All of the self-reported cannabis usage admissions (33/33) and readmissions (81/81) presented with additional aggravating factors for DKA such as medication noncompliance, polysubstance abuse, and infection. Finally, 20 of the overall 130 patients admitted during this timeframe presented with new onset DKA, where none reported cannabis usage, 20% (4/20) completed general toxicology screening, and none underwent cannabis specific toxicology screening.

From the observational retrospective analysis at this hospital, there is a need for awareness about substance abuse screening, especially in adults with a history of recurrent hospital admissions for DKA. Knowledge among health care providers and patient education regarding the effect of cannabis usage on metabolic factors and its diabetes complications, including diabetes self-management at time of drug usage, can be further explored in prospective studies.

References: (1) Umpierrez (2006) Diabetes Care, 29(12), 2755-2757. (2) Brown et al., (2017) JAMA, 317(2), 207. (3) Haffajee et al., (2018) NEJM, 379(6), 501-504.

Adipose Tissue, Appetite, and Obesity

MECHANISMS AND TREATMENT OF OBESITY IN HUMANS

The Treatment of Partial Lipodystrophy in the Setting of Neutralizing Antibody Against Metreleptin with Leptin Receptor Agonist REGN4461

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OR33-02

Background: An 18-year-old patient with atypical partial lipodystrophy had a transient initial metabolic response to metreleptin that deteriorated when neutralizing antibodies against metreleptin developed. A therapeutic trial with setmelanotide did not result in any metabolic benefit as desired. Because her status continued to deteriorate, we attempted to treat her with REGN4461, a fully human monoclonal antibody that is an agonist to the human leptin receptor (LEPR). **Clinical Case:** A compassionate use protocol (IND No. 144013) was initiated to treat the patient with REGN4461. The treatment consisted of 5 mg/kg intravenous infusion followed by 300 mg weekly subcutaneous injections of REGN4461. The primary endpoint was achievement of fasting triglycerides < 500 mg/dL without the need for ongoing plasmapheresis. Treatment-emergent adverse events were also followed. Here, we report her first 21-week response to treatment with REGN4461. The treatment resulted in a reduction of triglycerides from 1288 mg/dL to 344 mg/dl and allowed her to discontinue plasmapheresis. She lost 3.4 kilograms so far, and her liver size reduced per liver span measured by physical examination. Also, the liver MRI at week 12 showed a significant reduction in liver size and fat content (from 29.9% to 16.6%). Although her glucose control is still challenging, a slight reduction in her HbA1c was observed at week 12 along with improvements in her average glucose levels and total daily insulin requirement so far. No untoward signals were detected in her safety measurements. **Conclusion:** To date, treatment with REGN4461 offered substantial clinical benefit by improving the metabolic abnormalities in this unique patient. This experience represents the longest human exposure with REGN4461. The improvements noted in metabolic parameters and hepatic steatosis are similar to previous observations in lipodystrophic humanized LEPR mice. Our results suggest that REGN4461 showed clinical benefit even in the presence of neutralizing antibodies to metreleptin.

Thyroid

THYROID NEOPLASIA AND CANCER

How Does the American Joint Committee on Cancer 8th Edition Tumor, Node, Metastasis Staging System Perform in Patients Evaluated at a Major Middle Eastern Medical Center?

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MON-520

The American Joint Committee on Cancer (AJCC) Tumor Node Metastasis (TNM) Classification of Cancer 8th edition (AJCC8) was officially introduced in January 2018 as a replacement for the previous version (AJCC7). Validation studies using data obtained from large cancer registries in North America demonstrated the superiority of AJCC8 over AJCC7 for prediction of survival. Subsequent studies from Europe and East Asia have mostly shown similar findings. However, these data may not be generalizable to other parts of the world. In this first study from the Middle East (Saudi Arabia), we compared these two versions of AJCC staging for their concordance and prediction of outcome in a large unselected sample of patients (pts) with DTC managed at a major referral medical center. We also compared the AJCC staging systems with the American Thyroid Association (ATA) Risk Classification.

Of 814 consecutive pts seen during this period, 94 were excluded either due to their diagnosis being medullary or anaplastic thyroid cancer (37) or because of deficient data. The remaining 720 pts (149 males (20.7%), 571 females (79.3%) were included. The median age at the diagnosis was 37 yrs (range, 6-83). Total thyroidectomy was performed in 693 pts (96.3%) and central and/or lateral lymph node dissections in 487 pts (67.6%). I-131 was administered to 626 pts (87%). The tumors were classic PTC in 519 pts (72%), follicular variant PTC in 100 (13.9%), Tall cell PTC in 22 (3.1%), diffuse sclerosing PTC in 10 (1.4%), follicular thyroid cancer in 21 (2.9%) and other rare subtypes in 48 pts (6.8%).

The number (%) of pts within each stage group by AJCC7 and AJCC8 respectively are as follows: Stage 1: 514 (71.4%) vs. 597 (82.9%), Stage 2: 46 (6.4%) vs. 75 (10.4%), Stage 3: 63 (8.8%) vs. 11 (1.5%), Stage 4: 97 (13.5%) vs. 37 (5.1%).

