estradiol 0-24 hours after a dose of 100 mcg/m2 (max 100 mcg) of Triptorelin Pamoate. The results for LH greater than 8 uUI / L and estradiol of 80 pg / ml were considered positive - ***Results***: From 79 girls, mean age 8,02 years old (+/- 2,2) 41 were classified as likely PP (group 1) and 38 unikely PP (group 2) On group 1, 39 patients (95,1 %) had results of LH above 8 uUI/L. In this group, 5 patients (12.1%) had estradiol results below 80 pg / ml. Of the positive test, 3 patients (7,6%) %) had LH peak time 60 min, 4 patients (10,2%) had LH peak time 90 min, 31 (79,4%) had LH peak at time 180 minutes. In group 2, 3 patients (7,89 %) had values of estradiol above 80 pg/ml and 1 patient had values above 8 uUI/ml. Sensitivity was 95,1% specificity 97,4%, predicted positive value 97,5% and negative predicted value 95%. ***Conclusion***: Low dose LHRH test for precocious puberty with 100 mcg/m2 of Pamoate Triptorelin is a useful tool in the diagnosis of precocious puberty in girls, with high sensitivity and specificity and with lower cost than other diagnostic tools.

# Thyroid

## THYROID DISORDERS CASE REPORTS II

### *Pembrolizumab-Induced Thyroiditis with Negative Thyroid Peroxidase Antibody*

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**SAT-481**

***Introduction*:** Immune checkpoint inhibitors (ICI) have reformed oncology treatment through its immunomodulatory effect on T-lymphocytes to target metastatic and locally advanced cancers but have been known to produce immune-related adverse events (irAEs). Thyroiditis is a well-documented endocrinopathy occurring in patients receiving ICI; however, a Thyroid Peroxidase Antibody (TPO Ab) negative case of ICI induced thyroiditis suggests that its pathogenesis is independent of antibody mediated thyroid destruction and more associated with an alternative immunoregulatory mechanism. ***Case Description*:** A 60-year-old Caucasian, male with a 37-year smoking history and lung adenocarcinoma with metastasis to the brain was referred to Endocrinology clinic for evaluation of suppressed thyroid stimulating hormone (TSH) level. Patient was treated with a four-month course of IV Pembrolizumab every three weeks. TSH was <0.015 (NL 0.465-4.680 IU/mL) four weeks before being seen at the office. TSH level was normal 2.359 before starting immunotherapy. Patient reported occasional anxiety and heat intolerance, but did not experience other hyperthyroid symptoms. Physical examination in office demonstrated no significant thyromegaly, nodules, or tenderness. Vital signs were normal. Thyroid function tests obtained during the office visit were consistent with subclinical hypothyroidism. TSH was mildly elevated 7.545 with normal Free T4 of 0.94 (NL 0.78 - 2.19 ng/dL) and normal Free T3 level of 3.61 (NL 2.77 - 5.27 pg/mL). TPO antibodies were negative. Four weeks later, patient developed overt hypothyroidism; TSH level was higher 12.437 with low Free T4 of 0.71. Patient was then complaining of fatigue and cold intolerance. A diagnosis of drug-induced thyroiditis from Pembrolizumab was made. The patient was prescribed levothyroxine 75 mcg daily and followed closely. ***Discussion*:** While literature exists documenting the rare side effect profile of ICI endocrinopathies, few studies illustrate the implications and correlations of TPO Ab negative findings in ICI induced thyroiditis. The role of thyroid autoantibodies in the presumed antibody mediated pathogenesis of thyroid abnormalities is unclear and warrants further longitudinal studies to determine its function in these patients. This case report hopes to both identify the deficit of pathophysiological knowledge contextualizing irAEs while encouraging current healthcare practitioners to continue close monitoring of patients receiving ICI.

# Tumor Biology

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

### *Distinct DNA Methylation Signature in Neuroendocrine Tumors of Different Primary Sites and Hereditary Predisposition*

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**SUN-115**

Objective

There is scant data of the genome-wide methylome alterations in neuroendocrine tumors (NET). Thus, the goal of this study was to compare the DNA methylation signature of NETs with respect to various primary sites and inherited genetic predisposition syndromes including von Hippel-Lindau (VHL) and multiple endocrine neoplasia type 1 (MEN1).

Methods

Genome-wide DNA methylation analysis of 96 NETs (primary and metastatic) was performed by using the Illumina Infinium EPIC Array. Principal component analysis (PCA) and unsupervised clustering analyses were performed to identify distinct methylome signatures. The methylation status of genetic drivers such as *APC* were assessed by primary site.

Results

A total of 835,424 CpGs methylation sites were quantified. Hypermethylated CpG sites were detected more frequently in sporadic vs. MEN1-related vs. VHL-related NETs, respectively ($p < 0.001$ for all comparisons), while hypomethylated CpGs sites were more common in VHL-related NETs vs. sporadic and MEN1-related NETs ($p<0.001$ for both comparisons).

Small-intestinal NETs (SINETs) had the most differences at CpGs with the highest number of hyper- and hypomethylated CpG sites, followed by duodenal NETs

(DNETs) and pancreatic NETs (PNETs, p<0.001 for all comparisons). PCA showed distinct clustering of SINETs and three NETs of unknown primary. Sporadic, VHL-related and MEN1-related PNETs formed distinct groups on PCA. VHL-related NETs clustered separately showing pronounced CpG hypomethylation, while sporadic and MEN1-related NETs clustered together showing relative CpG hypermethylation. In a subgroup analysis, MEN1-related SINETs, DNETs and gastric NETs had distinct methylome signatures, respectively, with complete separation by PCA and unsupervised hierarchical clustering. Furthermore, we found CpG hypermethylation in the *APC* (adenomatous polyposis coli) gene, specifically in the 1A promoter, with higher methylation levels in gastric- and DNETs vs. SINETs, PNETs and NETs of unknown primary (p < 0.001 for all comparisons).

