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UROLOGY - CASE REPORT

Persistent Mullerian duct syndrome with transverse testicular ectopia and seminoma

Bilal Fırat Alp · Zafer Demirer · Ali Gürağaç · Oğuzhan Babacan · Erkan Sarı · Sebahattin Sarı · İbrahim Yavan

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Abstract Persistent Mullerian duct syndrome (PMDS) is a rare form of the 46 XY disorders of sexual differentiation, characterized by the presence of a uterus and fallopian tubes due to the failure of Mullerian duct regression in genotypically normal males. More than 150 cases have been recorded, most of them in adults. In most cases, the PMDS is discovered during surgery for inguinal hernia or cryptorchidism, or by the presence of transverse testicular ectopia (TTE). The presence of PMDS with TTE is even more uncommon. In TTE, both testes descend through the same inguinal canal into the same scrotal sac. Patients with TTE present with symptoms of unilateral cryptorchidism and a contralateral inguinal hernia. For patients with inguinal hernia and cryptorchidism associated with TTE, PMDS should be kept in mind, and radiologic evaluation such as ultrasonography or magnetic resonance imaging of the genitourinary system and karyotyping are recommended. Whereas radiologic evaluation could be helpful in the diagnosis of TTE, it cannot diagnose the malignancy itself. The case explained in this report will offer urologists additional useful treatment strategies for patients with inguinal hernia and cryptorchidism.

Keywords Persistent Mullerian duct syndrome · Transverse testicular ectopia · Inguinal hernia · Seminoma

B. F. Alp (✉) · Z. Demirer · A. Gürağaç
Department of Urology, Gulhane Military Medical Academy, Etlik 06018, Ankara, Turkey
e-mail: bilalfirat.alp@gmail.com

O. Babacan
Department of Pediatric Hematology and Oncology, Gulhane Military Medical Academy, Etlik 06018, Ankara, Turkey

E. Sarı
Department of Pediatric Endocrinology, Gulhane Military Medical Academy, Etlik 06018, Ankara, Turkey

S. Sarı
Department of Radiology, Gulhane Military Medical Academy, Etlik 06018, Ankara, Turkey

İ. Yavan
Department of Pathology, Gulhane Military Medical Academy, Etlik 06018, Ankara, Turkey

Introduction

Transverse testicular ectopia (TTE) is one of the rarest forms of testicular ectopia. In this condition, two testes are located on one inguinal side. One testis crosses the midline to meet its opposite mate at the internal inguinal ring, in the inguinal canal, or in the hemiscrotum. The condition has also been called "crossed testicular ectopia," "testicular pseudoduplication," "unilateral double testis," and "transverse aberrant testicular maldescent." TTE was first described by Lenhossek in 1886. Since then, about 100 cases have been reported in the literature [1]. TTE is associated with persistent Mullerian duct syndrome (PMDS) in approximately 20 % of cases [2].

PMDS was first described by Nilson as found in a man with inguinal hernia in 1939, presenting as hernia uteri inguinale. PMDS is characterized by the persistence of Mullerian duct (MD) structures (the uterus, fallopian tubes, and upper two-thirds of vagina) in otherwise normal, virilized males (karyotype 46 XY). The Mullerian system usually regresses in males, but occasionally, residual Mullerian structures exist. These well-developed MD derivatives may localize intra-abdominally or may herniate in the inguinal region [3–5].

In patients with PMDS together with TTE and hernia uteri inguinalis, malignancy could develop from residual testis or MD [6, 7]. In cases of TTE, the diagnosis of PMDS could usually be made during surgery with the presence of MD residues [8]. To protect testicular function and decrease morbidity, it is important for patients to be assessed thoroughly. Here, we report a case with an undescended testis and primary infertility and whom we have diagnosed with TTE and offered surgery in the event of PMDS and testicular malignancy.

Case Report

A 28-year-old male was transferred to our center, diagnosed with an undescended left testis and primary infertility. It was discovered that 14 years before, the patient had undergone a right inguinal hernia operation at another center.

