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Female form of persistent Müllerian duct syndrome: A rare case report and review of literature

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ABSTRACT

INTRODUCTION: Persistent Müllerian duct syndrome (PMDS) is a rare form of internal male pseudo-hermaphroditism characterized by the presence of rudimentary Müllerian structures in a virilized male often presenting as undescended testes. Thus, each patient diagnosed with undescended testes should promptly be investigated for PMDS because the early diagnosis has direct effects on outcome and prognosis.
CASE REPORT: A 26-year-old-male complained of long-standing abdominal pain two years ago and was diagnosed having bilateral undescended testes in the pelvic region. He underwent the orchidopexy about one year ago but, after 5 months of orchidopexy, he first complained of discomfort in the left and then right inguinal region due to an incisional hernia that presumed to have the ovotesticular disorder of sexual development. On the pelvic MRI exam, the Müllerian duct structures were observed and he was diagnosed as having PMDS.
DISCUSSION: In this case the patient had bilateral cryptorchidism with testes fixed in the para iliac region with respect to the uterus, indicating the female type of PMDS which is a rare type of PMDS. The case is proven genetically and Müllerian duct remnants have been resected to avoid malignant transformation.
CONCLUSION: Persistent Mullerian duct syndrome (PMDS) is a rare finding and may present as long-standing abdominal pain. Each patient diagnosed with undescended testes should promptly be investigated for PMDS. Diagnosis and management aim to preserve fertility and prevent malignant changes. Therefore, familiarity with this rare condition will lead to adequate management and prevention of complications.

1. Introduction

Persistent Müllerian duct syndrome (PMDS) was first described by Nilson in 1939 and since then about 300 documented personal cases have been reported in the literature [1,2]. PMDS is a form of male intersex caused by a defect in the Müllerian inhibiting factor (MIF), either by an insufficient amount of MIF or due to the insensitivity of the target organ to that factor [3]. Normally, Sertoli cells begin to produce MIF during week 7 of gestation, causing Müllerian duct regression [4]. Therefore, defect in MIF results in failure of regression and presence of a uterus, fallopian tubes, and the upper third of the vagina in males with a 46XY karyotype [5].

Persistence of the Müllerian duct may manifest as; PMDS, mixed gonadal dysgenesis, and intersex disorder of sexual development. The patients typically present with unilateral or bilateral undescended or partially descended testes with an inguinal hernia. However, some may have transverse testicular ectopia and hernia uteri inguinal [6].

PMDS is often misdiagnosed due to a lack of familiarity with the condition and wide variation in age presentation even some may remain undiagnosed [7,8]. Although the imaging techniques can help diagnose, accurate determination of PMDS is made by the appearance of abnormal internal genitalia during surgical procedures and genetic analysis. However, there is not always a perfect agreement between molecular and clinical data [3,9].

Abbreviations: PMDS, persistent Müllerian duct syndrome; MIF, Müllerian inhibiting factor; MRI, magnetic resonance imaging.

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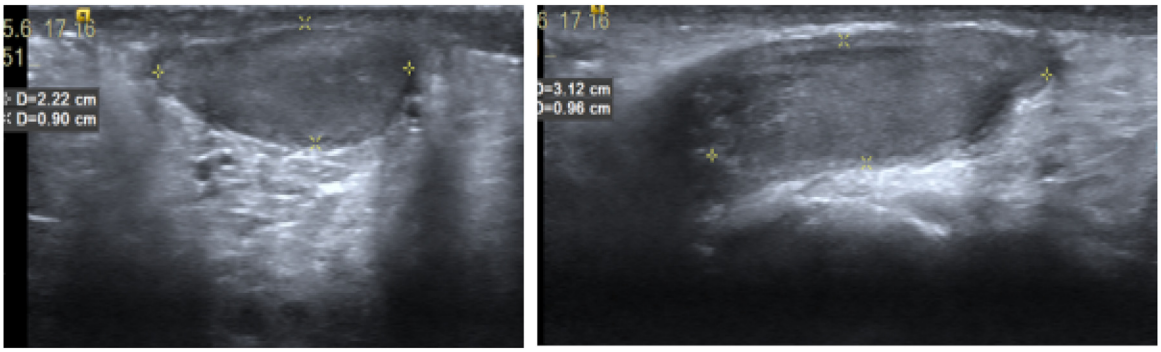

Fig. 1. Longitudinal Ultrasound images of both testes after orchidopexy, show small, heterogeneous and atrophic testes.

