recently diagnosed with type 2 Diabetes mellitus after he presented to his primary care physician with increased urinary frequency, frothy urine. He was found to have a hemoglobin A1c of 12.5% and blood glucose 408 mg/dl. Urinalysis was negative for nitrates and leukocyte esterase. Patient endorsed to have one sexual partner and safe sexual practices. Urinary gonorrhea and chlamydia antigens were negative. He was diagnosed with diabetes mellitus and was started on ertugliflozin, exenatide and bactrim for possible UTI. Three days later, the patient presented to the ED with dysuria, polyuria, rectal pain, nausea and fatigue. Patient appeared to be in distress with tachypnea and tachycardia. Physical exam showed signs of dehydration. Laboratory evaluation revealed blood glucose at 185 mg/dL. Given the history of recent diagnosis of diabetes mellitus and SGLT2 inhibitor use, euglycemic DKA was suspected. ABG revealed metabolic acidosis (arterial blood gas pH 7.32, pCO2 20, pO2 130) with elevated anion gap of 24, HCO3 level of 10 mmol/L (reference range 22 - 28 mmol/L) and beta-hydroxybutyrate of 5.7 mmol/L (reference range 0 - 0.3 mmol/L). The lactate levels were normal. Wbc count 20,100. Urinalysis showed glucose 4+, ketones 4+, WBC 4, negative for infection. Computed tomography scan of his abdomen and pelvis with contrast showed 3.7 x 2.7 cm prostate abscess and acute cystitis. Patient was treated for euglycemic DKA with infusion of insulin and dextrose 10% with 0.45% NS. Careful monitoring of his blood sugar was required as it dropped with slight increase in infusion rate. He was started on ciprofloxacin for prostate abscess. Patient's metabolic acidosis resolved and he showed clinical improvement. Endocrinologist was on consult. Patient was switched to insulin regimen for glycemic control. 

Conclusion: SGLT2i class of drugs has been increasingly used in the treatment of diabetes due to improved cardiovascular outcomes and renal protective effects. However, diagnosing DKA can be a concern while treating patients with this drug. While the SGLT2i is responsible for his euglycemic presentation, DKA was likely triggered by his SGLT2i use, euglycemic DKA was suspected. ABG on presentation revealed blood glucose at 185 mg/dL. Given the history of recent diagnosis of diabetes mellitus and SGLT2 inhibitor use, euglycemic DKA was suspected. ABG revealed metabolic acidosis (arterial blood gas pH 7.32, pCO2 20, pO2 130) with elevated anion gap of 24, HCO3 level of 10 mmol/L (reference range 22 - 28 mmol/L) and beta-hydroxybutyrate of 5.7 mmol/L (reference range 0 - 0.3 mmol/L). The lactate levels were normal. Wbc count 20,100. Urinalysis showed glucose 4+, ketones 4+, WBC 4, negative for infection. Computed tomography scan of his abdomen and pelvis with contrast showed 3.7 x 2.7 cm prostate abscess and acute cystitis. Patient was treated for euglycemic DKA with infusion of insulin and dextrose 10% with 0.45% NS. Careful monitoring of his blood sugar was required as it dropped with slight increase in infusion rate. He was started on ciprofloxacin for prostate abscess. Patient's metabolic acidosis resolved and he showed clinical improvement. Endocrinologist was on consult. Patient was switched to insulin regimen for glycemic control. 

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS II

Altered Mental Status and Hypercalcemia: A Rare Presentation of Pure Osteolytic Metastatic Prostate Cancer

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MON-LB66

Background: We present a rare case of hypercalcemia with the concomitant presence of parathyroid adenoma, secondary hyperparathyroidism due to kidney disease and hypercalcemia of malignancy. Mild hypercalcemia due to primary hyperparathyroidism often precedes the acute, more severe hypercalcemia of malignancy. Prostate cancers are usually known to cause osteoblastic lesions.

Steroid Hormones and Receptors

STEROID AND NUCLEAR RECEPTORS

Estrogen Receptor Beta Inhibits NFkbB Signaling to Inhibit Triple Negative Breast Cancer

