Thyroid

THYROID DISORDERS CASE REPORTS II

A Case of Impending Thyroid Storm in a Patient with Subacute Thyroiditis Following an Influenza Vaccine
Simona Stefan, MD, Whitlatch B. Hillary, MD
1Montefiore Medical Center/The University Hospital for Einstein, Bronx, NY, USA, 2University Of Maryland Medical Center, Baltimore, MD, USA.

SAT-464

Introduction: Thyroid storm is a rare, potentially fatal condition, affecting 1% of individuals with thyrotoxicosis. Although it can theoretically be seen in any cause of thyrotoxicosis, the most likely underlying etiology is Graves' disease. The rarity of thyroid storm due to thyroiditis makes the diagnosis challenging as the clinical and biochemical features overlap Grave's disease. Here we describe a rare case of severe thyrotoxicosis in a woman due to subacute thyroiditis that developed after receiving an influenza vaccine.

Case report: A 30 year-old Caucasian female with no known past medical history presented to the ED with worsening sore throat, odynophagia and anterior neck pain. Symptoms began 4 weeks ago prior to presentation, 1 day after receiving an influenza vaccine. Other symptoms included loss of appetite, chills, fever, fatigue, malaise, abdominal pain, diarrhea, palpitations, heat intolerance and 5lbs weight loss. She was treated by her primary care provider for suspected pharyngitis with a course of corticosteroids and antibiotics. Two weeks later, given worsening symptoms, was referred to the emergency room. On exam, she appeared anxious and was tachycardic (124 beats per minute) and tachypneic (28 breaths per minute). She had no lid lag, stare, thyromegaly or thyroid bruit. However, there was significant tenderness on palpation of the anterior neck.

Laboratory evaluation was notable for TSH <0.01 uIU/mL (0.39 - 4.0.8), free T4 5.19 ng/dL (0.58 - 1.64), free T3 10 pg/ml (2.53-3.87), ESR 95 mm/hr (0-20) and CRP 9.339 mg/dl (0.0-0.9) consistent with thyrotoxicosis. TSI was negative. Family history was negative for autoimmune disease. She continued on beta blockers with a steroid taper for 8 weeks. Thyroid function tests and inflammatory markers normalized within 3 months.

Conclusion:

Aside from the described patient, only three other cases of thyrotoxic crisis due to subacute thyroiditis have been reported in the literature. This case underscores the importance of thoroughly investigating the etiology of severe thyrotoxicosis, given the management and prognosis varies depending on underlying cause. Thyroiditis should be considered in the differential diagnosis of thyroid storm in patients who do not have a personal or family history of autoimmunity and present with neck tenderness in the setting of a precipitating event. Subacute thyroiditis is very uncommon after influenza vaccine, there have been 4 reported cases.

Bone and Mineral Metabolism

CLINICAL ASPECTS OF OSTEOPOROSIS AND VITAMIN D ACTION

Fracture Risk Assessment Models for Patients With T2DM
Andreea Maria Banica, Ms, MD1, Luciana Mihaela Oprea, Ms, MD1, Iuliana Ilie, Ms, MD1, Viviana Elian, Ms, MD, PhD2, Anda Caraageorgeheopol, MS, MD1, Carmen Iordachescu, Ms, MD1, Catalina Poiana, MD, PhD, FACE, CCD3, Madalina Musat, MS, MD, PhD1.
1”C.I. Parhon” National Institute of Endocrinology, Bucharest, Romania, 2“Carol Davila” University of Medicine and Pharmacy, “Prof. Dr. N. Paulescu” National Institute for Diabetes, Nutrition and Metabolic Diseases, Bucharest, Romania, 3Carol Davila University of Medicine and Pharmacy, C I Parhon Institute of Endocrinology, Bucharest, Romania.