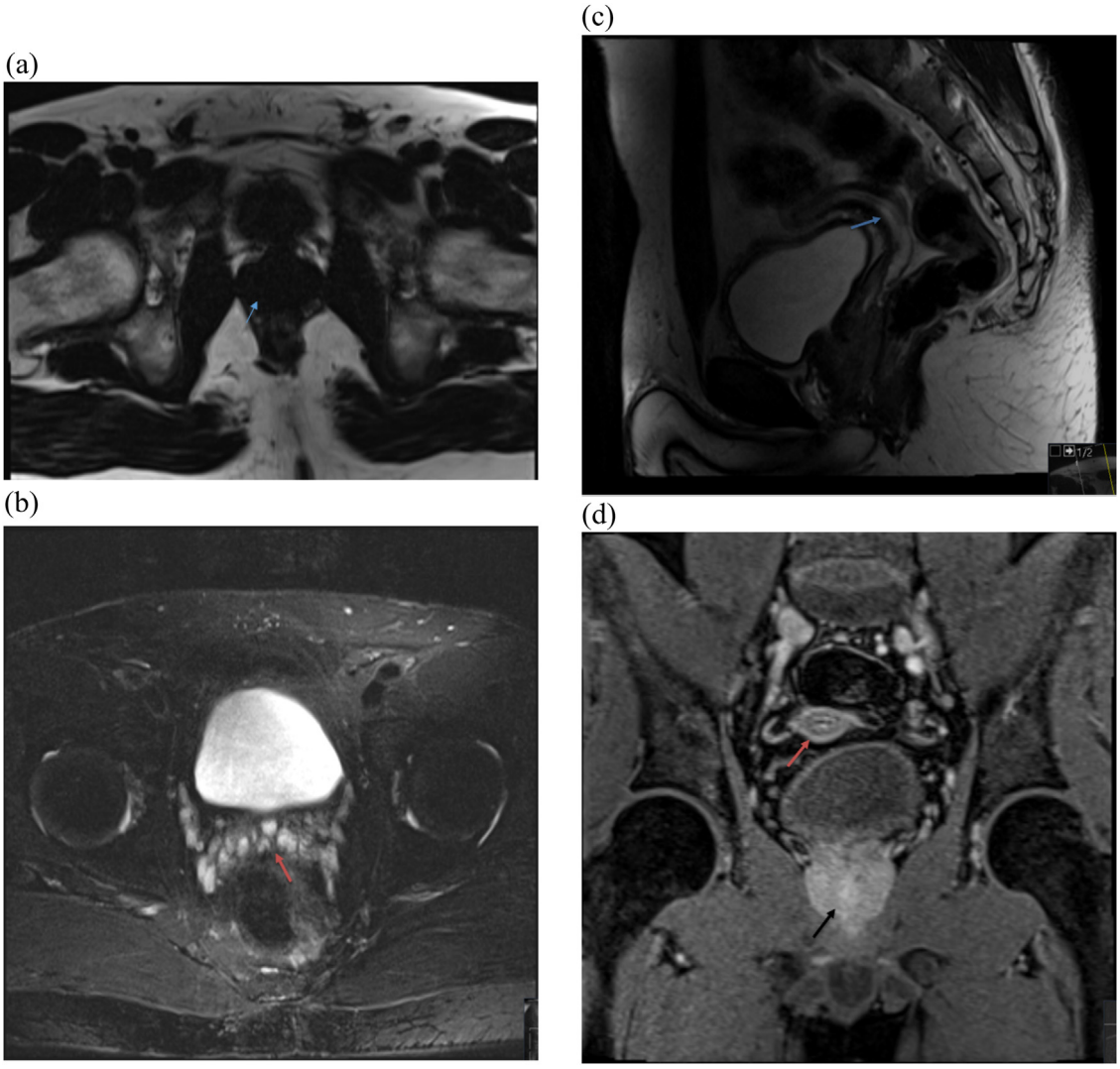

Fig. 2. (a) Axial T1 weighted MRI image shows a hypoplastic prostate (arrow).
(b) Axial fat sat T2 weighted MRI image shows a tubular cystic structure belonging to seminal vesicles (arrow).
(c) Sagittal T2 weighted MRI image shows an approximately 8 mm lumen width structure in the posterior of the bladder parallel to the bladder contour. The thickened wall around it compatible with the uterine wall.
(d) Coronal fat sat T1 weighted post contrast MRI image shows uterus (read arrow) and prostate (black arrow).

Generally, the patients with PMDS have a good prognosis especially if they diagnose earlier but, left untreated there is a high risk for malignant changes as well as infertility that may affect the quality of life. The common management of PMDS patients includes orchidopexy and resection of the Müllerian remnants to preserve fertility and prevent malignant changes. We present here a 26-year-old male with PMDS presented as bilateral undescended tests.

2. Patient information

A 26-year-old-male complained of long-standing abdominal pain two years ago and was diagnosed having bilateral undescended testes in the pelvic region in the para iliac area. He underwent the orchidopexy about one year ago but, after 5 months of orchidopexy, he first complained of discomfort in the left and then right inguinal region due to inguinal hernia that presumed to have the ovotesticular disorder of sexual development. On physical exam, he looked like a male, his both testes were palpable in the scrotum (after orchidopexy) and he had normal penis length. He had no past medical history, drug, or allergic history. He is an ordinary smoker, has 5 brothers and one sister. One of his brothers was examined for infertility. In the lab exam, he had total azoospermia and a low level of Müllerian Inhibiting Factor. In the genetic exam, his karyotype was 46 XY, increased heterochromatin in arm q in chromosome 9 and SRY positive but, no microdeletions. He also had a mutation in the gene for the type II MIS receptor (MISR-II). For further