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Incidentally Discovered Persistent Müllerian Duct Syndrome in a 45-year-old male presenting with germ cell tumor and bilateral cryptorchidism: A rare case report and review of the literature

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ABSTRACT

INTRODUCTION: Persistent Müllerian Duct Syndrome (PMDS) is a rare sexual disease. It is characterized by the presence of female reproductive structures such as uterus, cervix, fallopian tubes and upper part of vagina in a normal genotypically and phenotypically male. The diagnosis is usually incidental since the patients will present with normal external genitalia and secondary sexual characteristics. Imaging techniques such as magnetic resonance imaging (MRI), computed tomography (CT) scan, or ultrasound (US) could help in the diagnosis.
CASE PRESENTATION: A 45-year-old male presented with bilateral undescended testes since birth and 2 months history abdominal mass. CT scan showed a 13 × 17 × 20 cm solid pelvi-abdominal mass. The diagnosis of mixed germ cell tumor of the undescended testes was made based on the CT scan. During resection of the tumor, patient was found to have a uterus, fallopian tubes and ovaries.
DISCUSSION: Pathological investigation showed endometrial tissues with portion of lower uterine segment and cervix with remnant of testes with marked atrophy. No Ovarian tissues were found nor fallopian tube as well. The diagnosis of PMDS was made based on the pathological report.
CONCLUSION: PMDS is a challenging condition to diagnose. Radiological investigation can miss the presence of the Müllerian duct structures as in our case because of the unusual presentation of this condition. Early diagnosis and management is important as the malignant transformation is high due to the undescended testes.

1. Introduction

Persistent Müllerian Duct Syndrome (PMDS) is a rare genetic form of pseudo-hermaphroditism in males with normal external genitalia [1]. It has an autosomal recessive pattern of inheritance [2]. The main presenting symptom of PMDS is usually cryptorchidism. Differentiating PMDS from other sexual disorders such as mixed gonadal dysgenesis which is a type of Disorders of sex development (DSD) is mainly by the presence of external genitalia [3]. The incidence varies widely, but around 300 cases only reported in the literature [2]. This case report has been reported in line with the SCARE criteria [4].

2. Case Presentation

A 45-year-old male schizophrenic patient was referred to our institution with bilateral undescended testes and 2 months history of abdominal mass. On examination, the mass was pelvi-abdominal reaching the level of the umbilicus with empty scrotum. Laboratory workup was done and showed normal parameters. Abnormal laboratory results included alpha-fetoprotein (AFP) of 76 ug/L (normal range: <7 ug/L), beta-hCG of 1016 lU/L (normal range: <0.8 IU/L) and lactate dehydrogenase (LDH) of 976 IU/L (normal range: <333 IU/L). Computed Tomography (CT) scan was done and showed 13 × 17 × 20 cm solid pelvi-abdominal mass (Fig. 1). The mass was obstructing the lower left ureter with a moderate to

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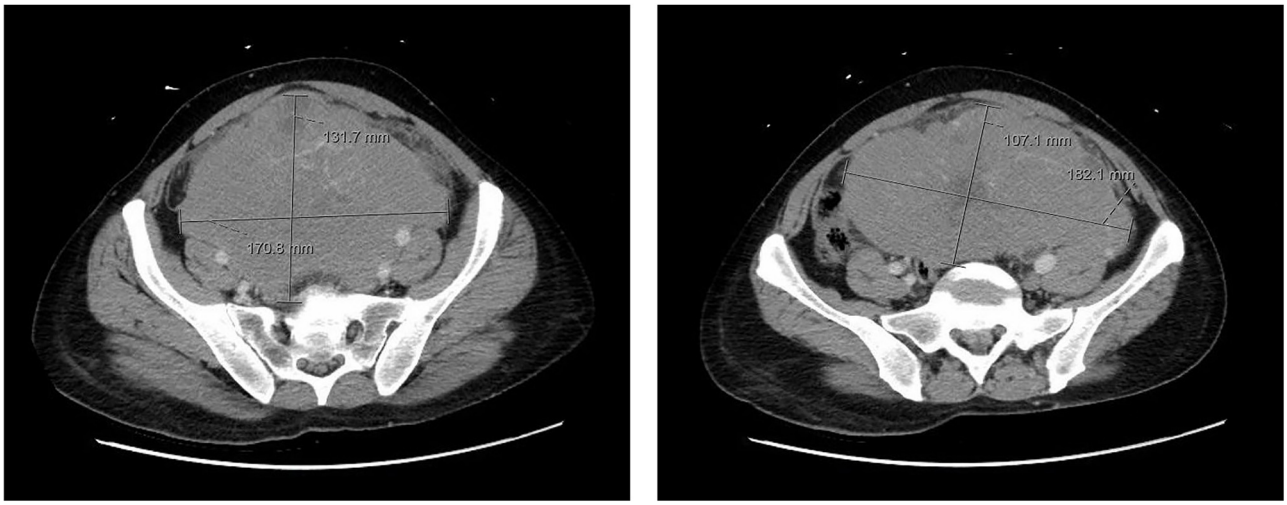

