[1]Yale New Haven Health - Bridgeport Hospital, Bridgeport, CT, USA, [2]Saba University School of Medicine, Saba, Netherlands Antilles, [3]Brigham and Women's Hospital, Boston, MA, USA.

SUN-700

Introduction

Sodium glucose co-transporter 2 (SGLT2) inhibitors have become an appealing treatment for diabetes due to their favorable cardiac and renal outcomes. However, reports continue to emerge describing potentially life-threatening adverse events such as Fournier's gangrene (FG) and diabetic ketoacidosis (DKA) associated with their use. Herein, we report a case of simultaneous FG and DKA in a patient taking canagliflozin.

Case Presentation

A 37-year-old woman with a history of type 2 diabetes mellitus, peripheral neuropathy, and morbid obesity (BMI of 45.8 kg/m^2) presented to the hospital with left gluteal pain associated with dysuria despite 5-day treatment with trimethoprim/sulfamethoxazole for a presumed urinary tract infection. Approximately 1 month prior, sitagliptin and canagliflozin were added to her regimen due to poor glycemic control on metformin (HbA1c 9.8%). On examination her temperature was 36.9°C, pulse 117 beats/minute, blood pressure 144/79 mmHg and respiratory rate was 19 bpm. She appeared lethargic and had suprapubic tenderness and induration in the left gluteal region extending to the perineum. Laboratory findings revealed an arterial pH of 7.23 and PCO2 of 34 mmHg, a blood glucose of 402 mg/dL, serum bicarbonate 12 mmol/L (20-30 mmol/L), an elevated anion gap of 24 mmol/L (7-17 mmol/L) and a lactate of 1.8 mmol/L. Urinalysis showed 4+ glucose and 1+ ketones. Serum β-hydroxybutyrate was 2.49 mmol/L (0.02-0.27mmol/L). A CT scan of the abdomen and pelvis showed marked inflammatory changes with subcutaneous edema and air within the medial left gluteal soft tissues and locules of air extending into the presacral soft tissues suggestive of Fournier's gangrene. The diagnoses of Fournier's gangrene and DKA were made. The patient was started on empirical antibiotic treatment and required six surgical explorations with debridement. Interestingly, initial DKA management included only subcutaneous insulin. Only when serum ketones were identified and the anion gap persisted, insulin infusion with aggressive fluid resuscitation was initiated with successful resolution of anion gap metabolic acidosis. She was discharged with a urinary catheter, vacuum dressing, colostomy with instructions to start insulin glargine 18U and discontinue the oral anti-diabetic medications.

Discussion

To the best of our knowledge, this is the first case describing the simultaneous occurrence of two potentially fatal adverse effects of SGLT2 inhibitor therapy; Fournier's gangrene and DKA. In light of the FDA's warnings and the growing popularity of SGLT2 inhibitor therapy it is important to be mindful of their more serious and potentially fatal complications. It is also important to promptly terminate SGLT2 inhibitors when harmful adverse effects are suspected to prevent further progression.

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES

U-Shaped Association of Plasma Testosterone, and No Association of Plasma Estradiol, with Incidence of Any Fracture and Hip Fracture in Older Men.

Bu Beng Yeap, MBBS, PHD[1], Helman Alfonso, PhD[2], Paul Chubb, BSc, PHD[3], Jacqueline Center, MBBS, PhD[4], Jonathan Beilin, MBBS, PHD[3], Graeme Hankey, MBBS, MD[1], Osvaldo Almeida, MD, PHD[1], Jonathan Golledge, MChir[5], Paul Norman, MB ChB, DS[1], Leon Flicker, MBBS, PHD[1].

[1]University of Western Australia, Perth, Australia, [2]Curtin University, Perth, Australia, [3]Fiona Stanley Hospital, Perth, Australia, [4]Garvan Inst of Med Research, Sydney, Australia, [5]James Cook University, Townsville, Australia.

