hyperaldosteronism and hypercortisolism with persistent hypertension following adrenalectomy.

Pediatric Endocrinology

PEDIATRIC ENDOCRINOLOGY CASE REPORT

Exogenous Cushing's Syndrome, Hypogonadism and Diabetes Secondary to Megestrol Acetate

Merilyn Baby, DO[1], Deepa Badrinath Murthy, MBBS[2], Melissa Kaori Litao, MD[3], Gail Shust, MD[4], Bina Cherryl Shah, MD[5].

[1]NEW YORK UNIVERSITY MEDICAL CENTER, Tappan, NY, USA, [2]NYU School of Medicine, New york, NY, USA, [3]New York University Medical Center, New York, NY, USA, [4]NEW YORK UNIVERSITY MEDICAL CENTER, New York, NY, USA, [5]NYU School of Medicine, Long Island City, NY, USA.

Introduction: Megestrol acetate (MA) is a synthetic progestin that is often prescribed for anorexic patients with HIV due to its effects on weight gain and appetite stimulation. It can cause several endocrine/metabolic abnormalities. Chronic use of MA can cause exogenous Cushing's Syndrome (ECS) and iatrogenic adrenal insufficiency (AI) due to its stronger affinity for the glucocorticoid receptor (GR). It can also cause gonadotropin suppression, diabetes and hyperprolactinemia. We present a case of a young woman with perinatal HIV/AIDS that developed ECS secondary to MA treatment in the setting of fatigue, rapid weight gain and irregular menses. **Case**: A 19 year old female with perinatal HIV/AIDS (CD4<200) was treated with MA (200mg/day for 5 months) for anorexia and weight loss. On exam she was pre-hypertensive (BP 138/62), obese (BMI 43.07, SDS +2.25; weight 114kg, SDS +2.34) with increased fat deposition over upper back and abdominal striae, excessive weight gain (21.5 kg in 5 months) suggestive of ECS. She had menarche at 13 years of age and had regular menses until starting MA, upon which she developed oligomenorrhea. A random serum cortisol level was <0.5ug/dl at 1pm with a low ACTH <1.5pg/ml and DHEAS of 13.4ug/dl. Her FSH was 3.4 mIU/L and LH 0.82 mIU/L, estradiol was <2pg/dl and total testosterone <2.5ng/dl consistent with secondary hypogonadism. Liver/kidney function, prolactin and lipid profile were normal. HbA1c increased from 5.3 to 6.4% in 8 months so she was started on metformin. ECS with AI, central hypogonadism and diabetes were all attributed to MA therapy. MA was discontinued gradually over two weeks. Stress dosing of glucocorticoids were advised as needed. **Results:** Gradual recovery of HPA axis was noted after discontinuation of MA. Two months after taper, serum ACTH level rose to 2.5pg/ml but AM cortisol level remained low at <0.5ug.dl. Her HPA axis showed partial recovery by 5 months with ACTH level of 53.2pg/ml and AM cortisol level of 5.5ug/dl. By 8 months after discontinuing MA therapy, AM cortisol was 9.3ug/dl, suggesting complete HPA axis recovery. Her HPG axis also normalized by 8 months with FSH 6.6 mIU/L and LH of 14.6 mIU/L, estradiol 32pg/dl with regular menses. Metformin was discontinued at 4 months due to hypoglycemia and HbA1C of 5.7%. Subsequently, euglycemia was achieved (HbA1C of 5.4%) within 9 months. BMI was stable (BMI 43.07, SDS +2.25; weight 114kg, SDS +2.34). **Conclusion:** Multiple endocrine abnormalities may occur due to MA therapy due to its affinity to bind with glucocorticoid and progesterone/androgen receptors. ECS and AI are known to occur with various forms of glucocorticoid use, but rarely can be seen with MA therapy. HPA axis, HPG axis and metabolic parameters should be evaluated and monitored carefully during MA therapy.

Pediatric Endocrinology

PEDIATRIC ENDOCRINOLOGY CASE REPORT

Growth Hormone Deficiency: Extending the Phenotypic Spectrum of SALL4-Related Disorders

Aneta Kodytková, Mgr.[1], Shenali Anne Amaratunga, MD[1], Daniela Zemková, RNDr.[1], Klára Maratová, PhD[1], Stanislava Koloušková, MD, CSc[1], Jan Lebl, MD, PhD[2].