Fig. 1. Transverse CT scan of the abdomen before the neoadjuvant chemotherapy showing a 13 × 17 × 20 cm solid pelvi-abdominal mass.

severe left hydronephrosis. The radiological diagnosis was mixed germ cell tumor of the undescended testes.

The patient received 3 cycles of BEP (Bleomycin, etoposide and cisplatinum) as a neoadjuvant chemotherapy. CT scan was repeated and showed reduction in the tumor size to 4.4 × 8 × 10.1 cm with the resolution of the left-sided hydronephrosis (Fig. 2). The previously abnormal laboratory markers showed improvement. AFP decreased to 5 ug/L, beta-hCG decreased to 1.5 lU/L and LDH decreased to 225 IU/L (normal range: <333 IU/L).

A midline incision was made to explore the whole abdomen. The tumor was identified and resected. During exploration, the patient was found to have a uterus, fallopian tubes and ovaries. Classical hysterectomy was done. After removal of the uterus, a closed cavity was found that is similar to the structure of the vagina, a sample was taken from it and was sent for pathology. Omentectomy, appendectomy and cholecystectomy were done combined with Hyperthermic Intraoperative Chemotherapy (HIPEC) and intraoperative radiotherapy (IORT) in the area of the tumor bed. The patient tolerated the operation and was extubated and was send to the ICU in a good condition the shifted to the ward without any complication. Pathological investigation revealed the presence of endometrial tissues with portion of lower uterine segment and cervix. No Ovarian tissues were found nor fallopian tube as well. But, remnant of testes with marked atrophy and tubular hyalinization with portions of viable epididymis, rete testis and vas deferens identified (Fig. 3).

3. Discussion

Persistent Müllerian Duct Syndrome (PMDS) is rare form of internal male pseudo-hermaphroditism. This condition defined by the presence of structures derived from the Mullerian duct (i.e uterus, cervix, fallopian tubes and upper part of vagina) in a normal genotypically and phenotypically male. Individuals diagnosed with PMDS manifest with normal external genitalia and secondary sexual characteristics [1]. This disorder caused by deficiency in the production of Müllerian inhibiting substance (MIS) from the immature Sertoli cells in the newly formed testes [2,5].

During the early stage of sexual differentiation, the embryo reproductive tract in both sex consists of Mullerian duct and Wolffian duct [6]. In a male fetus, Leydig cells and Sertoli cells of the newly formed testes start producing testosterone and MIS, respectively at the 8th week of gestation. Testosterone production will lead to Wolffian duct differentiation into epididymis, vas deferens and seminal vesicles. MIS, also known as anti-Müllerian hormone (AMH), production induce Mullerian duct regression. Also, MIS has

