performed in 992, and 576 were prescribed GH. NHW children were 1.4 (95% CI 1.04 - 1.8) times more likely than NHB children and 1.7 (95% CI 1.2 - 2.2) times more likely than Hispanic children to undergo GH stimulation testing. NHB children treated with GH had: 1) lower median peak GH concentration when compared with NHW (p=0.02) and Hispanic (p=0.08) children (NHB 4.7 [1.2, 8.3] ng/ml, NHW 7.2 [4.9, 9.7] ng/ml, Hispanic 7.1 [4.3, 11.9] ng/ml); 2) lower median height z-scores than NHW (p=0.01) but not Hispanic children (p=0.5); and 3) a greater height deficit from mid-parental height when compared with NHW (p=0.01) and Hispanic (p=0.002) children.

Discussion: Racial and ethnic disparities are present in the evaluation and treatment of children with disordered growth. This likely results from both over-investigation of NHW children as well as under-investigation and undertreatment of children from minority communities. The evaluation and treatment of children with short stature should be determined by clinical concern alone, but this is unfortunately not current practice.

Pediatric Endocrinology

HOT TOPICS IN PEDIATRIC ENDOCRINOLOGY

Topline Results of the CARE-PWS Phase 3 Study: Intranasal Carbetocin Improves Hyperphagia and Anxiety and Distress Symptoms in Prader-Willi Syndrome (PWS)

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Prader-Willi syndrome (PWS) is a complex genetic disorder associated with multiple neuroendocrine abnormalities including significantly decreased hypothalamic oxytocin levels, resulting in symptoms of severe hyperphagia (an unrelenting false sense of starvation) and multiple severe neuropsychiatric and behavioral issues. CARE-PWS, a multi-center, randomized, double-blind, placebo-controlled phase 3 study, has evaluated the efficacy, safety, and tolerability of intranasal carbetocin, a selective oxytocin receptor agonist, in participants with PWS. Eligible participants aged 7 through 18 with genetically confirmed PWS were randomized in equal proportions to three treatment arms for the 8-week placebo-controlled period of the study: carbetocin 9.6 mg, carbetocin 3.2 mg, or a matching placebo, administered by nasal spray three times a day with meals. The primary endpoint assessed changes from baseline to week 8 in Hyperphagia Questionnaire for Clinical Trials (HQ-CT) or Children’s Yale-Brown Obsessive Compulsive Scale (CY-BOCS) scores for the carbetocin 9.6 mg arm vs placebo, and the first secondary endpoint assessed changes from baseline to week 8 in HQ-CT or CY-BOCS scores for the carbetocin 3.2 mg arm vs placebo. Additional secondary endpoints included changes from baseline to week 8 in PWS Anxiety and Distress Questionnaire (PADQ) scores, and Clinical Global Impression of Change (CGI-C) scores evaluating the overall change in severity of PWS symptoms at week 8.

Due to COVID-19, enrollment was closed early with 119 evaluable participants for the primary analysis. In the carbetocin 9.6 mg arm, trends toward numerically greater improvements in HQ-CT and CGI-C scores relative to placebo were observed but did not reach statistical significance; however, the carbetocin 3.2 mg arm demonstrated a significant improvement in HQ-CT scores (LS mean improvement vs placebo -3.14 points, p=0.016). In the 3.2 mg arm, additional consistent evidence of improvements versus placebo was seen in multiple secondary endpoints, including CGI-C (p=0.027) and PADQ (p=0.027). Numeric trends toward improvement in CY-BOCS scores were observed in each dose arm, but did not reach statistical significance versus placebo. During the subsequent long-term follow-up period of the study, both carbetocin arms have experienced continued numeric improvements from baseline across multiple endpoints. Intranasal carbetocin was generally well-tolerated; the most frequently reported adverse event was flushing, which was generally mild and transient. In conclusion, results of the CARE-PWS study support that intranasal carbetocin appears to be safe and well tolerated, and reduces hyperphagia and anxiety and distress behaviors in PWS.