Conclusion

Various primary NET sites and genetically predisposed MEN1-related NETs have distinct DNA CpG methylation signatures. The methylome signatures identified in this study may be useful for non-invasive molecular characterization of NETs, through DNA methylation profiling of biopsy samples or circulating tumor DNA.

# Thyroid

## THYROID CANCER CASE REPORTS I

### *Unusual Presentation of Metastatic Follicular Thyroid Cancer*

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**SUN-486**

Distant metastasis of follicular thyroid cancer to the bone has been well documented. However, spinal cord compression as the initial presentation of metastatic follicular thyroid cancer without any thyroid symptoms is relatively rare. Here we discuss such a case. A 78-year-old female with history of HTN and melanoma presented to the ED with a 1-month history of middle back pain that progressed to lower extremity weakness, numbness, and inability to ambulate. MRI showed a T7 vertebral mass with cord compression and edema. Metastatic work up was unremarkable except for incidental bilateral thyroid nodules, the largest on the right lobe, at 1.6 cm, with peripheral calcifications. The patient underwent T6-T7 laminectomy with vertebral decompression, partial colpectomy, and T4-T10 fusion. Pathology of the thoracic vertebral mass was positive for CAM 5.2, cytokeran 7, TTF-1, and PAX8 consistent with either metastatic pulmonary adenocarcinoma or thyroid carcinoma. The patient denied shortness of breath, dysphagia, hoarseness, or neck tenderness. She had no personal history of hyperthyroidism or hypothyroidism, or radiation exposure. She also did not have any family history of thyroid cancer. Laboratory work up was significant for TSH of 3.71 mcU/mL (0.4-4.0 mcU/mL), Free T4 1.56 ng/dL (0.7-1.9 ng/dL), thyroglobulin (Tg) 6940 ng/mL (1.6-55.0 ng/mL), and thyroglobulin antibody (Tg Ab) 20 IU/mL (0-115 IU/mL). FNA of the right thyroid nodule showed follicular neoplasm with very similar morphological features to the epidural pathology, favoring a follicular carcinoma. She underwent total thyroidectomy. Pathology showed a 1.6 x 1.1 cm follicular carcinoma with capsular and angiolymphatic invasion, but with uninvolved margins of resection. TNM staging was pT1b, pNx, pM1. She was ablated with 109 mCi of I-131 after withdrawal therapy. Whole body scan after treatment revealed radioiodine avid metastatic disease at T7 and activity in the thyroid bed compatible with residual thyroid tissue. Patient completed 10 fractions of external beam radiotherapy to the spine for a total of 30 Gy. Three months follow up lab work showed Tg 580 ng/mL and negative Tg Ab with a suppressed TSH. Thyroid bed ultrasound did not show any residual tissue or abnormal lymph nodes. Ten-year survival rates in patients with bony metastatic differentiated thyroid cancer range from 13-21% (1). Metastatic thyroid carcinoma should be considered in the differential diagnosis of every patient with new onset bony metastasis and thyroglobulin should be considered as a tumor marker in the initial work up. Research shows increased survival with I-131 avidity and complete bone metastasis resection (1). 1. Ramadan, Sami et al. “Spinal metastasis in thyroid cancer.” *Head & neck oncology* vol. 4 39. 25 Jun. 2012, doi:10.1186/1758-3284-4-39

# Pediatric Endocrinology

## PEDIATRIC OBESITY, THYROID, AND CANCER

### *Impact of Vertebral Fracture on Auxological Profile and Insulin-Like Growth Factors of Children After Acute Lymphoblastic Leukemia Treatment*

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**MON-088**

Purpose: To investigate the overall prevalence of vertebral fractures (VF) following childhood acute lymphoblastic leukemia (ALL) treatment and examine the association of VF with growth trajectory and insulin-like growth factors. Methods: Children (n=172; 59.3 % male) diagnosed with ALL at age between 2 and 18 years were assessed for VF by screening the lateral thoracolumbar spine radiographs (Genant’s semi-quantitative method) when treatment was completed (baseline). Anthropometric measurements between pre- to post-treatment period were obtained and the association of VF with insulin-like growth factor-1 (IGF-1) and insulin-like growth factor binding protein-3 (IGFBP-3) were examined. Results: Thirty-five children (20.3 %) had vertebral fractures at baseline. Among children with vertebral fractures, 97.1 % had either mild or moderate deformity, and the 5th lumbar vertebrae was the most frequently injured site (20.0 %). Median lumbar spine bone mineral density Z-score was -1.0 (IQR of -1.6 and -0.8) in children with VF. Baseline Z-scores for height and weight were lower in children with VF than without VF (-0.5±1.3 and 0.0±0.9, P=0.01; -0.2±1.6 and 0.3±1.1, P=0.04, respectively). Height Z-score in children with VF had greater height decline than without VF (0.5±0.6 and 0.2±0.8; P=0.02). Children with VF had lower IGF-1 and IGFBP-3 Z-score than without VF at baseline (-1.2±1.0 and 0.0±0.8, P<0.01; -2.3±1.1 and -1.3±1.0, P<0.01). Decrease in IGF-1 level was associated