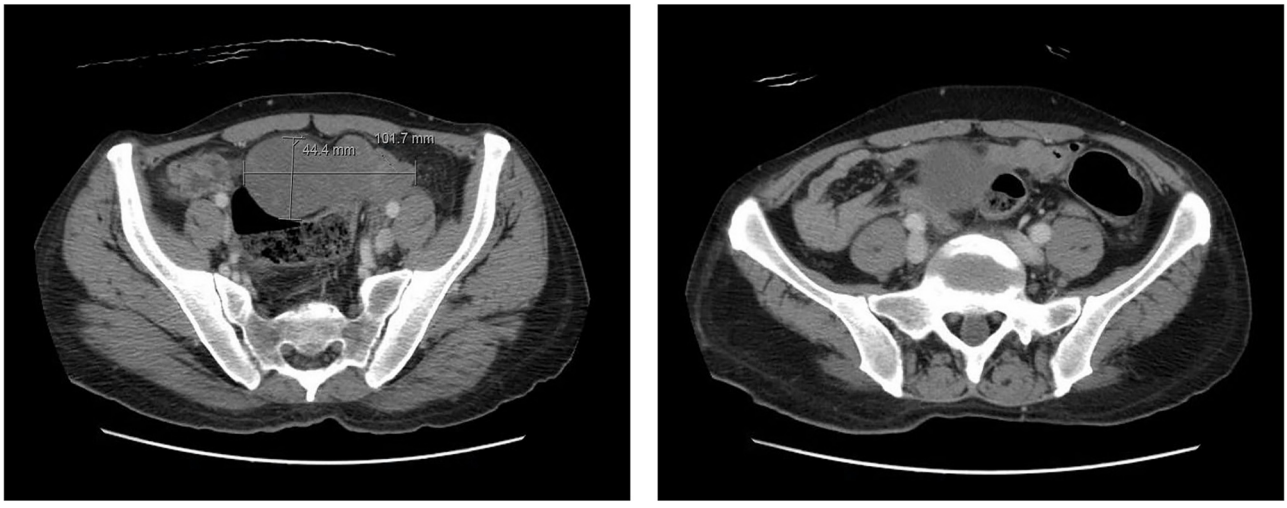

Fig. 2. Transverse CT scan of the abdomen after the patient received the neoadjuvant chemotherapy showing reduction in the tumor size to 4.4 × 8 × 10.1 cm.