[1]Motol University Hospital, Prague, Czech Republic, [2]Charles University, 2nd Faculty of Medicine, Prague 5, Czech Republic.

Background: The *SALL4* gene encodes sal-like protein 4, a transcription factor with eight zinc finger motifs that is essential for the development of the epiblast and primitive endoderm. In association with *TBX5* (T-box), *SALL4* is responsible for the establishment and morphogenesis of the thumb. Pathogenic *SALL4* variants have been reported to cause Duane-radial ray syndrome (also known as Okihiro syndrome), acro-renal-ocular syndrome and Holt-Oram syndrome. Hereby, we report on a family with radial hypoplasia and kidney dystopia in members of 4 consecutive generations, and short stature due to growth hormone deficiency (GHD) in the proband. **Clinical Case:** The male proband was born from the 3rd normal pregnancy at 39th week of gestation. He has no biological siblings. He was born small for gestational age (birth weight 2550 g, length 47 cm - both < 2SD) and had bilateral asymmetrical radial ray malformation consisting of radial hypoplasia, ulnar flexure and bilateral aplasia of the thumb, and pelvic dystopia of his right kidney. He had no cardiac malformations, clubfoot, ocular coloboma or Duane anomaly. He was examined for progressive short stature at the age of 3.9 years, where his IGF-1 was 68 ug/l (-1.0 SD), and peak GH in two stimulation tests was 6.2 ug/l. Other pituitary hormones were normal. His mother's and father's heights are 152.3 cm (-2.4 SD), and 177.8 cm (-0.4 SD), respectively. His father has malformation of the forearm that is milder than that of the son. The paternal grandfather is affected as well, with a radial defect with missing opposition of the thumb and height 164 cm (-2.3 SD). The family reports that the phenotype of radial dysplasia was apparent in the paternal grandfather's mother as well. Due to the suggestive monogenic dominant transmission of the developmental abnormality, we carried out whole exome sequencing that revealed a nonsense variant in the *SALL4* gene c.1717C>T (p.Arg573Ter) in the proband, his father, and paternal grandfather. The proband was started with regular GH therapy at age 6.5 years and experienced catch-up growth as expected in GHD. By the age 11 years, his height stabilized at about the 25th percentile in accordance to the mid-parent height with a target height of 171.5 +/- 8.5 cm. Puberty started spontaneously at the age 12.5 years. **Conclusion:** This is the first case demonstrating a patient with a congenital upper limb defect

based on a pathogenic variant of the *SALL4* gene where an isolated growth hormone deficiency (GHD) was detected and has been successfully treated with growth hormone. **Acknowledgements:** Genetic testing was funded by AZV grant NV18-07-00283.

Pediatric Endocrinology

PEDIATRIC ENDOCRINOLOGY CASE REPORT

Isolated Growth Hormone Deficiency as a Cause of Hypoglycemia Past Infancy

Amruta Thakkar, MD, Nella Aikaterini, MD.
TEXAS CHILDREN'S HOSPITAL, Houston, TX, USA.

Introduction: Hypoglycemia is a common manifestation of Growth Hormone (GH) deficiency in infancy, but is rarely seen beyond 1 year of age. Here, we describe the case of a 5 year 6- month- old child with recurrent episodes of hypoglycemia due to GH deficiency in the setting of malnutrition. **Experimental Methods / Case Presentation:** Case report and literature review **Results:** A 5y6m girl with history of atypical teratoid rhabdoid tumor, status-post surgical resection and adjuvant therapy with CNS irradiation (50.4 gray), presented with recurrent hypoglycemia despite continuous G-tube feedings. Child had undergone surgery and irradiation approximately 3 years prior to presentation. She was initially followed at the cancer survivor clinic but had been lost to follow up for 2 years. At presentation, whole blood glucose was 51mg/dL. Height was 93.5cm (-4 SDS) and BMI 10.6 kg/m2 (- 7.75 SDS); she appeared malnourished on exam with minimal subcutaneous fat. She was admitted to the hospital where blood glucoses ranged from 59-68 mg/dL, despite continuous enteral feeds. On evaluation, blood ketones were mildly elevated at 0.67 mmol/L (ref range < 0.3mmol/L), growth factors were low: IGF1 15 ng/mL (ref range 37 - 272 ng/mL); IGF-BP3 1.1 mg/L (ref range 1.1 - 5.2 mg/L), and other pituitary hormones were within normal range [stimulation test cortisol peak 31.9 mcg/dL, TSH 2.4 mIU/mL(Ref range: 0.700 - 4.100 uIU/ML), Free T4 1.2 ng/dL (Ref range 1.0-2.4 ng/dL)]. Hypoglycemia resolved within 48 hours of initiating empiric treatment with GH (0.2mg/kg/week) and patient's feeds were successfully compressed to 16 hours. Child was discharged home after passing an overnight 8-hour safety fast. **Conclusion:** Growth hormone deficiency can present as recurrent hypoglycemia outside the infantile period in the setting of malnutrition and needs to be considered in the differential diagnosis and evaluation of childhood hypoglycemia.

