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SUN-313
Serum osteocalcin is emerging as a potential marker of glucose homeostasis and risk of type 2 diabetes mellitus (T2DM). In mice, osteocalcin knockouts exhibit depressive-like behaviours but knockouts of a putative osteocalcin receptor, GPR158, are resistant to chronic unpredictable mild stress. Recently, osteocalcin release from bone has been suggested to mediate some aspects of the acute stress response. Here, we assess relationships between serum osteocalcin, depression and perceived stress in people with T2DM. Participants with T2DM were assessed for whether they met the DSM-5 criteria for Major Depressive Disorder using the research version of the Structured Clinical Interview for DSM-5 depression criteria (SCID-5RV). Subjective stress was assessed using the Perceived Stress Scale (PSS) with higher scores indicating greater subjective stress. Serum carboxylated (cOCN) and uncarboxylated (unOCN) osteocalcin were assayed from fasting morning blood by commercial ELISA. Among 87 participants (mean age 62.9±9.5, 52% women), 18 (26%) were experiencing a depressive episode (7 men, 11 women). Both serum unOCN and cOCN were associated with higher PSS scores in participants with depression (unOCN, r=0.566, p=0.014; cOCN, r=0.564, p=0.015) but not in those without depression (unOCN, r=0.002, p=0.985; cOCN, r=0.090, p=0.463). A significant interaction was found between depression and PSS scores predicting serum unOCN in a linear model adjusted for age, sex, body mass index, antidepressant use and HbA1c (F=6.225, p=0.015). The results are consistent with reports that osteocalcin release from bone may be a mediator of stress perception; however, among people with T2DM, this relationship was observed only among those currently experiencing a depressive episode.

Thyroid
THYROID NEOPLASIA AND CANCER
Clinicopathological Features of Papillary Thyroid Cancer After Fukushima and Chernobyl Accidents
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MON-508
The phenomenon of a sharp increase in the incidence of thyroid cancer worldwide is now under debate. Screening activity, diagnostic improvements or real rise in incidence as a result of unknown carcinogens are discussed. Studies in Belarus after Chernobyl showed that the synergistic influence of radiation and nitrates might lead to an increased thyroid cancer (TC) risk in children. For better understanding of the etiology, we compared the published clinical data of pediatric TC patients after the nuclear emergency of Fukushima with the observations we made after the Chernobyl accident.

In a large-scale survey after the Fukushima accident, 300,476 subjects were screened and by September 2018, 191 subjects were diagnosed with thyroid malignancy or suspected malignancy by fine needle aspiration. Mean age of TC patients was 17.8 years at presentation. Mean tumor size was 14.9 mm. Postoperative lymph node metastasis, extra-thyroidal invasion, and pulmonary metastasis were detected in 79%, 45%, and 2.1% of all cases, respectively. Only 4.8% TC cases were staged as low risk pT1aN0M0 (Suzuki et al. 2018). For comparison, in Belarus patients mean age was 13.0 years at presentation (1078 cases), mean tumor size 14.4 mm. Lymph node metastases were observed in 74%, pulmonary metastasis in 11% and extra-thyroidal extension in 48.5 - 64.1% (with respect to latency period). The low risk (pT1aN0M0) TC patients were diagnosed in 19.2% cases.

The most of TC cases from Japan and Belarus were clinically significant, not “overdiagnosed” and screened on time. Given that the accidental thyroid doses were very low in Japanese cases, it would be very important to evaluate and compare the exposure to endocrine disruptors as e.g. nitrates and low radiation doses from diagnostic procedures (dental X-ray examination and computed tomography).

Reference:
Suzuki S, Matsumoto Y, Ookouchi C, Nakano K, Iwadate M, Suzuki S, Nakamura I, Fukushima T, Mizunuma H, Yamashita S, Takenoshiba S. The clinicopathological features of childhood and adolescent thyroid cancer in Fukushima after the Fukushima Daiichi nuclear power plant accident. Thyroid. 2018; Supplement 1, (Poster 136).