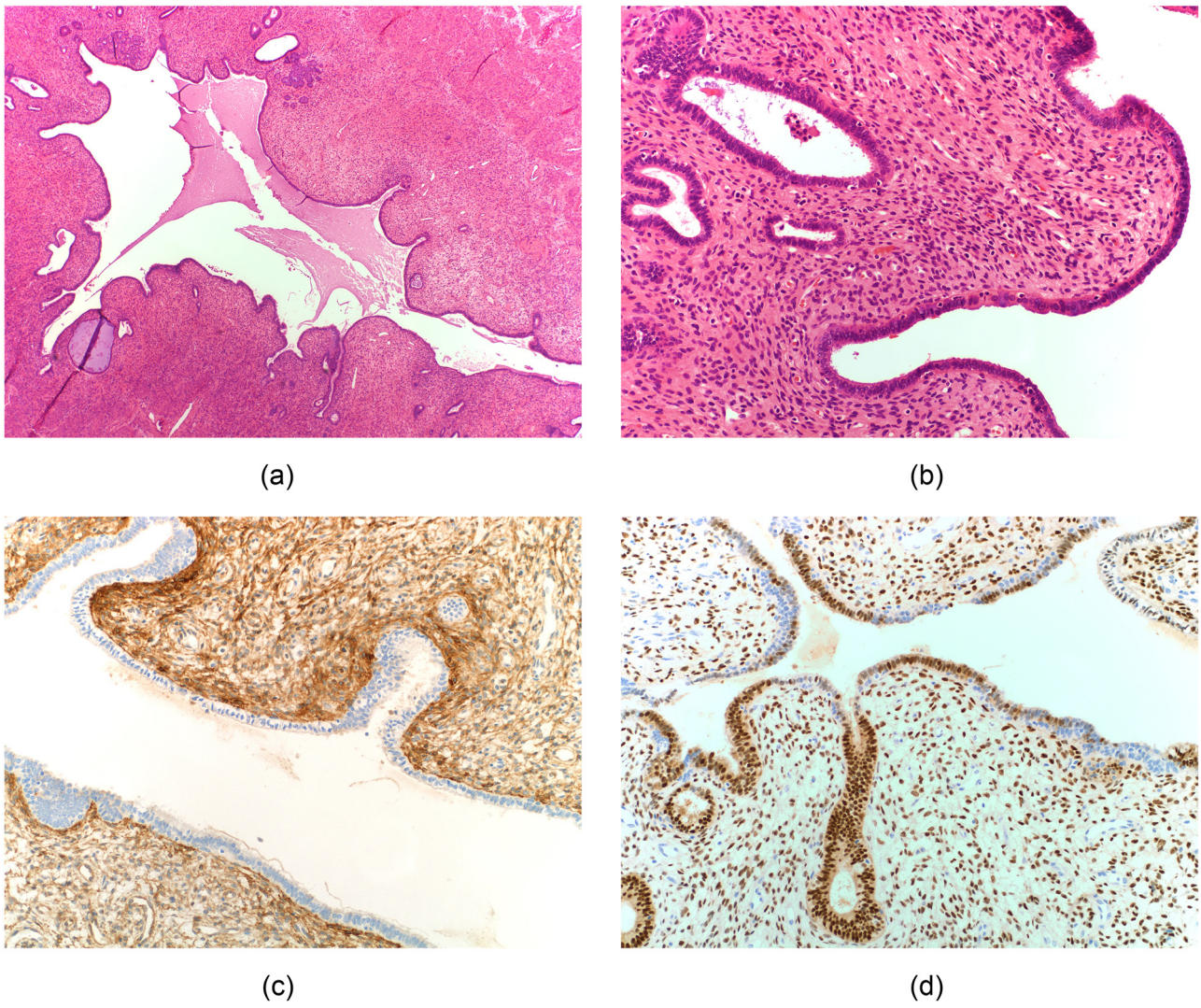

Fig. 3. Histopathology and immunohistochemistry: (a) Endometrial tissue with portion of lower uterine segment and adjoining stroma. H&E stain, 100× magnification. (b) Higher magnification showing details of endometrial epithelium and stroma. H&E stain, 400× magnification. (c) Immunohistochemical staining for CD10 showing positive expression in the endometrial stromal cells. (d) Immunohistochemical staining for Estrogen Receptor (ER) showing positive expression in both endometrial mucosa and stroma endometrial stromal cells.

major role in testicular descent. In females, the absence of testosterone causes Wolffian duct degeneration. While Mullerian duct differentiation begins in the absence of MIS into uterus, fallopian tubes and ovaries [6–8]

PMDS is categorized into male form and female form according to the anatomical structure. The most common form is the male form and constitutes more than 80% of the cases [1]. The male form defined by the presence of unilateral cryptorchidism with a contralateral inguinal hernia. It was further subdivided into two categories based on the content of the inguinal hernia. Hernia uteri inguinalis is the first subdivision in which the descended testes together with the ipsilateral corner of the uterus and the ipsilateral fallopian tube all herniate into the inguinal canal. The crossed testicular ectopia is the second subdivision in which the hernia sac will have both testes and the entire uterus and both fallopian tubes [1,9].

The female form, accounts only for up to 10–20% of cases. It is characterized by bilateral cryptorchidism and a fixed uterus to the pelvis with both testes attached to the round ligaments in both sides similar to the ovarian position. In this form, the clinical presentation depends mostly on whether structures derived from the Mullerian duct are mobile or not. If the uterus and fallopian tubes are mobile during testicular descent, this may cause the uterus and the fallopian tube to be pulled into the inguinal canal. Whereas if the Mullerian structures are immobile, they may block testicular decent [1,9].

The diagnosis of PMDS is usually incidental, since the Mullerian structures are undetectable during abdominal, scrotal or rectal examination [1]. Using imaging techniques such as Magnetic Resonance Imaging (MRI), CT, or ultrasound could help in the diagnosis. Since patients with PMDS have normal development of their genitals, screening or diagnosis of PMDS using these techniques is rarely performed [10]. In our case, the patient was diagnosed incidentally intraoperatively during the resection of germ cell tumor of an undescended testis. At first, the patient thought to have ovaries along with uterus, fallopian tubes and vagina but the pathological report of postoperative specimen showed remnant of testes without any ovarian tissues. Therefore, our case favors the second form of PMDS, the female form, in which the testes attaches to round ligament in an ovarian position with bilateral cryptorchidism without inguinal hernia [8].

The risk of malignancy in patients with PMDS and bilateral cryptorchidism increases by 35–50 time than normal people [1,11] therefore, surgical removal of the Müllerian Duct structures and

the undescended testis should be performed as soon as possible to eliminate the risk of malignant transformation [12].

4. Conclusion

PMDS is a challenging condition as the diagnosis is usually incidental due to the presence of normal male genitalia. It should be suspected in a male presenting with bilateral cryptorchidism or unilateral cryptorchidism and contralateral inguinal hernia. Early diagnosis and management of this condition is important as those patients have higher risk for malignant transformation.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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Ethical approval

Approval for case report has been exempted from our institution.

Consent

Written informed consent was obtained from the patient for publication of this case report.

Author contribution

Turki Z. Al Harbi – Writing the manuscript, Data collection, and Review of the Literature.

Kareem Ayman Azzam – Language Editing, Data collection, and Review of the Literature.

Ayman Azzam – Pre and Post-Operative patient Care and Revised the manuscript.

Tarek Amin – Pre and Post-Operative patient Care.

Nasir Bakshi – Histopathological Investigation and Figure Citation.

Registration of research studies

Not Applicable.

Guarantor

Dr. Ayman Azzam.
Dr. Tarek Amin.

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