SAT-LB313

Introduction: Beckwith-Wiedemann syndrome (BWS), a multisystem genomic imprinting disorder in chromosome 11p15.5 region, is an overgrowth syndrome often presenting with macroglossia, abdominal wall defects, hemihyperplasia, enlarged abdominal organs and an increased risk of tumors including neuroblastoma, rhabdomyosarcoma, unilateral Wilm's tumor, hepatoblastoma, adrenal cortical carcinoma and pheochromocytoma. Six cases of benign bilateral pheochromocytomas and one case of pheochromocytoma with lymph node metastasis in BWS have been described in the literature. We describe the first case of BWS with distant metastatic paraganglioma harboring an SDHB (succinate dehydrogenase subunit B) mutation.
Presentation: A 28-year-old male with BWS whose history included an omphalocele and diaphragmatic hernia in infancy, neuroblastoma resected at age 2, and left carotid paraganglioma (PGL) resected at age 22 presented with abdominal pain. CT A/P with contrast revealed a 3.3 x 4.4 cm hypervascular mass and multiple bone metastases. Workup revealed normal plasma/urine metanephrines, elevated plasma dopamine of 178 pg/ml (normal <20) and elevated chromogranin A of 190 ng/ml (normal <90). ^{68}Ga-dotatate PET CT showed hypermetabolic 4.4 cm mass (SUV 83), right hypopharynx mass (SUV 49), and many dota avid areas throughout the skeleton. The abdominal mass was resected and pathology was consistent with PGL. Due to unusual presentation, patient underwent hereditary cancer genetic testing (67 gene panel) and pathogenic mutation (c.713delT) in the SDHB gene was identified, consistent with hereditary PGL syndrome IV.
Conclusion: While pheochromocytomas and other tumors are commonly found in association with BWS, PGLs are not. This is the first documented case of a patient with BWS having distant metastatic PGL. Malignant transformation of hereditary and sporadic pheochromocytomas and paraganglioma (PPGLs) is more common in SDHx associated PPGLs (>40% of metastatic PPGLs are related to an SDHB mutation). Hereditary PGL syndromes should be suspected in the case of PGLs that are recurrent, early onset (<45 years), extra-adrenal and/or metastatic. With additional genetic testing, our patient with an already rare growth disorder was found to have hereditary PGL syndrome IV caused by a pathogenic mutation in the SDHB gene. This unique case highlights the rationale and importance of systematic genetic cancer screening in the diagnostic evaluation of PPGLs.

Pediatric Endocrinology

PEDIATRIC GROWTH AND ADRENAL DISORDERS

Clinical Utility of 21-Deoxycortisol in Congenital Adrenal Hyperplasia

Bill Curtin, MS[1], Donald Walt Chandler, PhD[2], Brett Holmquist, PhD[1].
[1]Endocrine Sciences, Calabasas Hills, CA, USA, [2]Endocrine Sciences, LabCorp, Calabasas Hills, CA, USA.

SAT-LB13

Introduction Congenital Adrenal Hyperplasia (CAH) is most often caused by mutation of the 21-hydroxylase gene (CYP21), which results in underproduction of cortisol with overproduction of precursor steroids and their metabolites by the adrenal glands. Historically the most common biomarker used for detecting CAH in pediatric patients is 17-Hydroxyprogesterone (17OHP). Another less commonly used biomarker for 21-Hydroxylase deficiency is 21-deoxycortisol (21DOF), which increases from very low levels in normal patients to high levels in affected patients as 17OHP rises to very high levels. In this study we performed retrospective analysis of serum 21DOF concentration in specimens that had been genotyped for mutations in the CYP21A2 gene, or had been submitted to our laboratory for provocative adrenocorticotropin (ACTH / Cosyntropin) stimulation testing. Methods: Biochemical testing for 21DOF concentration was measured by LC-MS/MS. Briefly, a TX-4 HPLC system (Thermo-Fisher) with Agilent® 1100 pumps (Agilent Technologies, Inc.) and a Sciex® 5000 (Danaher) triple quadrupole mass spectrometer in positive mode atmospheric pressure chemical ionization (APCI) was used for detection in Multiple Reaction Monitoring (MRM) mode. Genetic testing was performed using the CAHDetx test, which detects the 12 most common small mutations and large gene deletions/conversions in CYP21A2. Genetic Correlations: 21DOF was quantifiable (above the LLOQ of the assay) in 4% (n=24/600) of specimens where no mutation was detected. 21-DOF was quantifiable in 42% (122/292) of specimens with 21-hydroxylase enzyme mutations as determined by the CAHDetx test. Those mutations included In2G, I172N, V281L and others. Some mutations such as Q318X did not result in a detectable increase in 21-deoxycortisol. ACTH Stimulation Response: 21-deoxycortisol was below the quantitation limit in both the baseline and stimulated samples in ~35% (52/148) of submitted samples. The 21-deoxycortisol was quantifiable in only the stimulation sample in ~45% (65/148) of ACTH stimulation submitted, and was quantifiable in both baseline and stimulated samples in the remaining ~20% (30/148) of ACTH stimulation pairings. The extent of 21-deoxycortisol increase ranged from 1.2-fold to 116-fold with a median 14-fold increase. Clinical Significance: The use of 21-deoxycortisol may be beneficial in reducing the rate of false positives in CAH diagnosis when used in concert with other steroid hormones, and may eventually reduce the need for provocative testing to confirm CAH diagnosis.

Thyroid

THYROID DISORDERS CASE REPORTS IV

Case Report: Killian-Jamieson Diverticulum Presenting as a Thyroid Nodule

Branavan Ragunanthan, M.D., James K. Salem, MD.
SUMMA HEALTH SYSTEM, Akron, OH, USA.

SUN-LB86

Title: Case Report: Killian-Jamieson Diverticulum Presenting as a Thyroid Nodule
Introduction: Multitudinous endocrine and non-endocrine disorders cause thyroid nodules, thus in an effort to diagnostically exclude various thyroid malignancies, endocrinologists are obligated to perform a thorough investigative workup. A Killian-Jamieson diverticulum