Persistent Müllerian Duct Syndrome (PMDS): a Rare Anomaly the General Surgeon Must Know About

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Abstract Persistent Müllerian duct syndrome is a rare condition occasionally encountered in men with normal phenotype but with presence of Müllerian duct structures. In India, owing to neglect and lack of facilities, we encounter this condition in adult males. We encountered on the same day in the operation theatre two phenotypic males aged 40 years and 10 months who had inguinal hernia on one side along with contralateral undescended testis. Both patients intraoperatively had uterus with fallopian tubes and underwent subtotal hysterectomy with preservation of vas. Repair of inguinal hernia with fixation of the testis in the scrotum was done. Though rare, every surgeon operating upon inguinal hernia or undescended testes or cryptorchidism needs to know about the presence of the uterus in a phenotypic male patient at any age. High degree of suspicion and awareness is needed to diagnose this condition. Early treatment is needed to maintain fertility and to prevent the occurrence of malignancy in remnant müllerian structures.

Keywords Persistent Müllerian duct syndrome · Phenotypic male · Uterus · Subtotal hysterectomy · Undescended testis · Inguinal hernia

Abbreviations

PMDS Persistent Müllerian duct syndrome
MIF Müllerian inhibitory factor
MGD Mixed gonadal dysgenesis
TTE Transverse testicular ectopia

Introduction

Persistent Müllerian duct syndrome (PMDS) is a rare disease that occurs in men with a completely normal phenotype and is characterised by the presence of Müllerian duct structures. Organogenesis of the male external genitalia is not affected. There is failure of regression of the müllerian structures, resulting in the presence of a uterus, fallopian tubes and the upper third of the vagina in males with a 46XY karyotype. Persons affected with this syndrome show the presence of male and female reproductive systems together. We report two cases of transverse testicular ectopia seen by us on the same day in our rural secondary care set-up. Almost as if lightening striking twice at the same place, we discuss these 2 cases of this rare disorder.

Case Report

We report a 40-year-old male, a father of five children, who presented to us with right undescended testis and left irreducible hernia which pre-existed for many years. On examination, he was a healthy male with well-developed left hemiscrotum and palpable testis and irreducible inguinal hernia on the right side which was firm and mildly tender. His right-sided hemiscrotum was underdeveloped. On exploring the left inguinal region, the sac consisted of a greater omentum along with the both testes (the right testis was smaller than the left testis which was normal) with a well-formed uterus with fallopian tubes in between the two gonads (transverse testicular ectopia with PMDS). Both the testes had normal epididymis with their vas and blood supply which was distinct from that of the uterus and cervix. Subtotal hysterectomy preserving the vas on both sides was done. Both the testes were fixed in their respective hemiscrotum, and repair of the hernia sac on the left side was followed by Bassini repair. The patient had an uneventful recovery and was discharged on post-operative day 4 (Fig. 1).

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Fig. 1 Contents of the hernia sac on the left side in the first case. The uterus is held in the babcock clamp

Fig. 2 Subtotal hysterectomy with bilateral orchidopexy being performed in case 2

On the same day, a 10-month-old male child presented to us with left inguinal hernia and undescended testis on the right side. The child was first born of non-consanguineous marriage with no significant family history of ambiguous genitalia. Phenotypically, the child was a normal male with well-developed left hemiscrotum and a palpable testis with another mass just above it. The right hemiscrotum was partially developed with impalpable testis. On exploring the left inguinal region, a wide neck sac consisting of the left testis with uterus and two fallopian tubes between the two gonads was seen. The right testis could be pulled into the sac by gentle traction on the uterus. This testis was similar in volume and consistency as the left testis (Fig. 2). Here, also, we performed subtotal hysterectomy with bilateral orchidopexy. Vas was preserved on both the sides. Post-operative period was uneventful. No associated genitourinary malformations were found in both the cases.

Discussion

Müllerian duct derivatives are present in a male foetus up to 8th week of gestation, and their regression is mediated by müllerian inhibitory factor (MIF) produced by Sertoli cells. The only müllerian remnant in a normal male is the utriculus prostaticus. Failure of synthesis or release of MIF or defect in end organs or error in the timing of release of MIF causes persistence of müllerian structures, the condition known as PMDS [1]. Since testosterone levels are normal, the Wolffian duct development progresses in the normal direction, leading to normally developed external genitalia. MIS is a member of transforming growth factor beta (TGF- β) family. MIS secretion is independent of the pituitary secretions. MIS induces the degeneration of basement membrane of epithelial and mesenchymal cells. Some of the PMDS patients have defect in MIS

gene located at 19p13, and others have defective gene for type II MIS receptor (MISR-II), located at 12q13. Approximately 85 % of PMDS cases are due to mutation of either MIS or MISR-II genes, in similar proportions. In 15 % of cases, the cause for PMDS is unknown [2].

