(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

with the presence of VF (OR=0.3(95 % CI of 0.2-0.5), P<0.01). Conclusion: Substantial number of children encounter VF after ALL treatment is completed and the presence of VF might be associated with compromised auxological state, prominent height decline and IGF-1 deficiency.

Diabetes Mellitus and Glucose Metabolism

TYPE 1 DIABETES MELLITUS

Partial Beta-Cell Destruction: An Atypical Case of Immune Checkpoint Inhibitor Diabetes Mellitus

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SAT-667

Background: Autoimmune diabetes mellitus (CPI-DM) caused by immune checkpoint inhibitors (CPIs) is rare-occurring in approximately one percent of patients exposed to this form of cancer immunotherapy. Typically, this immune related adverse event occurs after treatment with PD-1/PD-L1 inhibitors. It is characterized by abrupt insulinopenia leading to acute hyperglycemia. Beta cell autoantibodies are positive in approximately half the cases. DKA is common at the time of diagnosis. Recovery of beta cell function has been reported in only two case reports. In one case, spontaneous resolution occurred following cessation of CPI therapy and in the other the patient was treated with infliximab for concurrent inflammatory arthritis prior to resolution of CPI-DM.

Clinical Case: A 50-year-old woman was started on adjuvant pembrolizumab for stage IIIC melanoma following surgery. She had no prior history of diabetes mellitus, thyroid disease, or other autoimmune disease. Pre-infusion random blood glucoses (RBG) were 84 - 105 mg/dL. After 36 weeks, she developed hypothyroidism (TSH 17.5 (0.5-4.1 mIU/L), FT4 6 (10-18 ug/dL)) and started levothyroxine. Pembrolizumab was continued. For nine weeks following her diagnosis with CPI- hypothyroidism, her pre-infusion RBG ranged from 102-133. At 45 weeks (15 cycles) after initiating pembrolizumab, her RBG was 260. She was not on glucocorticoids and had no other signs of inflammation or stress. Pembrolizumab was continued. Just prior to her 17th cycle, 48 weeks after initiating adjuvant pembrolizumab, her RBG was 482 with a normal anion gap and HCO3, and her A1c was 8.9%. Her last dose of pembrolizumab was held. She started metformin and liraglutide. In just three weeks, a random c-peptide was inadequate at 1.7 (0.8-3.5 ng/mL) with a recent RBG of 220 and A1c of 10.3%, showing the acuity and extremity of her hyperglycemia. Over the course of the year, she has achieved excellent glucose control (A1c 6.3-7.1) on this regimen with preservation of insulin production (c-peptides 1.4-1.8 with matched RBG 92-129). She never required insulin. Her beta cell autoantibodies are negative.

Clinical Lessons: This is a case of CPI-DM in which the patient did not have complete loss of beta-cell function. The acuity of her hyperglycemia is not consistent with new onset type 2 diabetes. At diagnosis, her c-peptide was inadequate suggesting insufficient insulin production rather than insulin resistance. Therefore, her hyperglycemia is more consistent with CPI-DM than type 2 diabetes. Atypically, she did not progress to fulminant beta cell failure, which could have been due to cessation of pembrolizumab (which is not unique to this case), initiation of liraglutide and metformin, or other unknown immunologic responses that inhibited full beta cell loss. This case raises the possibility of preventing fully insulin dependent CPI-DM if hyperglycemia is caught and treated early.

Adrenal

ADRENAL CASE REPORTS I

A Case of Metastatic Pheochromocytoma Associated with Beckwith-Wiedemann Syndrome

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SAT-231

Introduction:
Beckwith-Wiedemann Syndrome (BWS) is an autosomal dominant disorder of chromosome 11p15 that results in increased IGF-2 and CDK1NC. This leads to excessive cell proliferation and tumor formation. The following highlights a case of metastatic pheochromocytoma in a patient with BWS.
Clinical Case:
A 30-year-old male presented with sudden onset blurry vision without any associated complaints. His past medical history was significant for BWS. His family history was negative for uncontrolled hypertension, sudden death, thyroid cancer or hyperparathyroidism. Physical examination was notable for an elevated systolic blood pressure of 200/160 mm of hg and fundoscopy revealed features of hypertensive emergency. Laboratory investigations revealed an elevated plasma normetanephrine [10445 pg/ml (normal: <148)], metanephrine [93 pg/ml (normal: <57)], total metanephrine [10538 pg/ml (normal: <205)], epinephrine [134 pg/ml (normal:<50)], norepinephrine [23526 pg/ml (normal: 112-658), total catecholamine level [23660 (normal: 123-671pg/ml)] and dopamine [403 pg/ml (normal<30)] levels. His PTH, corrected serum calcium, gastrin, insulin, carcinoembryonic antigen, calcitonin levels and basal metabolic panel were all normal. MRI of the abdomen demonstrated bilateral adrenal nodules with a large mass encasing the celiac axis along with evidence of hepatic lesions. I-123 MIBG scan showed mild radioactive tracer uptake in the adrenal nodules and mass near the celiac axis but not in the hepatic lesions. PET scan confirmed MRI findings and was negative for any evidence of malignancy in the chest, pelvis and skeleton. MRI of the brain was negative for metastasis as well as pituitary abnormalities. Ultrasound-guided liver biopsy was positive for malignant cells that stained positive for chromogranin and synaptophysin confirming the diagnosis of metastatic pheochromocytoma. He was treated with phenoxybenzamine, diltiazem and lisinopril. He underwent cycles of cyclophosphamide, vincristine and dacarbazine. Genetic testing revealed a variant in SDHD gene which was of uncertain significance. Repeat biochemical testing on follow up after a year and a half showed a decreased plasma normetanephrine [487pg/ml] and metanephrine