evaluation, he was referred for radiologic studies. On the ultrasound exam, both testes were in the scrotum but, were smaller than normal with heterogeneous texture and seemed to be atrophic [Fig. 1]. On the pelvic MRI exam, the urethral outlet continued in the lobulated contoured soft tissue center, consistent with the hypoplastic prostate. A tubular cystic structure belonging to seminal vesicles was observed adjacent to the hypoplastic prostate [Fig. 2a and b]. On sagittal images, an approximately 8 mm lumen width structure in the posterior of the bladder parallel to the bladder contour was seen. The thickened wall around it belonged to the uterine layer. It is distinguished by thin septation in the middle of a cystic structure that surrounds the bladder all around and ends in the anterior, compatible with Mullerian duct anomaly [Fig. 2c and d]. However, no typical ovarian tissues were detected. The patient was operated in the urology section by a qualified urologist and Mullerian duct remnants were resected [Figs. 3a–c and 4]. There were no changes in intervention and he was discharged after 48 h hospitalization without any complications.

3. Discussion

PMDS is defined as the presence of Müllerian derivatives, uterus, and fallopian tubes in otherwise normally masculinized 46, XY subjects [9]. Müllerian duct derivatives are present in male fetuses until the 8th week of gestation. Thereafter, it regresses by MIF, a glycoprotein produced by fetal Sertoli cells [10]. Therefore, defect in MIF either by an insufficient amount of MIF or due to insensitivity of the target organ to that factor results in failure of regression and presence of a uterus, fallopian tubes, and the upper third of the vagina in males with a 46XY karyotype [3,5]. Fertility is rare but possible if at least one testis is scrotal, and its excretory ducts are intact. Testosterone levels and sexual function are usually normal except if testicular degeneration is found [11]. Our patient had a low level of MIF and total azoospermia but, his testosterone level and sexual function were normal.