It was observed that the patient had external secondary sexual characteristics, and penis size and appearance were normal. While palpation occurred in the right testis scrotum, the left testis scrotum and the inguinal area could not be palpated. In addition, during his medical examination, the patient was found to have an approximately 10 cm incision scar and hernia in his right inguinal area (Fig. 1). The rest of the physical examination was unremarkable.

It was observed that the patient who had been married for 2 years and was infertile, and previous semen analysis revealed azoospermia. Scrotal-pelvic ultrasonography (US) performed at another center showed a second ectopic testis in the inguinal region. Moreover, this second ectopic testis was deformed and atrophic. A magnetic resonance imaging (MRI) performed at another center found a multilocular cyst in the left scrotum but did not observe the left testis. This MRI found the right testis (3 × 2 × 3 cm) present in the scrotum that the right inguinal area had dilated ductus deferens and observed the ejaculatory duct of the neighboring right rectus muscle of the ectopic testis (27 × 17 mm) (Fig. 2a, b).

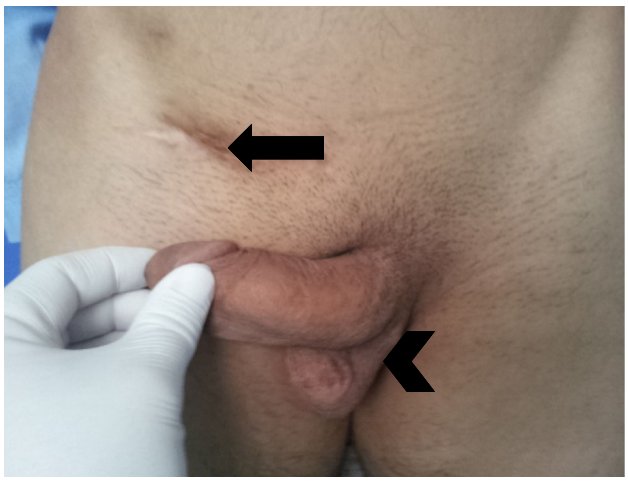

Fig. 1 Right herniorrhaphy incision scar (*black arrow*) and empty left scrotum (*black arrow head*)

Scrotal-pelvic US performed in our center found the size of the right scrotum normal. The right inguinal canal had a 17-mm hernia defect that had an intestinal segment, and an approximately 27 × 11-mm ectopic tissue was discovered (Fig. 3a). Moreover, parenchymal calcifications and two tumor-like parenchymal lesions with hyperechoic, internal bleeding amorphisms, 7 × 10 and 6 × 7 mm, were discovered in the lower half of the testis. (Fig. 3b).

The patient's full blood and biochemical tests were normal. Complete blood count, serum urea, creatinine, electrolytes, and blood sugar were within normal ranges. Tumor markers and hormonal analysis levels were normal; lactic dehydrogenase level was 319 U/L (normal 220–450 U/L), beta-human chorionic gonadotropin level was 0 mIU/mL (normal 0–5 mIU/mL), alfa-fetoprotein level was 3.1 ng/mL (normal 0–9 ng/mL), follicle stimulating hormone level was 26.6 IU/L (normal 1.4–18.1 IU/L), and luteinizing hormone level was 14.9 IU/L (normal 1.5–9.3 IU/L). However, total testosterone level was 226.7 ng/dL (normal 241–877 ng/dL). The patient was observed to have karyotype analysis, 46 XY. As a result of the endocrinology consultation, the postoperative pathology result and the hormone levels need to be evaluated, and testosterone replacement was recommended if necessary.

During the surgical exploration, two testes were observed one of which was in the right hernia and the ectopic one was on the superior of hernia. Additionally, possible MD residues between the two testes were apparent in the hernia sac (Fig. 4a, b). Due to the suspicion of a tumor in the ectopic testis, a radical orchiectomy with the excision of MD residues and right inguinal herniorrhaphy was performed. The right testis was normal and placed in the right scrotum.