Pediatric Endocrinology

PEDIATRIC ENDOCRINOLOGY CASE REPORT

Maffucci Syndrome, Calcium Homeostasis, and Endocrine Challenges in Management

Olivia Z.B. Ginnard, D.O., Lindsay C. Burrage, MD, PhD, Lefkothea P. Karaviti, MD, PhD.
Baylor College of Medicine, Houston, TX, USA.

Maffucci syndrome is a rare disorder characterized by enchondromatosis and hemangiomata. It can occur due to sporadic, de novo, mosaic pathogenic variants in the gene encoding isocitrate dehydrogenase 1 (*IDH1*) or isocitrate dehydrogenase 2 (*IDH2*). *IDH1* variants are associated with endocrine manifestations, such as pituitary adenomas. However, literature is limited in describing other clinical features and available treatments in severe phenotypes. We report a pediatric patient with uniquely complex and severe Maffucci syndrome. Case: A 5-year-old boy was evaluated by pediatric endocrinology for chronic hypercalcemia as part of a multidisciplinary evaluation of his severe Maffucci syndrome. Past medical history included prematurity, restrictive lung disease, developmental delay, seizures, 2-OH glutaric aciduria, angiomas, and bicytopenia. Physical exam revealed angiomas, scoliosis, and severe bony deformities throughout the entire skeleton. During admission, laboratory assays revealed normal parathyroid hormone, phosphorus, 1,25-OH2D, and C-telopeptide; elevated serum calcium and PTH-related peptide; and low 25-OHD, alkaline phosphatase, and osteocalcin. Low-dose ACTH stimulation test yielded a peak cortisol level of 16.8. A 24-hour urine study confirmed hypercalciuria. Renal ultrasound demonstrated nephrocalcinosis. Skeletal survey revealed diffuse and chondromatous changes of nearly every bone. Whole-exome sequencing detected a presumed, mosaic de novo *IDH1* variant. DEXA scan revealed total body BMD z-score of -3.8. **Discussion:** Hypercalcemia in Maffucci syndrome is a rare phenomenon. The most likely etiology was due to the severe and chronic bony breakdown from the underlying progressive enchondromatosis. Subsequently, the body attempted to adapt to these chronic processes with abnormal mineral homeostasis, as seen in his laboratory assays. Chronic primary hyperparathyroidism was not likely, as his PTH, phosphorus, and 1,25 OH2D levels were not congruent with that diagnosis. Familial hypocalciuric hypercalcemia was not likely, as his urine calcium clearance ratio was >0.01. Finally, his slightly elevated PTHrP level was not due to PTHrP-mediated hypercalcemia of malignancy, as his bone marrow biopsy was negative. The options for short-term hypercalcemia management had their own inherent risks and were not suitable for long-term management. Although there is a lack of pediatric data to guide therapy in Maffucci syndrome, decision was made to proceed with bisphosphonate infusion given the benefits in the setting of his nephrocalcinosis, chronic hypercalcemia, and results of his DEXA scan. Given the rarity of Maffucci syndrome, few characteristics are well-described in the pediatric population. A multidisciplinary approach is necessary to review the severity of the disease and to determine the best treatment approach based on this information.

Pediatric Endocrinology

PEDIATRIC ENDOCRINOLOGY CASE REPORT

Metreleptin and Metformin Use in an Infant With Congenital Generalized Lipodystrophy Secondary to AGPAT2 Mutation

Cintya Schweisberger, DO, Jill Diane Jacobson, MD, Emily Paprocki, DO.
Children's Mercy Hospital, Kansas City, MO, USA.

Background: Congenital generalized lipodystrophy (CGL) is a rare inherited disease characterized by widespread loss