MON-389

Fracture Risk Assessment Models for Patients with Type 2 Diabetes
Key Words: Type 2 Diabetes, Osteoporosis, FRAX

Introduction

Bone mineral density (BMD) measurement, a tool used to diagnose osteoporosis (OP) and to predict fracture risk, has not been found very useful in type 2 diabetic (T2DM) patients. They have a 69% higher fracture risk despite having higher hip and lumbar spine BMD than the non-diabetic population. The aim of this study was to examine the impact of 3 different fracture risk assessment (FRAX) models using surrogate adjustments for T2DM in predicting osteoporotic fracture risk over 10 years.

Material and Methods

Observational retrospective study included 98 patients with OP or osteopenia: 94 women and 4 men admitted in the National Institute of Endocrinology between 2011-2019. 50 % (n= 49) of the patients had T2DM, while the other half were non-diabetic patients. BMI, BMD, lipid profile, serum creatinine, calcium, phosphorus, 25(OH) vitamin D, HbA1c were assessed. BMD was measured on a GE Lunar osteodensitometer. The risk of major osteoporotic fracture in 10 years was assessed with FRAX adjusted for Romania. For diabetic patients, FRAX was adjusted by adding 10 years to patients’ age (model 1), by using rheumatoid polyarthritis as a substitute for T2DM (model 2) or by lowering T score with 0.5 DS (model 3).

Results

Non-diabetic patients had a lower BMI (p=0.001) and a lower BMD (p=0.03) than diabetic patients. A higher BMI correlated with a higher hip BMD (p=0.004).

For diabetic patients, FRAX risk without adjustment was statistically significant lower than FRAX risk calculated with model 1 and 2 (p<0.001) for both major and hip fracture risk. Unadjusted FRAX risk was lower than the one calculated with model 3 only for hip fracture risk (p=0.001). Model 1 FRAX adjustment led to a statistically significant risk of both major osteoporotic fracture (p= 0.004) and hip fracture (p=0.04) over 10 years in diabetic patients than
non-diabetic patients, though diabetic patients had higher BMD. The same observation was made when FRAX was adjusted by model 2 (p=0.001) or by model 3 (p=0.001). HbA1c correlated inversely with FRAX adjusted with all three models. Discussion FRAX calculator does not include T2DM among secondary causes of OP and this precludes a proper risk assessment independent of BMD. Trabecular bone assessment (TBS) captures a larger portion of the diabetes-associated fracture risk than BMD, however TBS it is not fully independent of the BMD. We examined 3 models of adjusted FRAX in T2DM patients that showed an important increase in fracture risk prediction when adding BMD - independent risk factors into FRAX calculator.

Conclusion T2DM patients have a greater risk of major osteoporotic fracture in 10 years at the same BMD compared with non-diabetic population. New models of FRAX adjusted for T2DM are needed in assessing the intervention threshold for OP/osteopenia of patients with T2DM.

Reproductive Endocrinology

CLINICAL STUDIES IN FEMALE REPRODUCTION I

SSRI Use in the Peripartum Period Regulates Mammary Gland Parathyroid Hormone Related Protein (PTHrP) by a Serotonylation-Dependent Mechanism

Celeste Sheftel, BA, Luma C. Sartori, UG, Laura L. Hernandez, PhD

UNIVERSITY OF WISCONSIN MADISON, Madison, WI, USA.