Pathologic examination reported MD residues, an 8-mm germ-cell tumor (histologic subtype is seminoma) of ectopic testis tissue, and neighboring testis tumor tissue with intratubular germ-cell neoplasm (Fig. 5). In thoraco-abdomino-pelvic computerized tomography (CT) examination, liver and retroperitoneal cysts were observed. The patient's postoperative first and third month checkups showed continually increasing FSH and LH serum levels, and tumor markers with total testosterone serum levels (340.3 ng/dL) within normal limits were observed. Due to postoperative serum testosterone being within normal levels, hormone replacement therapy was not indicated. Due to the patient having stage 1 seminoma, postoperative prophylactic radiotherapy was initiated. All clinical

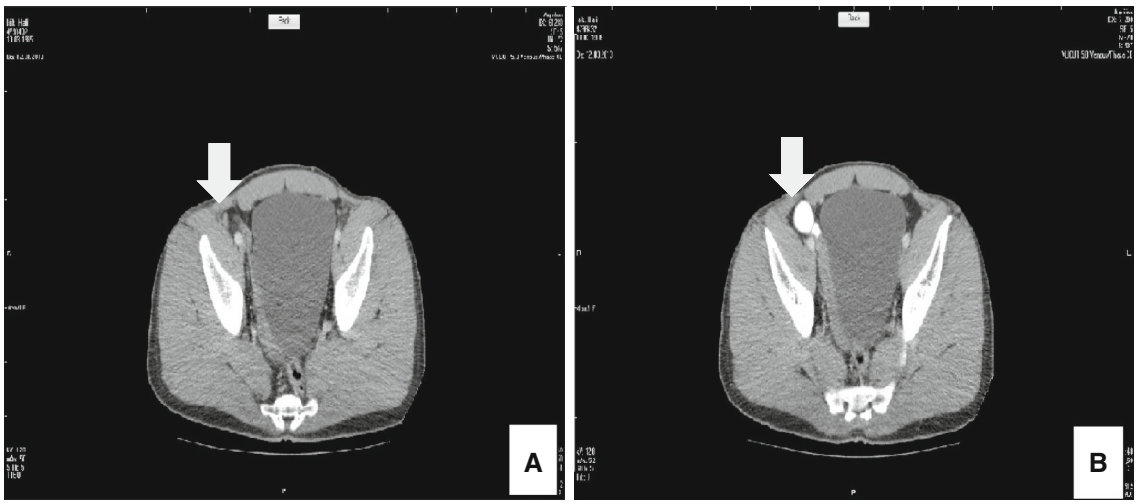

Fig. 2 Magnetic resonance imaging findings: **a** hernia sac including MD residue, **b** ectopic testis

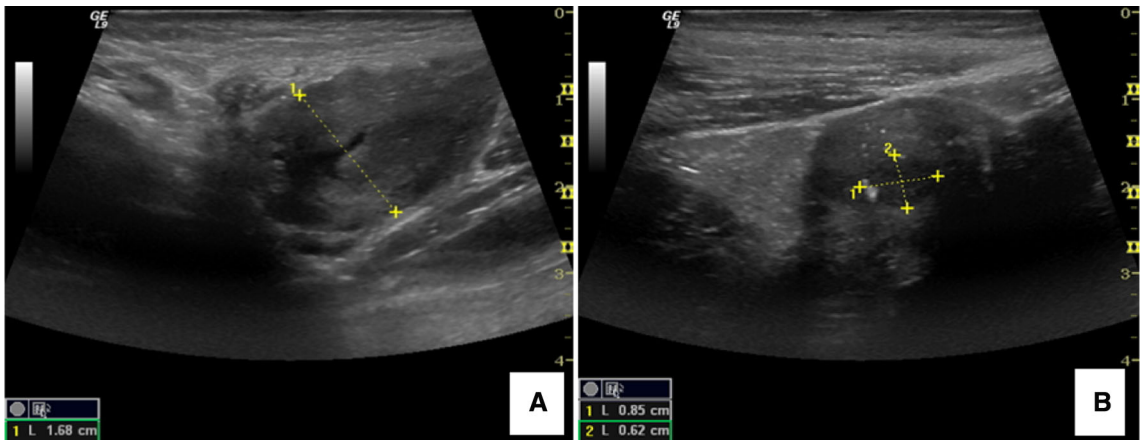

Fig. 3 Ultrasonography findings: **a** the right inguinal canal with hernia defect, **b** parenchymal calcifications and hyperechoic internal bleeding amorphisms in the ectopic testis