PMDS can occur sporadically or inherited either as X-linked or autosomal recessive sex-limited trait. Mutation in MIS and MISR-II gene has autosomal recessive transmission [3]. The mode of transmission is heterogeneous, and the presence of consanguinity in few cases and the occurrence of PMDS in several pairs of brothers suggest an autosomal recessive male-restricted transmission [4]. It is present since birth, but patient may present to the physician at any stage of life: infant, child or adulthood.

PMDS or persistent müllerian duct syndrome is a rare phenomenon, and a high degree of suspicion is essential in diagnosing it. Clinically, PMDS cases are divided into three categories:

1. Majority (60–70 %) with bilateral intra-abdominal testis, in a position analogous to ovaries (female variant) (Fig. 3).
2. Smaller group (20–30 %) with one testis in the scrotum, associated with contralateral inguinal hernia whose contents are the testis, uterus and tubes (classical presentation of hernia uteri inguinale, male variant) (Fig. 4).
3. Smallest group (10 %) where both the testes are located in the same hernial sac along with the müllerian structures (transverse testicular ectopia (TTE), male variant) [5] (Fig. 5).

PMDS accounts for 30–50 % of all cases of TTE. There are two anatomic variants: male or female. In the male form or hernia uteri inguinale, one testis is normally descended in the scrotal sac. The uterus and ipsilateral fallopian tube and sometimes contralateral testis and the tubes are either in the inguinal

Fig. 3 Presentation of bilateral intra-abdominal testis

canal or can be brought into the inguinal canal by gentle traction [6]. Female form is less common and is characterised by the presence of bilateral cryptorchidism with both the testes embedded in the broad ligament in the ovarian position with respect to the uterus in the pelvis. Vas deferens is adherent to the lateral walls of the uterus and courses along the cervix in both forms [6]. Von Cenhossek in 1886 first described transverse testicular ectopia, and in 1895, Jordan described the association of PMDS with transverse testicular ectopia in which one testis crosses the midline, and both are seen in the contralateral inguinal canal or hemiscrotum. The 10-month-old child in our setting had similar presentation [7, 8].

Transverse testicular ectopia has been classified into three types on the basis of various associated anomalies: those associated with inguinal hernia alone (40–50 %), those associated with persistent or rudimentary Müllerian duct structures (30 %) and those associated with other anomalies without müllerian remnants, e.g. inguinal hernia, hypospadias, pseudohermaphroditism and scrotal abnormalities (20 %) [9].

Preoperative diagnosis of PMDS is difficult, but all patients (of any age group) who present with bilateral cryptorchidism

Fig. 4 Classical presentation of hernia uteri inguinale

Fig. 5 Male variant of transverse testicular ectopia

or one-sided inguinal hernia with contralateral undescended testis or one-sided inguinal hernia with a palpable mass above the normally descended testis should ideally be investigated for chromosomal studies and ultrasonography or MRI to assess the presence of uterus with fallopian tubes and testis. However, most studies have found ultrasonography to be of limited value in picking up müllerian structures [7]. Diagnosis of PMDS is based on a combination of high index of suspicion and anatomic, clinical and imaging findings. Simple per rectal examination may reveal the presence of uterus with fallopian tubes. MRI has also been done to detect the mass when PMDS presents as an intra-abdominal mass. In our case, owing to cost restraints and unavailability of MRI, we did not resort to it. Imaging should be complemented by karyotyping.

Differential diagnosis of PMDS includes disorders of sexual differentiation with defective regression of the müllerian derivatives including mixed gonadal dysgenesis (MGD). Biopsy is required to confirm the sex and to differentiate from MGD. A workup to rule out associated genitourinary malformation should be done. In our case, both the patients had no associated genitourinary malformation.

In both our cases, we had a high index of suspicion, and we explored the inguinal hernia site first. On recognising the condition, the inguinal incision was extended to Pfannenstiel incision facilitating a complete lower abdominal exploration and adequate procedure. Distinguishing other intersex disorders from PMDS is important, as the management is different. In the presentations such as ours where the patient is a fully virilised male with asymmetric gonads, the differential diagnosis will include MGD (it refers to individuals who usually have a differentiated gonad on one side and a streak gonad or streak testis on the other side) with karyotype showing mixed chromosomal pattern (XO/XY). However, on abdominal exploration, in such cases, the internal gonad is likely to be dysgenetic, which neither shows normal testicular form nor

consistency, but sometimes shows a streak gonad. This can mostly be picked up by the naked eye, though gonadal biopsy is essential to confirm the above and rule out in situ cancer. Where the surgeon is in doubt, a gonadal biopsy and delaying the definitive procedure to a second sitting are recommended. If exploration of hernia shows uterus with ovaries (ovarian tissue can be identified by naked eye), most likely, the diagnosis will be a fully virilised female due to congenital adrenal hyperplasia.

