EVALUATING TUMOR RISK AND SUBSEQUENT MANAGEMENT IN PATIENTS WITH MIXED GONADAL DYSGENESIS.

Olivia ZB Ginnard[1], Lefkothea Karaviti[2]

[1] Baylor College of Medicine, Department of Pediatrics, Endocrinology & Metabolism

[2] Texas Children's Hospital/ Baylor College of Medicine, Pediatrics, Endocrine & Metabolism

Background: The timing of gonadectomy for mixed gonadal dysgenesis (MGD) depends on the MGD phenotype-specific risk of germ cell malignancy. We summarize the initial evaluation and considerations of a patient with Turner syndrome with partial XYY MGD, and discuss the current recommendations pertaining to tumor risk and timing of gonadectomy.

Materials/Methods: Case: An 11-year-old girl was referred to the Pediatric Endocrinology Clinic for short stature. Past medical history was significant for hearing loss, snoring, tonsillar hypertrophy, learning difficulties in math, and persistent slow growth, with height at the 0.15th percentile and mid-parental height at 25th percentile at time of presentation. Physical exam revealed low-set ears and Tanner 1 breasts and pubic hair. At chronological age 11 years, bone age was consistent with 7 years and 10 months. Laboratory assays revealed normal IGF-1, IGFBP-3, and thyroid function, and elevated FSH and LH; low AMH confirmed primary ovarian failure. Chromosomal microarray analysis revealed mosaicism for a 45, X cell line in 13/20 (65%) cells and a 47, XYY cell line in 7/20 (35%) cells. Pelvic US revealed a small uterus with unidentifiable, likely streak ovaries.

Results: Discussion: Disorders of sex differentiation comprise karyotypes such as 45, X; 47, XXY; and variants of both (MGD). The various MGD phenotypes are dependent on the degree of testicular development, which varies from normal-appearing males with azoospermia to our patient's Turner female phenotype. As the degree of germ cell cancer risk is also dependent on gonadal differentiation or "testicularization" and location, current gonadectomy guidelines recommend earlier gonadectomy in more virilized patients and for abdominal gonads. Given the gravity of this decision, a multidisciplinary care approach is paramount, with early involvement of the affected child in open and transparent discussion.

Conclusions: Conclusion: Given the 7–10% risk of gonadoblastoma development in patients with Turner/Partial XYY MGD and abdominal streak gonads, the evaluation of risks outweighs the very low quality data supporting a strong recommendation in the literature against routine gonadectomy in gonadal dysgenesis. An open and transparent discussion of gonadectomy including endocrinology, gynecology, and psychology was held with the parent and child, with a decision to pursue gonadectomy.