Comparing AJCC8 with the ATA risk stratification system in 709 pts in which data were available, we found a high

correlation with 96.8% of ATA low risk group being stage 1 in AJCC8, 2.9% stage 2 and 0.3% stage 3 and none in stage 4. The ATA intermediate risk group was 87.4% AJCC8 stage 1, 12.3% stage 2, 0.4% stage 3 and none in stage 4. The ATA high risk group was 19.1% in AJCC8 stage 1, 33% in stage 2, 9.6% in stage 3 and 38.3% in stage 4.
In addition, AJCC8 was more predictive of the outcome with 80% of pts with evidence of disease (biochemically and structurally incomplete) being in AJCC8 stage 3 or 4 compared with 60% in AJCC7. For ATA staging, 8.6%, 22.4% and 67.7% of low, intermediate and high risk groups had evidence of disease at the last follow up, respectively.
Conclusion: In this Middle Eastern population, AJCC8 downstaged a significant percentage of pts with DTC from higher stages in AJCC7. It also correlated better with the outcome and with the ATA risk classification system.

Thyroid

THYROID DISORDERS CASE REPORTS II

New Breast Cancer Therapy Atezolizumab, Leads to Thyroiditis.

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SAT-475

Background: A NSABP B 59 trial is currently underway to check the efficacy of an experimental drug, Atezolizumab (Anti-PDL 1 monoclonal antibody) in the treatment of triple negative breast cancer. In the trail, the drug is added to the usual neoadjuvant chemotherapy given before surgery and prolonged treatment with it is continued after surgery to reduce the recurrence. Listed adverse effects are immune medicated hyperthyroidism in 2% of population.
Clinical Case:
32 y old Asian woman was diagnosed with triple negative left breast cancer in May 2018. She was started on paclitaxel, carboplatin and study medication Atezolizumab/Placebo in June 2018 and she received 4 cycles of the same and then it was stopped in August 2018. She was started back on the same in September 2018 which ended in November 2018. Patient tested positive for BRCA1 gene mutation and underwent bilateral mastectomy in December 2018. The study medication was restarted in January 2019.
Patient is received a total of 11 doses of study medication and was due to receive 16 doses if she had finished the trial in June 2019. Patient received radiation therapy starting in January 2019 till February 2019.
On her oncology visit in April 2019 patient was found to have a suppressed TSH of 0.009 with a high free thyroxine of 1.72 and an elevated free T3 of 5.4. She was referred to endocrinology for evaluation of thyroid abnormalities, as the study medication can cause thyroid problems. She denied symptoms of hyperthyroidism. TPO, TSI and anti-thyroglobulin antibodies were negative. Thyroid uptake scan showed uniformly decreased tracer distribution in both thyroid lobes consistent with thyroiditis.
As per the protocol for the study medication as well as recommendations by the American Society of oncology, we waited for normalization of the thyroid function test before resuming the study medication. In July 2019, TSH normalized to 2.99 and free T4 0.97.
She was noted to have low random cortisol level of 3.27 at 1000AM. ACTH stimulation test was performed and she responded appropriately.
Hence could not take the remainder of the study medication that were scheduled until June 2019. She is on observation phase since June 2019 and currently doing well.

Neuroendocrinology and Pituitary

ADVANCES IN NEUROENDOCRINOLOGY

Evidence that Urocortin 2 Contributes to the Suppressive Effect of Metabolic Stress on LH Secretion in Female Mice

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SUN-257

Pulsatile luteinizing hormone (LH) secretion is disrupted by numerous stimuli including metabolic stress. Insulin-induced hypoglycemia is a model of metabolic stress that suppresses LH secretion in numerous species including mice. Our recent work provides evidence that this inhibition of LH secretion occurs via suppression of neurons that contain kisspeptin (Kiss1), neurokinin B (NKB) and dynorphin (Dyn) in the arcuate (ARC) nucleus (KNDy cells). Thus, our current objective is to identify the neural components responsible for the suppression of KNDy cells during metabolic stress. Several lines of evidence support the hypothesis that the neuropeptide urocortin 2 (UCN2) has a key role in the inhibition of LH during stress in rats. First, ICV injection of UCN2 suppresses LH secretion. Second, an antagonist to the receptor for UCN2 reverses the suppression of LH during metabolic stress. Finally, restraint and osmotic stress increase *UCN2* mRNA abundance in the paraventricular nucleus (PVN). To determine if UCN2 neurons in the PVN are activated during metabolic stress we performed immunohistochemistry for UCN2 and c-Fos in tissue collected 120 min after saline or insulin (0.75mU/kg) injection (n = 2/group, ovariectomized, adult, C57/BL6). Insulin significantly increased both the number of UCN2 cells (saline: 109.0 ± 8.5, insulin: 156.3 ± 10.8 cells) and the percentage of UCN2 cells that expressed c-Fos (saline: 13.1 ± 2.5%, insulin: 31.2 ± 0.8%). Next, we administered UCN2 (7.23nmol) via ICV injection to determine if this molecule suppresses LH secretion and/or mRNA abundance of KNDy genes. LH was measured in serial blood samples collected from 60 min prior to and 30-90 min following injection. Tissue was collected 3 h after ICV injection to confirm injection site and quantify mRNA abundance in ARC micropunches. In saline-treated mice (n = 5 successful injections), mean LH concentration and the number of LH pulses did not differ across sampling periods (mean: 6.4 ± 0.4 ng/mL vs. 6.0 ± 0.4 ng/mL; pulses: 2.6 ± 0.2 vs. 3.0 ± 0.3, pre vs. post). In contrast, in mice with successful UCN2 injections (n = 4) there was a significant reduction in both mean LH and the number of LH pulses following UCN2 (mean: 5.0 ± 0.3 ng/mL vs. 1.4 ± 0.2 ng/mL; pulses: 3.0 ± 0.0 vs. 0.25 ± 0.25, pre vs post). UCN2-treated animals had a significant reduction in the abundance of mRNAs encoding