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SUN-LB135

Triple Negative Breast Cancer (TNBC) affects approximately 15-20% of BC patients, yet accounts for a disproportionately higher rate of BC morbidity and mortality, in part due to lack of targeted therapies. We have shown that...
estrogen receptor beta (ERβ) is expressed in approximately 20% of TN breast tumors and that ligand-mediated activation of ERβ with estradiol (E2) or ERβ-selective agonists decreases tumor cell proliferation, invasion and migration in vitro and in vivo. Therefore, we aimed to elucidate the mechanisms by which ERβ elicits its anti-cancer effects in TNBC. RNAseq analysis of ERβ-expressing MDA-MB-231 cells demonstrated that ERβ significantly downregulates NFκB signaling in the presence of E2. ChIPseq for ERβ in these cells revealed that ERβ primarily associated with estrogen response elements, but 12% of all ERβ binding sites were located at NFκB consensus motifs. Using an NFκB reporter construct and qPCR, ERβ was shown to block TNFα-mediated induction of NFκB signaling and NFκB target gene expression. RNAseq analysis of MDA-MB-231-ERβ cells treated with TNFα or E2+TNFα revealed substantial global inhibition of TNFα regulated genes in the presence of E2. ChIPseq for NFκB demonstrated that ERβ significantly alters NFκB’s cistrome whereby it can both diminish NFκB binding and redistribute NFκB throughout the genome. ChIPseq also demonstrated that ligand-mediated activation of ERβ significantly diminished an activating histone mark (H3K27Ac) at many of these NFκB target genes while enhancing a repressive mark (H3K27Me3). The addition of H3K27Me3 at these loci was shown to occur through the recruitment of the histone methyltransferase, EZH2. Drug-mediated blockade of EZH2 activity reversed suppression of NFκB target gene expression by ERβ. Knockdown of NFκB or Mutation of ERβ’s DNA binding domain rendered ERβ incapable of associating with DNA, recruiting EZH2, methylating NFκB target gene loci, repressing NFκB target gene expression and inhibiting proliferation. Interestingly, ERβ was shown to elicit more potent anti-cancer effects in TNBC cells expression a constitutively active form of NFκB. These finding suggest that a primary mechanism by which ERβ functions as a tumor suppressor is through inhibition of NFκB pathway activity. Our studies have also revealed that ERβ functions as a molecular switch for EZH2 and repurposes it for tumor suppressive activities, as EZH2 has previously been reported to enrich NFκB signaling in TNBC. These findings could address the paradox that high EZH2 expression is associated with worse TNBC patient outcomes, while high H3K27Me3 expression is associated with improved patient outcomes. Currently, a Mayo Clinic Breast Cancer SPORE prospective phase II clinical trial is underway to investigate the efficacy of estradiol for the treatment of metastatic ERβ+TNBC and to further evaluate the cross-talk between ERβ, EZH2 and NFκB signaling.

Cardiovascular Endocrinology
ENDOCRINE HYPERTENSION AND ALDOSTERONE EXCESS II

Mineralocorticoid Receptor Mediates Sex-Dependent Anticontractile Effect of Perivascular Adipose Tissue in Obese Mice.
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SUN-LB93

Obesity, a condition of excessive fat mass and subclinical inflammation, reached epidemic proportions with higher prevalence in women compared to men worldwide. Expansion of the perivascular adipose tissue (PVAT) is observed in obesity and clinical studies indicate a positive correlation between PVAT amount and body mass index. PVAT, a fat depot surrounding most of the vessels, modulates vascular function by releasing PVAT-derived factors such as adipokines.

Thyroid
THYROID DISORDERS CASE REPORTS II

Carbohydrate Crash: A Rare Case of Thyrotoxic Periodic Paralysis
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SAT-LB81

Introduction Thyrotoxic Hypokalemic Periodic Paralysis (TPP) is an uncommon diagnosis in the western world and may be the initial presentation of hyperthyroidism. Case A healthy 37 year old Asian male was visiting the US when he had sudden onset lower limb weakness after carbohydrate rich meal on Saturday night. He reported hand tremors for 1 month and a 10kg weight loss. On examination he was anxious with a fine hand tremor, BP 158/80mmHg, and HR 106bpm. He had grade 2/5 power to lower limb proximal muscles and brisk reflexes. Thyroid and eyes were normal. Laboratory results significant for potassium (K) 3.2mmol/l, TSH 0.005 (0.270-4.4iu/ml), FT4 2.6 (0.8-2.2ng/dl), FT3 12.4 (2.77-5.27 pg/ml) and TSH Receptor antibody was 23.9% (<16%). Thoracolumbar MRI was normal. Repletion of K resulted in total resolution of paresis. He was given propranolol and methimazole and chose to complete workup in China. Clinical Lesson: TPP results in paralysis due to hypokalemia and hyperthyroidism and can be the initial presentation of hyperthyroidism. It is most common in Asian males 20-40 years with incidence 1.9%, but only 0.2% in the west. Proximal muscles are affected more. Attacks may be precipitated by carbohydrate load, rest after exercise, or stress. Patients tend to present on weekends between 2100-0900hrs. It is hypothesized that K metabolism is diurnal, with influx to muscle at night or at rest. Once euthyroid, TPP will not recur unlike familial hypokalemic periodic paralysis which is recurrent and of earlier onset. The underlying reason remains unclear. It may be related to the action of thyroxine on Na/K-ATPase pump. TPP is usually associated with Graves’ disease, but other causes of hyperthyroidism have been reported. TPP is a treatable rare illness in Asians, and very uncommon in the West. Physicians must be aware of its subtleties, as it may be confused with other more common conditions. References: Chang-Hsun Hsieh, Shi-Wen Kuo, Dee Pei, Yi-Jen Hung, Sandra Chyi-Fan, Ling-I Wu, Chih-Tsueng He, Tsao-Chin Yang, Wei-Cheng Lian, and Chien-Hsing Lee, Thyrotoxic periodic paralysis: an overview, Ann Saudi Med. 2004 Nov-Dec; 24(6): 418-422. doi:10.5144/0256-4947.2004.418

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