SAT-033

Osteoporosis resulting in bone fractures is a major cause of morbidity in older men. Previous studies implicated reduced exposure to estradiol (E2) with increased fracture risk in men. The extent to which circulating androgens contribute to maintenance of bone health is uncertain. We examined associations of different sex hormones with incidence of any bone fracture or hip fracture in older men. We analysed 3,307 community-dwelling men aged 76.8±3.5 years, median follow-up period of 10.6 years. Medical information was collected by questionnaire. Frailty was assessed using the FRAIL scale (1). Early morning plasma testosterone (T), dihydrotestosterone (DHT) and E2 were assayed by mass spectrometry, sex hormone-binding globulin (SHBG) and luteinising hormone (LH) by immunoassay. Incidence of any fracture and hip fracture were determined via data linkage to emergency department presentations and hospital admissions. Risk of fracture according to sex hormone concentrations was analysed. Hazard ratio of fracture according to sex hormone quartiles (Q1-4) was assessed using Cox regression models adjusted for age, medical comorbidities and frailty. In 30,355 participant-years of follow-up, the incidence of any fracture was 1.1% and hip fracture 0.5% per participant per year. Incident fractures occurred in 330 men, including 144 hip fractures. Probability plots suggested non-linear relationships between hormones and risk of any fracture and hip fracture, with higher risk at lower and higher concentrations of plasma T, lower E2, higher SHBG and higher LH. In fully-adjusted models, there was a U-shaped association of plasma T with incidence of any fracture (Q1: reference group, Q2: fully-adjusted hazard ratio [HR]=0.69, 95% confidence interval [CI]=0.51-0.94, p=0.020; Q3: HR=0.59, CI=0.42-0.83, p=0.002; Q4: 0.85, CI=0.62-1.18, p=0.335). A similar U-shaped association of T was found with incidence of hip fracture (Q1: HR=1.0; Q2: HR=0.60, CI=0.37-0.93, p=0.043; Q3: HR=0.52, CI=0.31-0.88, p=0.015; Q4: HR=1.04, CI=0.65-1.68, p=0.866). DHT, E2 and LH were not associated with incidence of any fracture or hip fracture (all p>0.050). SHBG was not associated with incidence of any fracture, but was associated with hip fracture (Q4 vs Q1: HR=1.76, CI=1.05-2.96, p=0.033). In conclusion, we found a non-linear or U-shaped association of T with fracture risk, with no association of E2. Mid-range plasma T was associated with lower incidence of any fracture and

hip fracture, and higher SHBG with increased risk of hip fracture. Circulating androgen rather than estrogen may be a biomarker for hormone effects on bone driving fracture risk. A randomised controlled trial of T therapy powered for the outcome of fracture may be warranted and should recruit men with baseline T in the lowest quartile of values.
Reference: (1) Hyde Z, et al. J Clin Endocrinol Metab 2010; 95: 3165-3172.

Tumor Biology

TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS

Refractory Paraneoplastic Non Islet Cell Tumor Hypoglycemia (NICTH) from Hepatocellular Carcinoma Managed with Somatostatin Analogue and Glucocorticoids

Mahwash Fatima Siddiqui, MD, Amy Vora, MD, Sadia Ali, MD, Sasan Mirfakhraee, MD.
University of Texas Southwestern Medical Center, Dallas, TX, USA.

SAT-117

Non islet cell tumor hypoglycemia (NICTH) is a rare paraneoplastic syndrome generally seen in tumors of mesenchymal and hepatic origin. This syndrome is characterized by life threatening hypoglycemia caused by over expression of high molecular weight insulin-like growth factor 2 (IGF 2). The main stay of treatment is surgical resection of the tumor with no clear medical management being reported as standard of care.

