of 12 subjects with thyrotoxicosis and were treated with antithyroid drugs. Overall 85.5% of referred subjects were treated and after one-year follow up management was found to be adequate in 81% subjects. 

Conclusions The evolving trend of diagnosing children having nonspecific symptoms with SCH is a matter of concern as many are subjected to the burden of unwanted prolonged treatment and frequent testing as highlighted in our study. Delayed presentation of CH in our study warrants active surveillance of children at birth for thyroid disorders to avoid long term adverse effects on mental development.

Neuroendocrinology and Pituitary ADVANCES IN NEUROENDOCRINOLOGY

Female Mice Lacking Brain Insulin Production Exhibit Learning Deficits, Anxiety, and Reduced Hippocampal Cyclin D1 Expression

Stella Katharina Baehring, BA Hons1, Timothy P. O’Leary, PhD2, Danae M. Holenka, BSc1, Hong Li, MSc1, Kyungchan Kim, PhD Candidate1, Arya E. Mehran, PhD2, Paul Pavlidis, PhD2, Eun-Kyoung Kim, PhD2, Shernaz X. Bamji, PhD2, James D. Johnson, PhD2.

1 UNIVERSITY OF BRITISH COLUMBIA, Vancouver, BC, Canada. 2 Daegu Gyeongbuk Institute of Science and Technology, Daegu, Korea, Democratic People’s Republic of, 3 University of British Columbia, Michael Smith Laboratories, Vancouver, BC, Canada.

SUN-240

Insulin dysregulation independently underlies diabetes and Alzheimer’s Disease (AD) pathology. However, the former has also been shown to be a risk factor for the latter. The ancestral insulin gene (Ins2), but not the pancreas-specific Ins1 gene, is transcribed locally within the brain in mice. We confirmed that neuronal expression of Ins2 is most prominent within the hippocampus, a brain region with established roles in learning and memory, and that it was reduced by a diet known to promote neuronal dysfunction. It is not yet clear, however, how insulin produced locally within the brain influences hippocampal function, learning and memory. To eliminate brain-derived insulin, we used young and old mice with germline Ins2 knockout (Ins2−/−) and their normal complement of wildtype Ins1 alleles, which had equivalent pancreatic insulin and normal glucose homeostasis. Using the Morris water maze, we found that learning and memory performance of female Ins2−/−mice was significantly impaired relative to wild-type mice, whereas the performance of male Ins2−/−and wild-type mice did not differ. During acquisition training, the swim-speed in female Ins2−/−was faster than wild-type mice, suggesting increased stress reactivity and motivation to escape from water. Indeed, anxiety-like behavior was increased in female mice as assessed by the open-field test. Using RNA sequencing to profile isolated hippocampi, we found that femaleIns2−/−mice had a significant reduction in Cyclin D1 (Ccdn1) compared with littermate controls. This observation points to a possible defect in hippocampal neurogenesis, a physiological hallmark of impaired memory and emotionality implicated in both, diabetes and AD. Together these data suggest that Ins2 plays sex- and brain region-specific roles in neuronal function and perhaps adult neurogenesis.

Adrenal
ADRENAL CASE REPORTS I

When Acne, Hirsutism and Menstrual Irregularities Are More Than PCOS

Paola Rios, MD, Gabriela Zuniga, MD, Alex Manzano, MD.
Mount Sinai Medical Center, Miami Beach, FL, USA.

SAT-210

Background: Polycystic ovarian syndrome (PCOS) mimics non-classic congenital hyperplasia (NCCAH), presenting with hyperandrogenic symptoms. NCCAH is usually diagnosed later in life, where 21-hydroxylase (21OHD) is the most common deficiency. There are more than 300 mutations in 21OHD, being V281L one of the described mutations.

Clinical Case: 23 y/o female patient GOPO comes to the office complaining of irregular periods, frontal hair loss, weight gain, acne and hirsutism. She has had noticed these changes since menarche; however, her acne was getting worse. Was seen 2 months prior to presentation by her gynecologist who order a free Testosterone that was elevated (6.4 pg/mL, n<4.2 pg/mL), with normal TSH (1.1 uIU/mL, n,0.45-4.5). She was not taking any medication. Her mother has history of 2 spontaneous abortions and her sister has acne and hirsutism as well. On physical exam BMI was 26, it was noticed comedones and papules on her face, back and shoulders. Ferriman-Gallwey scale was >8. At the initial visit due to the clinical scenario, it was thought that she had hyperandrogenic syndrome, probably secondary to PCOS. Serum blood test were ordered and showed an elevated total testosterone (71 ng/dL, n,8.48ng/dL), free testosterone (8.4 pg/mL, n<4.2 pg/mL), 17-OH pregnenolone performed by liquid chromatography-tendem mass spectrometry (LC-MS/MS) was (429 ng/dL, n,35-290 ng/dL luteal phase) and androstenedione LC-MS/MS (1941 ng/dL, n,41-262 ng/dL) which confirmed NCCAH diagnosis due to 21OHD. She had no desire to become pregnant at the time of evaluation; however, was concerned about fertility and genetics. Was started on OCPs and genetic testing was positive for V281L mutation in the CYP21A2 gene, being homozygous for this
Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS I

Rare Case of Ectopic Cushing Syndrome Caused by ACTH Secreting Thymic Neuroendocrine Tumor in a Patient with Multiple Endocrine Neoplasia Type I.