Pediatric Endocrinology

PEDIATRIC ENDOCRINOLOGY CASE REPORT

22q13 Duplication in Newborn With Dysmorphic Features: The Role of SOX10 in Disorders of Sex Development

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Background: The 46,XX testicular disorder of sex development (DSD), also known as 46,XX male reversal, is a rare form of DSD and clinical phenotype shows complete sex reversal from female to male. The sex-determining region Y (SRY) gene can be identified in most 46,XX testicular DSD patients; however, approximately 20% are SRY-negative. Here we present a 2 week old with discrepant prenatal karyotype and infant phenotype.

Case: This 2-week-old had dysmorphic features (bitemporal narrowing, broad and flat nasal bridge, bilateral epicantal folds) and multiple genetic anomalies; IUGR, hypertelorism, cleft lip and palate, ASD, small kidneys, sacral dimple. Physical exam revealed palpable inguinal masses and microphallus without hypospadias. Postnatal karyotype showed a 46,XX chromosome complement with duplication of 22q13-pter. He was negative for SRY gene by FISH. Microarray analysis confirmed the duplication encompassing the SOX10 gene. Lab evaluation showed LH 10.81 mIU/ml, FSH 3.21 mIU/ml and total testosterone 241 ng/dl. These values are consistent with activation of the hypothalamic–pituitary–gonadal axis during the neonatal period in males.

Conclusion: Our case along with previous cases supports the existence of a gene on chromosome 22q that can trigger testis determination in the absence of SRY. Potential mechanisms responsible for ovotesticular disorder in the XX (SRY−) individual could involve activation of testis
6-Year-Old Girl With a Luteinized Follicular Ovarian Cyst and an Estradiol Level > 1,000 PG/ML

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**Background:** Precocious puberty in girls is defined as onset of secondary sexual characteristics, such as breast development, before 8 years of age. To differentiate between central and peripheral precocious puberty, laboratory and imaging evaluation is helpful. When gonadotropins are low but estradiol is elevated, results may suggest a primary ovarian source of estrogen production. Small ovarian cysts are not uncommon, are benign and self-resolve. However, large ovarian cysts are rare, let alone ones requiring surgical removal.

**Clinical Case:** A 6-year 7-month-old girl presented with several days of breast tenderness and palpable bilateral breast tissue noted by her mother. There was no history of vaginal bleeding. There were no reported exposures to estrogen-containing products. Her mother reached menarche at age 14 years. The patient was born full term and was otherwise healthy. On exam, her height was at the 90-95th percentile (mid-parental height at the 95th percentile) and her growth velocity was 10.9 cm/yr. She had Tanner 2 breasts (1 cm breast bud on the left and 1.5 cm on the right), Tanner 1 pubic hair and no axillary hair, body odor, acne or café-au-lait macules. A bone age was read as 6 years at a chronological age of 6 years 7 months. She did not have signs of systemic inflammatory response, need for respiratory support, or glucocorticoids. His insulin requirements continued to increase up to 4 u/kg/day with sustained hyperglycemia indicating an exceptional state of insulin resistance. On Day 6 of admission metformin was initiated, on Day 9 insulin requirements declined and he was discharged on an insulin regimen close to 1.5 u/kg/d.

**Conclusion:** This case describes the rare finding of a large luteinized follicular ovarian cyst that required surgical removal in a 6-year-old girl in the setting of a significantly elevated estradiol level. Luteinized follicular cysts have been described in newborns, though rare. To our knowledge, this is the first described case of a luteinized follicular cyst in this patient’s age group. Laboratory and imaging evaluation should be considered in girls presenting with precocious puberty, despite the extent of thelarche, as the clinical examination does not always correlate with degree of estradiol elevation. This is especially important if clinical changes are acute and other features are consistent with puberty, such as rapid linear growth.