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Independent case reports

Persistent mullerian duct syndrome and transverse testicular ectopia: embryology, presentation, and management

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Abstract

Background: The finding of persistent mullerian duct syndrome (PMDS) with transverse testicular ectopia (TTE) is rare. We present nonidentical triplets with PMDS with TTE.

Cases: Triplet A presented with a right inguinal hernia and left nonpalpable testis at 4 months of age. Ultrasound demonstrated 1 testis in the right hemiscrotum. Laparoscopy revealed both testes in the right inguinal canal with a thick midline structure. Triplet B presented at 6 months of age in the exact manner with similar intraoperative findings as triplet A. No additional mullerian structures were identified in triplets A and B. Both underwent laparoscopic left orchiopexy and open right inguinal herniorraphy/orchiopexy. A portion of vas was noted in the path specimen of triplet B. Triplet C presented at 7 months of age with a nonpalpable left testis. Laparoscopy demonstrated bilateral fallopian tubes and a midline uterine remnant. Open bilateral orchiopexy was performed, and bilateral biopsies confirmed testes. All 3 were 46-X,Y.

Conclusion: Persistent mullerian duct syndrome with TTE may be encountered when performing laparoscopy for patients with nonpalpable testis. The persistent mullerian remnants vary among individuals and alter the normal anatomy, thus may complicate diagnosis and surgical management.

The finding of persistent mullerian duct syndrome (PMDS) with transverse testicular ectopia (TTE) is a clinically rare event. In this form of male sexual differentiation syndrome, affected individuals have mullerian remnants in a variable location (scrotal, inguinal, or intraabdominal) and both testis located on 1 anatomic side [1]. The anomaly combines defects in regression of fetal mullerian structures with aberrant testicular descent. The underlying mechanisms for this genitourinary finding has been hypothesized and subsequently researched, with many concepts demonstrated in animal models [2]. There are complex interactions between genetics, hormones, and anatomic factors, but many controversies persist [3,4].

This series focuses on the finding of PMDS with TTE in nonidentical triplets. Limited previous literature has described familial associations in brothers and identical twins only [5,6]. Consistent with many published descriptions,

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each infant boy's anomaly was discovered during surgery for unilateral inguinal hernia with contralateral cryptorchidism. All triplets initially underwent diagnostic laparoscopy followed by inspection of genitourinary structures and subsequent surgical repair. The intraoperative findings of both testes on the right anatomic side (with nonpalpable testes located intraabdominally) were identical for all 3 boys. The midline mullerian remnant was most prominent in triplet C.

1. Case series

This study was exempted by the Institutional Review Board at Kaiser Permanente, Los Angeles Medical Center.

The nonidentical triplets were born by cesarean delivery at 31 weeks gestation to a 31-year-old prima gravida mother. They were conceived through in vitro fertilization because of the father's decreased sperm cell count. All 3 boys had normal-appearing male genitalia. Postnatal hospital courses of approximately 1 month per child were uneventful.

Triplet A was initially evaluated at 4 months of age for right inguinal hernia and left nonpalpable testis. Preoperative testicular ultrasound visualized only 1 testicle, located in the right hemiscrotum. He underwent diagnostic laparoscopy, laparoscopic left orchiopexy, open right inguinal hernia repair, and open right orchiopexy. Intraoperatively, the left vas deferens appeared to approach the left internal ring, but the left testicle was located near the right internal ring (Fig. 1). A thickened midline structure with peritoneal covering was dissected to skeletonize the left cord structures in preparation for orchiopexy. The right testicle was in the right scrotum with a fibrosed complex hernia sac that thinned as it ascended to the internal ring.

Triplet B presented at 6 months of age, also with right inguinal hernia and nonpalpable left testis. He underwent identical surgical procedures as triplet A (diagnostic laparoscopy, laparoscopic left orchiopexy, right open orchiopexy, and right inguinal hernia repair). Intraoperatively, the left testicle was located near the right internal ring with a visible gubernaculum inserting through this right internal ring. The right testicle was retracted up into the abdominal cavity. Dissection of the left vas deferens for orchiopexy, which traveled through a thickened fold of midline peritonealized tissue, was somewhat difficult. On the right side, cord and sac structures were dissected free and visualized multiple times before suture ligation, but postoperative pathology of the hernia sac noted a 1-cm segment of vas deferens (of unknown laterality) present in the specimen.

Triplet C underwent surgery at 7 months of age for a nonpalpable left testis only. He had diagnostic laparoscopy followed by open bilateral orchiopexy, bilateral gonadal biopsies, biopsy of midline mullerian duct remnant, and open bilateral inguinal hernia repair. Intraoperatively, his anatomic findings were the most apparent of the triplets, with bilateral fallopian tubes/fimbria and midline uterine remnants. The right testis was in the right scrotum, and the left testis near the right internal ring. Laparoscopic dissection of the vas was particularly difficult with the midline abnormality obscuring normal anatomic landmarks, so conversion to an open procedure was made (Fig. 2). Postoperative pathology showed normal testicular tissue bilaterally, and fibrovascular tissue and nerve twigs in the midline structure.

After the above intraoperative discoveries, genetics consult was completed. All 3 boys were found to be 46-X, Y by chromosomal analysis, and no further abnormalities were noted by the geneticist.

2. Discussion

Persistent mullerian duct syndrome as a distinct entity can be explained by inadequate mullerian suppression from hormonal influences. The primary responsible glycoprotein is mullerian inhibiting substance (MIS) or antimullerian hormone. It is created and released by testicular Sertoli cells, causing mullerian duct regression [7]. The hypotheses for PMDS causation include failure of synthesis or release of MIS, the failure of end organs to respond to MIS, or a defect in the timing of the release of MIS [3].

Experiments have since discovered specific mutations in MIS and the MIS receptor genes, mapping these to chromosome 19 (MIS) and chromosome 12 (MIS type II specific receptor) [8]. Mutations cause lack of MIS secretion or lack of translocation to the surface membrane causing inactivity of the MIS receptor. These lead to persistence of mullerian structures, with approximately 85% of human cases because of mutations inherited in an autosomal recessive pattern. The remaining 15% of cases have an unknown case and may be related to complex malformations of the urogenital region [9].

The relationship between PMDS and TTE is less clear. Traditionally, testicular descent is independently described as occurring in 2 stages: transabdominal phase and inguinoscrotal phase. The transabdominal phase was thought to be controlled by MIS, but animal studies have shown that this stage of descent is regulated primarily by insulin-like hormone 3 and androgen's effect on the gubernaculum. Mullerian inhibiting substance appears only to augment gubernacular activity [4]. The inguinoscrotal phase appears to be controlled by neurotransmitter release from the genitofemoral nerve, with androgens necessary to "preprogram" the response of the gubernaculum to genitofemoral nerve released calcitonin gene-related peptide [10]. Overall, congenital undescended testis could be caused by any abnormality in the complex hormonal or anatomical mechanisms. The simple anatomic connection of the testis to the persistent mullerian ducts has even been argued to cause cryptorchidism in PMDS [8].