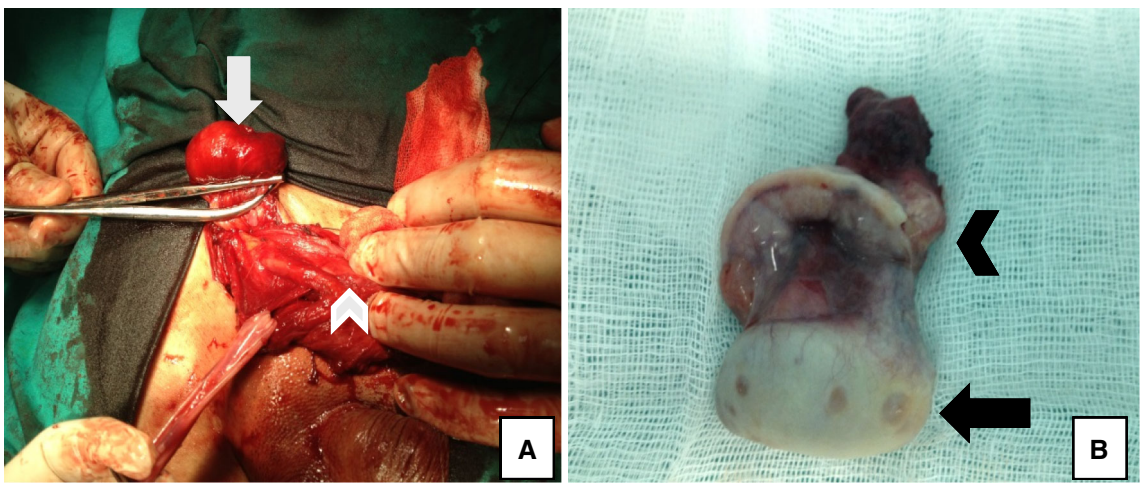

Fig. 4 Intraoperative findings: **a** ectopic testis (*white arrow*) and hernia sac including MD residue (*white arrow head*), **b** material of orchiectomy (*black arrow*) and hernia sac (*black arrow head*)