Some of the PMDS patients have a defect in the MIS gene located at 19p13, and others have a defective gene for type II MIS receptor (MISR-II), located at 12q13. PMDS can occur sporadically or inherited either as an X-linked or autosomal recessive sex-limited trait. Approximately 85% of PMDS cases are due to mutation of either MIS or MISR-II genes, in similar proportions, and have autosomal recessive male-restricted transmission. In 15% of cases, the cause of PMDS is unknown [5]. Our patient had a mutation in the gene of the type II MIS receptor.

There are two types of anatomic variants of PMDS, the male form, and the female form. The most common variant is the male form, encountered in 80–90% of cases, which manifests as a hernia uteri inguinal or crossed testicular ectopia. The second anatomic variant of PMDS is the female form, seen in only 10–20% of cases and is characterized by bilateral cryptorchidism, with the testes fixed within the round ligaments in an 'ovarian position' with respect to the uterus. The gonads are fixed within the pelvis [12]. Our patient had the female type PMDS, manifested as bilateral cryptorchidism fixed in the para iliac region concerning the uterus. The

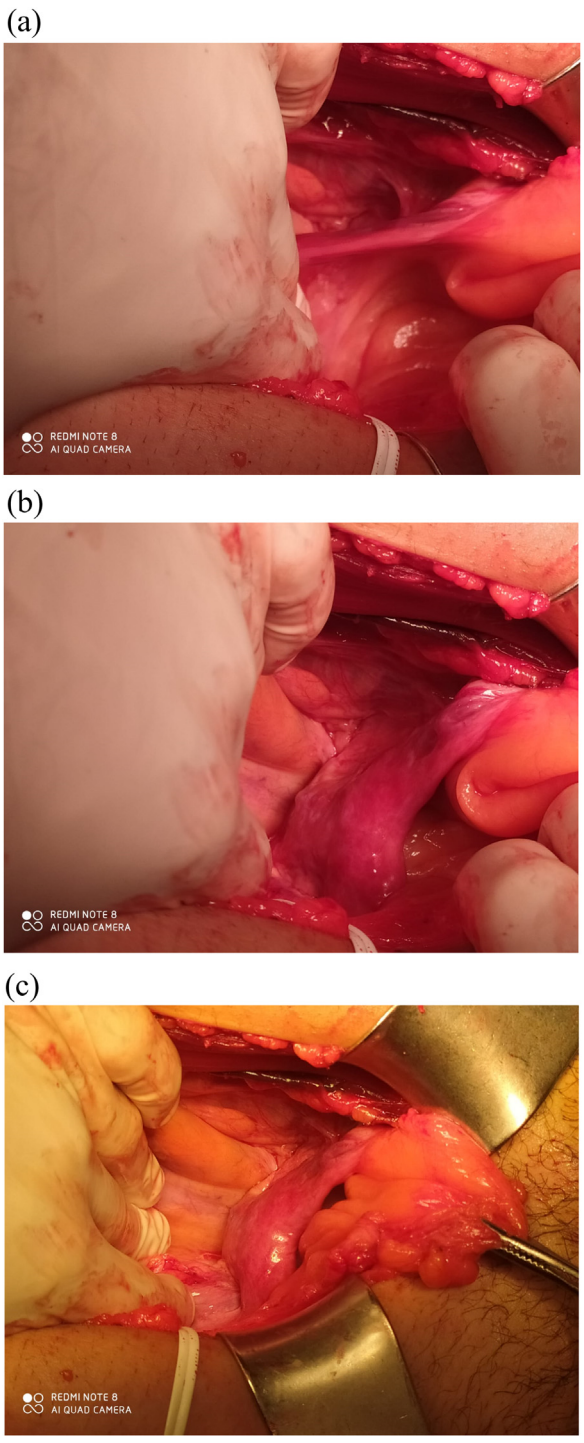

Fig. 3. (a) Intraoperative picture showing the posterior wall of the uterus and the right fallopian tube.
(b) Intraoperative picture showing the anterior wall of the uterus, ends with a blind ended vagina behind the urinary bladder.
(c) Intraoperative picture showing the uterus with both fallopian tubes. The peritoneal tissues are pulled cranially with forceps.

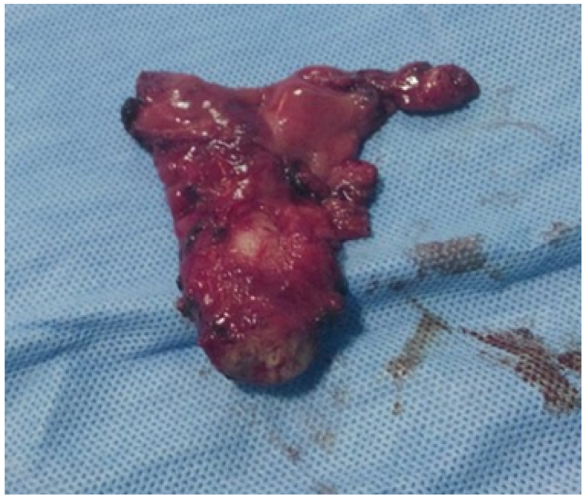

Fig. 4. The picture shows surgically excised Müllerian duct structures.

resected Mullerian duct remnants were also consistent with the uterus. The diagnosis is often challenging but, a holistic approach to diagnosis should be sought, encompassing a variety of imaging techniques and surgical interventions. Imaging modalities as ultrasound, multi-detector CT, and MRI can help diagnose. MRI with its multiplanar capabilities and high spatial resolution plays an important role in the identification of different genital structures and their relationship to adjacent pelvic organs [1,13].