Distinguishing intersex disorders from PMDS is important as the management is different. In the literature, there are case reports of PMDS patients with infertility as well as patients with three to five children, so there is no definitive documentation of PMDS with infertility. Josso et al. reported that if the gonads are placed in the scrotum, fertility is retained [2]. Martin et al. documented spermatogenesis in a patient with TTE [10]. Fertility is rare in patients with PMDS. Imbeaud et al. reported three cases of PMDS with testicular degeneration and opined that anatomical abnormality may favour testicular torsion and early loss of testis [11].

Management of PMDS is controversial. Earlier studies [8, 12] opined that while removing the müllerian remnants, there is a high probability of damage to vas deferens and its blood supply with no disadvantage of conversion into malignancy, so they should not be removed. Thiel and Erhard reported the death of a 14-year-old boy with PMDS, due to metastasis of adenocarcinoma arising from the müllerian remnant [14]. Romero et al. reported a 39-year-old man who developed adenocarcinoma of endocervical origin, arising from the müllerian remnant [13]. The overall incidence of malignant transformation in these testes is 18 % similar to the rate in abdominal testes [15]. There have been reports of embryonal cell carcinoma, seminoma, choriocarcinoma and teratoma in patients with cryptorchidism and persistent Müllerian duct. Apart from malignancy, retained müllerian remnants which are in connection with the prostatic utricle are known to cause recurrent UTI, stones and voiding disturbances [5].

Surgical management is aimed at preserving fertility by performing orchiopexy for repositioning of the testis into the scrotum if feasible or at least getting the testis to a palpable suprascrotal location. Herniorrhaphy with hysterectomy and bilateral salpingectomy with preservation of the vas deferens retained to preserve fertility should also be done [16, 17]. Orchiectomy is indicated for testes that cannot be mobilised or have undergone a malignant change or if streak/dysgenetic gonads have been detected [18]. Routine orchiectomy should not be done as the capacity of the virilisation must be preserved.

Laparoscopic management of PMDS with bilateral cryptorchidism is reported by El-Gohary [19]. If facilities of endoscopy are available, then diagnostic laparoscopy can be performed to assess the internal gonadal status. Some authors do staged procedure whereby after histopathological

confirmation of testicular structure, bilateral orchidopexy with preservation of vas is done along with removal of uterus and bilateral fallopian tubes. Brandli et al. believed that laparoscopically, the müllerian structure should be divided in the midline, and if there is lack of adequate visualisation of the vas deferens, that conversion to an open approach is a better option. Pfannenstiel incision provides superior exposure and is the safest possible approach to the müllerian structures and blood supply [20]. They recommend a minimal division of the persistent müllerian structures which ensured an adequate placement of the testis in the scrotum or a staged procedure for the same [19].

Excision of MDS is considered essential to prevent sexual maturation hypertrophy of the uterus and accumulation of blood causing abdominal discomfort and mass [1]. Current surgical recommendation for MDS includes proximal salpingectomies and a hysterectomy, leaving an intact pedicle of myometrium as it facilitates preservation of fertility and hormonal functions, especially when the child is young [4]. For TTE, transseptal fixation or modified Ombredanne technique, in which both cords and vessels of two testicles pass through the same inguinal canal, is recommended, but this carries a risk of damage to both vas and vessels of the two testes whenever there is trauma or infection [21].

Manjunath et al. (2010) recommended stripping/destroying the mucosa of the retained müllerian remnants to reduce the risk of malignancy and, simultaneously, to prevent the damage to the vas deferens and disruption of collateral blood supply to the testes [5]. In both cases, we identified the vas deferens and blood supply to the testis which was running high up, and subtotal hysterectomy was done; both the testis were fixed in their respective hemiscrotum after adequate mobilisation.

It is necessary for every surgeon not just a paediatric surgeon to know about this condition, as it can be encountered in our routine practice while operating upon any patient with indirect inguinal hernia or undescended testis or cryptorchidism. The best treatment option for this condition according to us is to do subtotal hysterectomy along with preserving the vas on both the sides so that we do not tamper with the fertility, and the risk of malignancy due to persistence of müllerian structures is reduced.

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