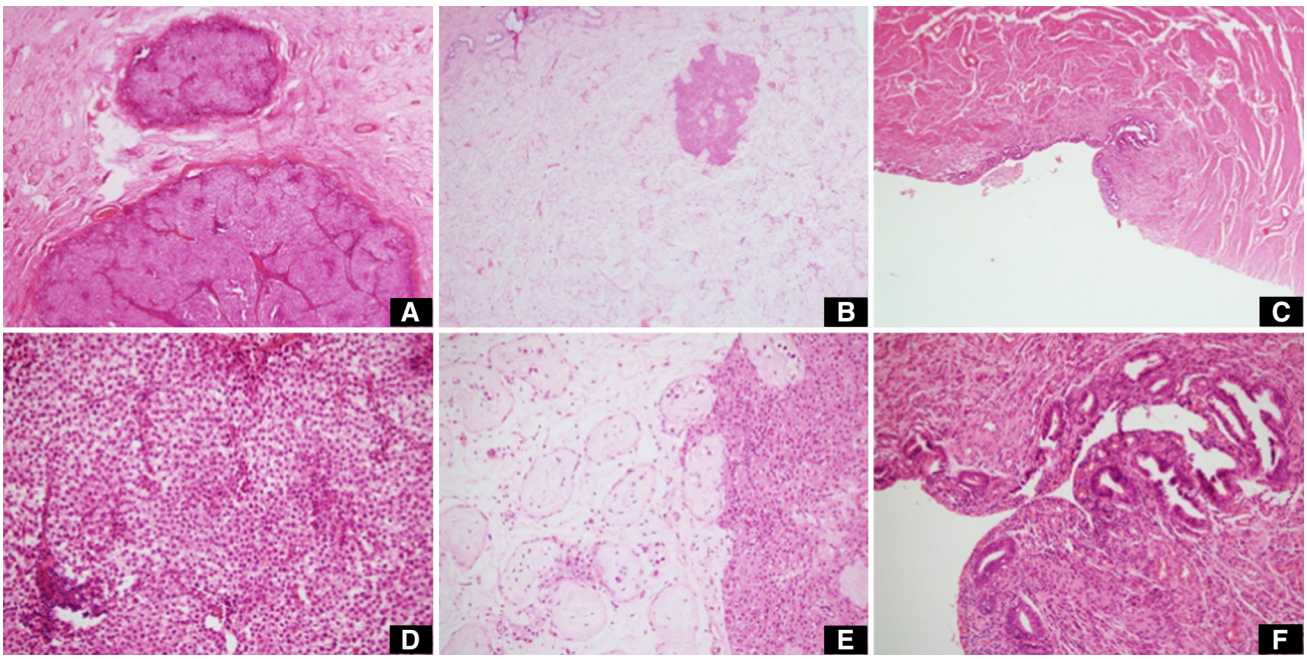

Fig. 5 Histopathology findings: **a** and **d** seminoma with well-margined nodul in testis, **b** and **e** atrophic and sclerotic seminiferous tubule in whole stroma and hypertrophic Leydig cells, **c** and **f** glandulary and stromal findings reminds endometrium and MD residue

findings and laboratory analyses were normal in the post-operative fifth week.

Discussion

Mullerian inhibiting factor (MIF), also known as anti-Mullerian hormone, and testosterone play important roles in genital differentiation in male fetuses. MIF, which is secreted from the Sertoli cells, regresses the MD, and testosterone, which is released from the Leydig cells, plays a role in the development of epididymis, vas deferens, and seminal vesicles from the Wolffian ducts. PMDS is characterized by the persistence of MD structures (uterus, fallopian tubes, and upper two-thirds of vagina) in otherwise normal, virilized males (karyotype 46 XY) [5]. Hypotheses for PMDS etiology include failure of synthesis or release of MIS, failure of end organs to respond to MIS, or a defect in the timing of MIS release [2, 4, 9, 10]. The Mullerian system usually regresses in males, but occasionally, residual Mullerian structures exist. These well-developed Mullerian duct derivatives may localize intra-abdominally or may herniate in the inguinal region [5]. Ninety percent of these patients have partially undescended testes with hernia uteri inguinalis, and 10 % of them have intra-abdominal testes at ovarian positions and MD structures [11].

TTE is a rare form of testicular ectopia of uncertain embryologic etiology. Suggested embryologic explanations are adherence and fusion of developing Wolffian ducts, aberrant gubernaculum, testicular adhesions, defective internal inguinal ring, and traction on a testis by persistent MD structures [1]. Main clinical characteristics are unilateral cryptorchidism and contralateral inguinal hernia [2]. Additional genitourinary abnormalities, such as hypospadias, peno-scrotal transposition, seminal vesicle cyst, common vas deferens, renal agenesis, horseshoe kidney, and uretero-pelvic junction obstruction, are reported in patients who have TTE. Disorder of sexual differentiation (DSD) exists in nearly one-third of patients who have TTE [2]. TTE is separated into three subtypes with the following concomitant anomalies: Type 1 is the most common form and has only inguinal hernia; in Type 2, TTE is associated with PMDS; Type 3 is a rare form in which, in addition to PMDS, there are other anomalies, such as inguinal hernia, hypospadias, DSD, and scrotal anomalies [12]. These concomitant anomalies can be explained by traction of the testes by the unregressed MD structures or by both testes dialing in the direction of the same scrotal compartment [1]. In our case, there was male-type PMDS and Type 3 TTE combined.