SAT-009

During lactation, a woman experiences a considerable amount of bone loss and recent studies suggest bone deficits persist years postpartum. Furthermore, selective serotonin uptake inhibitors (SSRIs), which are often prescribed to women experiencing peripartum depression, have been linked to osteopenia. Serotonin signaling can increase parathyroid hormone related protein (PTHrP), a bone remodeling protein which liberates calcium for the milk. Additionally, fluoxetine (a common SSRI) results in increased mammary gland serotonin content and PTHrP, and treatment during the peripartum period reduced maternal bone mineral density. One proposed mechanism of serotonin action is by its covalent addition to proteins by transglutaminase (TG2), termed serotonylation. We therefore investigated whether the combination of fluoxetine and lactation can exacerbate maternal bone loss and the underlying mechanism. We hypothesized that SSRI-induced serotonin signaling in the lactating mammary gland increases PTHrP through a serotonylation-dependent mechanism. Treatment of mouse mammary epithelial cells (HC11) with fluoxetine significantly upregulates PTHrP gene expression and the concentration of its downstream effector, cAMP, over control (P < 0.0004). Furthermore, treatment of the HC11 cells with fluoxetine in addition to a TG2 inhibitor, monodansylcadaverine, restores PTHrP mRNA expression to levels observed in the control. Small g-proteins have emerged as a common target protein for serotonylation. Currently, our data suggest that the g-proteins, RhoA and Rab4, are potential serotonylation targets in the mammary gland. Together these data suggest that the molecular process of serotonylation in HC11 cells links serotonin signaling to increased PTHrP expression. Future work is directed at using the cre-lox system to genetically ablate serotonylation using a WAPCre/TG2lox transgenic mouse to determine whether decreasing serotonylation in vivo in the mammary gland during lactation improves maternal bone mass.

Tumor Biology

TUMOR BIOLOGY: DIAGNOSTICS, THERAPIES, ENDOCRINE NEOPLASIAS, AND HORMONE DEPENDENT TUMORS

The Roles of Two Insulin Receptor Isoforms in Triple Negative Breast Cancer Growth

Chifei Kang, PhD1, Gadi Shlomai, NY2, Annie James, MS1, Irini M. Antoniou, MS1, Tiffany Scully, PhD1, Abora Ettela, MS1, Nathan G. Kase, MD1, Teresa Wood, PhD2, Derek LeRoith, MD, PhD1, Emily Jane Gallagher, MB, BCCh, BAO, PhD1.

1 Icahn School of Medicine at Mount Sinai, New York, NY, USA, 2 Rutgers-New Jersey Medical School, Newark, NJ, USA.

SUN-131

Systemic hyperinsulinemia is believed to be an important factor in the progression of a number of cancers, including breast cancer by activating the insulin receptor (IR) signaling cascade in the tumor cells. The IR is expressed in two isoforms, IR-A and IR-B. IR-B is the full-length isoform, while IR-A is lacking 12 amino acids in the α-subunit due to exon 11 alternative splicing. IR-A is predominantly expressed in cancer tissues, while IR-B is mostly expressed in metabolic tissues. The IR and closely related insulin-like growth factor 1 receptor (IGF-1R) are expressed in different ratios in cancer cells. Compared with estrogen receptor positive breast cancers, triple negative breast cancers (TNBC) frequently have higher ratios of IR to IGF-1R. Hyperinsulinemia is associated with increased prevalence of TNBC in pre-menopausal women. Although new targeted therapies are emerging, among breast cancer subtypes TNBC continues to carry the worst prognosis and therefore developing a greater understanding of the links between IR signaling and TNBC progression is critical. The aim of this study is to understand the role of IR-A and IR-B on proliferation, metastasis and metabolism in breast cancer cells. We stably overexpressed human IR-A (IR-A OE) and IR-B (IR-B OE) in TNBC MDA-MB-231 (231) and murine c-myc/vegf overexpressing Mvt1 cells with lentiviral transduction using pLVX-ires-puro HIV-1-based expression vectors with cDNA encoding the human IR-A, IR-B and control cDNA sequences. Native murine IR was silenced using lentiviral transduction of shRNA in the Mvt1 cells. Overexpression of IR was confirmed at a protein level by western blot, and RNA isoform expression was confirmed using real time PCR. Cell proliferation assays were performed in DMEM/10% FBS and revealed that MDA-MB-231 cells with IR-A OE cells had 15% higher proliferation rates than 231 IR-B OE cells. We then examined the IR signaling pathways by western blot in DMEM/10% FBS. No differences in phosphorylated or total ERK1/2