Müllerian structures should be removed whenever possible to avoid the risk of malignant transformation and surgical intervention aims are to preserve fertility and prevent malignant changes [1,14]. In our case, all Mullerian duct remnants were resected and orchidopexy was already done to preserve fertility.

This case is the rare form of PMDS which had an unusual presentation and is one of the documented case, proved by genetic analysis and surgical intervention. However, the lake of a long-time follow-up after treatment may be the only limitation of this case report.

This work has been reported in line with the SCARE 2018 criteria [15].

4. Conclusion

Persistent Mullerian duct syndrome (PMDS) is a rare finding and may present as long-standing abdominal pain. Each patient diagnosed with undescended testes should promptly be investigated for PMDS before any intervention. Diagnosis and management aim to preserve fertility and prevent malignant changes. Thus, familiarity with this rare condition will lead to adequate management and prevention of complications.

Declaration of Competing Interest

The authors report no declarations of interest.

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Ethical approval

The manuscript has got an ethical review exemption from the Ethical Review Committee (ERC) of our institution, as case reports are exempted from review according to the institutional ethical review committee's policy.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editor of this journal.

Author contribution

All of the authors have participated sufficiently in the manuscript and take public responsibility for its content. Habib Ahmad Esmat helped in writing the manuscript, selecting the case and images, and corresponding with the journal. Nevra Zehra Elmas and Busra Ozcan helped in supervising the manuscript. Gulparkha Manalai Osmani provided as the review of literature and Fuat Kızıla, who is the urologist helped us in preparation of information about the operation note and intraoperative pictures. All of the authors have read and approved the final manuscript.

Registration of research studies

Not applicable.

Guarantor

The corresponding author (Dr. Habib Ahmad Esmat) is the Guarantor for the work and he has the responsibility of access to the data, and controlling the decision to publish.

Provenance and peer review

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