Yamuna Gorantla, MD, Jorge Soria Moncada, MD, Juan Sarmiento, MD, Ambika Ambler, MD, Malini Ganesh, MD. Cook County Hospital, Chicago, IL, USA.

SUN-938
Introduction
Cushing syndrome (CS) represents an uncommon manifestation of MEN1 and can be caused by both ACTH dependent or independent etiologies. Among them, ectopic ACTH secretion from a Thymic neuroendocrine tumor (TNET) in MEN1 is rare, with very few cases reported so far in literature. We report a case of Ectopic Cushing syndrome (ECS) in a MEN1 patient (pt) with multiple tumors, secondary to ACTH-secreting TNET.

Case description:
A 44 year old male presented to our institution for nausea, vomiting, dizziness. He had initial workup which revealed multiple tumors (papillary thyroid cancer, thymic mass, parathyroid adenomas, bilateral adrenal nodules, macroadenoma, peripancreatic nodules). Given concern for MEN 1, genetic testing was performed which was confirmative. Hormonal workup at this time for adrenal nodules was negative including low dose dexamethasone suppression test(DST). The immobile thymic mass was found to be poorly differentiated NET on biopsy with Ki-67 >50% with vascular invasion and adhesions to lung/ chest wall on VATS, not amenable to surgery. The pt declined chemotherapy and radiotherapy due to poor social support. Six months later, he presented with complaints of shortness of breath, proximal muscle weakness, anasarca. Evaluation revealed AM cortisol >60 ug/dL(range 6.7-22), high-dose DST Cortisol >60 ug/dL, 24hr urine free cortisol: 8511mcg (range 4-50) and ACTH level: 278pg/mL(range 6-50) confirming ACTH-dependent CS. Special stains from the previous TNET biopsy demonstrated positive staining for ACTH confirming ectopic ACTH secretion. Ketokonazole and chemotherapy with Etoposide and Carboplatin was started, however he clinically deteriorated and expired a few weeks after diagnosed of ECS.

Discussion:
TNET in MEN 1 is rare, with a prevalence of 3-8%. TNET are unusual neoplasms that account for 2% to 7% of all mediastinal tumors. TNET in MEN1 rarely secrete functional hormones with very few reported Ectopic ACTH secretion. MEN1 associated ECS from TNET is an aggressive disease with local invasion of adjacent mediastinal structures or metastasis being common, resulting in poor prognosis as demonstrated in few case reports including our case. Radical surgery of involved adjacent structures and adjuvant local RT can provide local disease control.

Conclusion:
Our pt is a rare case of ECS from TNET in MEN1 with poor prognosis. A special feature of this case is that the patient had initial negative evaluation for hypercortisolemia, however 6 months later he presented with signs and symptoms of severe hypercortisolism, with evaluation confirming transformation into ACTH producing TNET. This conversion is very rarely found in literature and adds to the unique presentation of the case.

Diabetes Mellitus and Glucose Metabolism

METABOLIC INTERACTIONS IN DIABETES

Metabolic and Functional Regulation of T Cells by Insulin and Insulin like Growth Factor 1

Kaitlin Kiernan, BS1, Nancie J. Macleer, MD,PHD2.
1Duke University School of Medicine, Durham, NC, USA, 2Duke Univ Medical Center, Durham, NC, USA.

SUN-649
Obesity leads to altered immunity characterized by increased risk of autoimmunity, poor response to infection, and impaired vaccine response. T cells play an important role in this obesity-associated immune response; however, the mechanisms by which T cells are altered in obesity remain unknown. Our goal is to identify nutritionally regulated hormones and cytokines that link whole body nutrition and immunity, and to understand the mechanisms by which such factors can alter T cell response in obesity. To that end, we have identified the hormones insulin and insulin-like growth factor-1 (IGF-1) as potential links between nutritional status and T cell metabolism and function. Insulin is secreted from pancreatic beta cells in response to increasing blood glucose levels, and circulating insulin levels are elevated in obesity due to insulin resistance in metabolic tissues. IGF-1 levels are influenced by protein intake and nutrition status, and free (bioactive) levels of IGF-1 are elevated in obesity. To study the role of insulin and IGF-1 on T cell function and metabolism, we treated activated CD4 T cells with physiologic levels of insulin or IGF-1 in vitro for 24 hours. Treatment of CD4 T cells with insulin or IGF-1 increased glucose uptake, glycolytic metabolism, and mitochondrial metabolism while altering inflammatory cytokine production. In particular, both insulin and IGF-1 decreased IFN-γ production, whereas IGF-1 specifically increased IL-17 production from both bulk activated CD4 T cells and T cells skewed toward a T helper 17 (Th17) phenotype. Using a T cell-specific insulin receptor (IR) conditional knockout mouse, we found that loss of IRsignaling decreased glucose uptake and mitochondrial metabolism and increased IFN-γ production by activated T cells. Moreover, IR appears to be required for both insulin and IGF-1 effects on T cells.