Neuroendocrinology and Pituitary
CASE REPORTS IN CLASSICAL AND UNUSUAL CAUSES OF HYPOPITUITARISM II
Atypical Presentation of Isolated Adrenocorticotropic Hormone Deficiency and Sheehan's Syndrome
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MON-243
Introduction: Isolated adrenocorticotropic hormone (ACTH) deficiency is a rare pituitary hormone deficiency defined by secondary adrenal insufficiency and normal secretion of all other pituitary hormones. Patients present with fatigue, weakness, weight loss, anorexia, nausea, low cortisol levels and low ACTH levels. Isolated ACTH deficiency is more common in males and usually presents in the fifth
decade of life. Main mechanisms involved in the pathogenesis are genetics and autoimmune causes, traumatic brain injury and infarction of the pituitary postpartum, known as Sheehan’s syndrome. Sheehan’s syndrome is characterized by postpartum hemorrhage, failure to lactate and menstrual irregularities and it can occur from immediate postpartum period to years after delivery. The most common hormone deficiencies are prolactin and growth hormone. Empty sella is the most common finding on brain MRI. We are reporting a case of a woman in her third decade with isolated ACTH deficiency due to Sheehan’s syndrome two years postpartum, able to lactate, with normal menes and normal brain MRI. Clinical Case: A 33-year-old woman G3P3A0 with hypothyroidism who was referred to Endocrinology clinics due to tiredness, fatigue and weakness. She reported postpartum hemorrhage requiring 4 PRBC transfusions and IV steroids after last pregnancy 5 years ago. Patient was able to lactate after pregnancy and continued in her usual state of health until 3 years ago when she referred loss of consciousness with traumatic head injury due to hypoglycemia. At Endocrinology office physical examination and vital signs were unremarkable, including no blood pressure or heart rate variations with positional changes. Despite hypothyroidism being adequately controlled, she continued with extreme fatigue and weakness affecting her quality of life, for which cortisol and ACTH levels were ordered. Laboratories showed normal electrolytes, negative autoantibodies, cortisol 0.20 μg/dL (5-25 μg/dL) and ACTH 22 pg/mL (10-60 pg/mL) suggesting partial isolated ACTH deficiency. ACTH stimulation test was done and noted with suboptimal response. Evaluation of other anterior pituitary hormones was normal. Brain MRI showed normal pituitary gland. She was started on hydrocortisone in AM and PM and symptoms resolved. Conclusion: Immediate recognition of isolated ACTH deficiency due to Sheehan’s syndrome is necessary due to the availability of effective treatment and morbidity and mortality associated with this serious condition. To our knowledge isolated ACTH deficiency due to Sheehan’s syndrome in which the patient was able to lactate and normal findings on brain MRI has not previously been reported. References: Shivaprasad C. Sheehan’s Syndrome: Newer advances. Indian J Endocrinol Metab. 2011 Sep; 15(3): S203-207. DOI:10.4103/2230-8210.84869.

Thyroid

THYROID NEOPLASIA AND CANCER

Primary Thyroid Lymphoma Developing from a Background of Lymphocytic Thyroiditis: First Report in Mice

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OR21-05

Primary thyroid lymphoma is rare, accounting for less than 5% of all thyroid malignancies. It typically develops in patients with Hashimoto thyroiditis who have approximately a 70 fold higher risk than other patients. The mechanisms underlying the development of thyroid lymphoma remain unclear, and no mouse model has been described. For our studies of papillary thyroid cancer and lymphocytic thyroiditis, we crossed TPO-Cre-ER transgenic mice and hBRAFV600E knock-in mice onto the NOD. H2b4 background to establish TPO-Cre-ER_hBRAFV600E NOD.H2b4 strain where papillary thyroid cancer is induced by the injection of tamoxifen and thyroiditis by the administration of iodine in the drinking water. Mice injected with corn oil or drinking regular water served as control. In 3 of 121 mice, TPO-Cre-ER_hBRAFV600E NOD.H2b4 mice injected with corn oil and drinking iodinated water we observed the development of thyroid lymphoma. At about 6 months after the injection of corn oil, these mice developed a marked increase in the size of the thyroid gland, which appeared hypoechoic on thyroid ultrasound. Fine needle aspiration on the thyroid gland under ultrasound was performed, along with measurement of TPO antibodies, H&E thyroid histology; immunohistochemistry, and flow cytometry at the time of sacrifice. Histology established a diagnosis of Hodgkin lymphoma with the typical Reed Sternberg cells. Flow cytometry identified an increased frequency of CD8+ effector memory T cells in the thyroid lymphoma. TPO antibodies were significantly higher in mice with thyroid lymphoma than in those without, perhaps suggesting their utility as predictive biomarkers. In summary, we report a mouse model of thyroid lymphoma that evolves from a background of lymphocytic thyroiditis with a predictable natural course that can be monitored by thyroid ultrasound and TPO antibodies. This model can be used to study the mechanisms and development of thyroid lymphoma in patients.

Healthcare Delivery and Education

EXPANDING CLINICAL CONSIDERATIONS FOR PATIENT TESTING AND CARE

Evaluation of the Timeliness of Serial Denosumab Administrations at the University of Colorado Hospital

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MON-137

BACKGROUND:
Denosumab is an antiresorptive medication commonly used in the treatment of osteoporosis that works by slowing bone loss. This medication should not be delayed or interrupted without initiation of an alternative treatment (i.e. bisphosphonates) as studies have shown that this can lead to rapid bone loss, very high markers of bone turnover, and increased vertebral fracture (VF) risk. It is unknown how frequently dosing is delayed in practice settings and how best practices can ensure timely dosing. Our study aimed to (1) evaluate the frequency and causes of delayed denosumab doses at our institution and (2) compare the incidence of delayed doses before and after implementation of a new electronic ordering process.

METHODS:
We performed a retrospective chart audit for all patients receiving two or more denosumab doses at our institution between 1/1/16-8/11/18 and categorized those whose doses were >/=214 days (7 months) as delayed. We reviewed...