TTE is associated with PMDS in approximately 20 % of cases [2]. However, the relationship between TTE and PMDS is not clear, since the role of MIS in testicular descent is not well understood. It seems that MIS increases gubernaculum activity. Inguinal hernia usually accompanies TTE, but the condition may be difficult to diagnose correctly [2]. TTE is sometimes diagnosed before surgery, but PMDS is usually diagnosed after surgery with the determination of MD structures in histologic examination

[8]. In suspected cases, US, CT, MRI, and laparoscopy may be helpful in diagnosis of TTE [13–15]. As in our case, it may be diagnosed easily by performing radiologic imaging, such as US or MRI. Before puberty, in patients with bilateral cryptorchidism, the serum anti-Mullerian hormone level also aids diagnosis [5, 16]. It has been reported that 65 % of TTE patients are diagnosed during hernia operations [17]. The most important differential diagnosis of PMDS is mixed gonadal dysgenesis (MGD). In MGD, in addition to residual MD structures, there can be ambiguous genitalia. In addition, in MGD, the chromosomes are usually 45 X/46 XY.

PMDS patients usually have normal virilization, but most of them are infertile. Five of 150 patients reported in the literature have offspring, and only two patients have 2–3 million sperm in semen analysis [5]. Causes of infertility are specified as testes hypoplasia and ejaculatory duct obstruction due to compression by MD structures. The patient admitted to our clinic complained of infertility and inguinal hernia.

Seminoma is the most common testicular germ-cell tumor, representing 50 % of cases. In PMDS, the testes are usually histologically normal, apart from lesions because of long-standing cryptorchidism. The overall incidence of malignant transformation in these testes is 18 %, similar to the rate in abdominal testes in otherwise normal men. There also have been reports of embryonal carcinoma, seminoma, yolk sac tumor, and teratoma in patients with PMDS. Malignancy arising from the Mullerian remnants also has been reported, for example, adenocarcinoma (esp. clear-cell), squamous cell carcinoma, papillary cystadenocarcinoma, or adenosarcoma arising from the remnants of MD [5, 7]. Our patient was diagnosed with stage 1 seminoma and revealed no recurrence on follow-up.

There is still debate about surgical treatment for PMDS. Reasons for this debate are ectopic testes, cancer formation risk of residual MD structures, and the risk of damage to the testicular artery and vas deferens by orchidopexy surgery. Transseptal orchidopexy is a surgical treatment option for TTE patients [10]. If surgery is chosen, residual MD structures should be removed carefully, to avoid damaging the vas deferens and testicular vessels. However, in patients with TTE, the vas deferens is usually much shorter and its lower segment is embedded in the wall of the uterus [4]. Due to the risk of tumor, there are advocates for removal of MD structures. To keep vas deferens and testicular circulation, some recommend only hernia repair and orchidopexy, without MD structure removal [2, 12]. If MD structure removal is chosen, proximal salpingectomy should be leveled and the myometrium pedicle left intact. The fallopian structure attached to the testis upper pole should be left, without separating the testis from its mesenter, to prevent epididymis injury [5, 11]. Our case included a right-incarcerated inguinal hernia and TTE. Because of the atrophic ectopic testis and cancer suspicion, the orchiectomy was performed with a hernia pouch and residual MD structure excision.

Usually, undescended testes are found in the inguinal channel or intra-abdominally, and appropriate surgical procedures are performed. However, rarely, undescended testes are found with TTE, and very rarely, they can be found with residual MD structures, called PMDS. Therefore, in patients with inguinal hernia and cryptorchidism, possible TTE and PMDS must be considered. These patients require complete, detailed, preoperative radiologic evaluation of the genitourinary system and karyotyping. In addition, due to the risk of tumor in the undescended testis, necessary surgical intervention must be made to prevent life-threatening testicular cancers.

Conflict of interest The authors declare that there is no conflict of interest in this manuscript.

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