elevated TPOAb levels. 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 (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 epidermal 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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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 vertebra 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±2.9, 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 with radiographic severity of VF. Conclusion: Children with leukemia (ALL) had higher prevalence of VF at baseline. VF was associated with decreased height growth and lower levels of IGF-1 and IGFBP-3.