We present the case of a 72 year old Cambodian man with no history of diabetes mellitus who presented to our institution with severe hypoglycemia complicated by a seizure and was found to have hepatocellular carcinoma (HCC). Hypoglycemia occurred during times of fasting. Laboratory evaluation revealed a serum glucose of 30mg/dl with insulin level of 2.2 mcIU/mL [2.6 - 24.9 mcIU/ml], C-Peptide of 0.17 ng/mL [0.80 - 3.85 ng/ml], BHB <0.1 mmol/L [0.0 - 0.3 mmol/L] and Proinsulin of <0.4 pmol/L [< or = 18.8 pmol/L]. Hypoglycemic agents screening was negative. Insulin Antibody was negative <0.4 U/mL [<0.4 U/mL] and adrenal insufficiency and hypothyroidism was ruled out. Patient was found to have an elevated IGF 2: IGF 1 ratio of 78 confirming the diagnosis of NICTH. IGF 2 level was 780 ng/ml [333 - 967 ng/ml] while IGF-1 was < 10 ng/ml [32-200 ng/ml] He was not a candidate for surgery due to portal vein involvement and tumor radioembolization was unsuccessful. Despite Prednisone dose of 10 mg twice daily and frequent complex carbohydrate meals, he still continued to have hypoglycemia ultimately requiring hospitalization. During hospitalization, he was treated with 50% dextrose infusion, 37.5 grams of dextrose gel every three hours and frequent small meals. Hypoglycemia remained refractory and a trial of diazoxide was ineffective. He was then started on octreotide with titration to 100mg every 8 hours with significant reduction in hypoglycemic episodes. He continues to remain on octreotide, Prednisolone 20mg twice a day, dextrose gel and dextrose infusion. Goal is to wean dextrose infusion and transition him to Pasireotide 40mg monthly.

Hepatocellular carcinoma has been associated with NICTH in the literature. NICTH is characterized by an IGF2:IGF1 ratio >10 as there is no commercially available assay for big IGF II. Definitive treatment involves surgical resection or tumor debulking. Octreotide has antiangiogenic and antineoplastic properties and unfortunately, few studies have shown improved survival and quality of life in patients with advanced HCC. In the case of our patient, tumor was unresectable and NICTH improved with octreotide and prednisolone.

Thyroid

THYROID DISORDERS CASE REPORTS II

Untreated Primary Hypothyroidism Presenting as Pica with Concurrent Hyponatremia and Rhabdomyolysis

Mehwish A. Mirza, MD[1], Ricky Ayala, MD[1], Jacqueline Savage, MD[2].
[1]University of Connecticut School of Medicine, Farmington, CT, USA, [2]Hartford Hospital, Hartford, CT, USA.

SAT-487

Background:

Psychosis is a rare but known presentation of hypothyroidism, whereas other mental health disorders are less commonly associated. Pica, the consumption of non-nutritive, non-food substances, has not been reported to be associated with hypothyroidism. We describe a case of untreated severe hypothyroidism in which the patient presented with pica that reversed with treatment with levothyroxine.

Clinical case:

A 65-year-old female with a history of cigarette smoking and chronic marijuana use was brought to the emergency department by family after she was found attempting to eat non-food objects such as pens and a toothbrush. She reported new onset unsteady gait and having frequent falls over the past several months in addition to being increasingly forgetful. She complained of fatigue and reported recent unintentional weight loss, but denied cold intolerance, skin or hair changes, or constipation. On admission, she was noted to be hypothermic with body temperature between 94-95 degrees Fahrenheit. Physical examination was essentially unremarkable with normal thyroid size and reflexes. No pretibial edema was noted. Admission labs showed hemoglobin of 14.0 g/dL with a white cell count of 8000 cells/uL, without evidence of anemia or infection. Sodium was low at 123 mmol/l and creatinine kinase was elevated at 989 U/L which peaked at 1356 U/L during her admission. CT of the head was negative for any acute intracranial process. Further workup was significant for TSH 85.6 mIU/L (0.27-4.20 mIU/L), free T4 <0.1 ng/dL (0.80-1.90 ng/dL), total T4 0.7 mcg/dL (5.1-11.9 mcg/dL), total T3 < 25 ng/dL (76-181 ng/dL), and TPO antibody 416 IU/ml (<9 IU/ml). AM cortisol was 27.0 ug/dL (6.2-19.4 ug/dL) at 8 AM, ruling out hypocortisolemia. The patient had not seen a medical provider in 10 years, had no recent health maintenance, and had no prior known history of thyroid disease. She was given IV fluids and started on oral levothyroxine 100 mcg daily due to the severity of hypothyroidism. Her sodium improved to 130 mmol/l over the next 4-5 days.