Persistent Müllerian Duct Syndrome - A Case Presentation

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Abstract

Introduction and Objectives. Persistent Müllerian duct syndrome is a relatively rare form of male pseudohermaphroditism in which Müllerian duct derivatives (uterus, fallopian tubes and upper vagina) are seen in an otherwise differentiated male patient with a normal 46XY karyotype.

Materials and Methods. We report the case of one patient that was evaluated in our clinic using physical examination, imaging, measurement of tumor markers and surgical exploration.

Results. The patient had an atrophic right testicle and a hypoplasic left testicle and presented primary infertility. Taking into account the existent risk of malignancy of the müllerian derivatives, laparoscopic hysterectomy was performed.

Conclusion. Controversy remains as to the ideal surgical treatment regarding the müllerian structures, but orchidopexy should be performed in all cases. Laparoscopic exploration associated with excision on the derivatives is safe and should be taken into account.

Key-words: Persistent Müllerian duct syndrome, PMDS, pseudohermaphroditism, laparoscopic exploration, cryptorchidism.

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Introduction and Objectives

Persistent Müllerian duct syndrome (PMDS) is a relatively rare form of male pseudohermaphroditism in which Müllerian duct derivatives (uterus, fallopian tubes and upper vagina) are seen in an otherwise differentiated male patient with a normal 46XY karyotype [1]. Patients are phenotypically male and usually present when young, with unilateral or bilateral undescended testes and an inguinal hernia into which prolapses an infantile uterus and fallopian tubes [2,3]. It was first described in 1939 by Nilson [4], who first described this association in a man with inguinal hernia as hernia uteri inguinale.

PMDS is caused by either lack of Müllerian inhibitory hormone (MIH) or due to lack of sensitivity of the target organ to MIH by dysfunction of the MIH Receptor [5,6]. Mutations cause lack of MIH secretion or lack of translocation to the surface membrane causing inactivity of the receptor.

Usually it is an incidental finding during check-ups or surgery in patients with unilateral or bilateral cryptorchidism and ipsilateral inguinal hernia. Sometimes they may associate transverse testicular ectopia (TTE) [7,8] and also most of the patient associate primary infertility [9].

Materials and Methods

We report the case of a 36 year old male who presented for left inguinal pain and male infertility, clinical examination showed the lack of left testicle in the left scrotal sac and magnetic resonance imaging (MRI) showed a uterine like structure posterior of the bladder.

On clinical examination the right scrotal sac was empty, while the left scrotal sac contained a hypoplasic testicle. Phenotypically the patient was a male, with male pattern of external genitalia and secondary sexual characteristics, while the body hairness was significantly reduced. The patients past history included primary infertility. Testicular tumoral markers were all within normal limits, while from a hormonal point of view, the patients presented a compensated hipergonadotrophic hypogonadism. The genetic evaluation noted a normal 46XY karyotype, with the presence of the sex-determining region Y (SRY) protein gene.

Ultrasound showed postero-lateral of the bladder a structure of 43/20 mm echographically similar to a uterus. The prostate was normal, while only the left seminal vesicle was identified by echography. The left scrotal sac showed a uniform oval structure of approximately 19/10 mm conforming to a testis, while the right scrotal sac contained a 7 mm structure without the certainty of being a testis, also no structure suggestive of testicular parenchyma was identified in an ectopic location.

MRI confirmed the ultrasound findings. It showed a triangular structure oriented to the internal inguinal rings and the prostate, with a 5 mm wall and T2 signal suggestive for uterine stratification - Figure 1. Also the absence of the right seminal vesicle was noted - Figure 2, hypoplasic left testicle, without identifying an ectopic right testicle and with the identification of a 7mm structure suggestive for right testicle in the right scrotal sac.

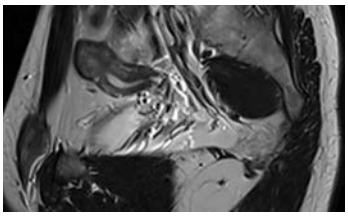


Fig. 1. IRM aspect showing the structure, with triple T2 stratification, suggestive for uterine stratification.

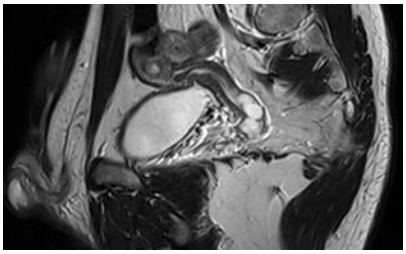


Fig. 2. The structure is localized posterior to the bladder, tractioned to the left, where we can identify a left unique seminal vesicle.

After the multidisciplinary evaluation the patient we have opted for excision of the structure. Subsequently the patient was planned for exploratory laparoscopy and excision of the formation. We used a three trocar laparoscopic transperitoneal access. Access was obtained using the open technique, after that two 10 mm and one 5 mm trocars were inserted. On exploration of the peritoneal cavity we identified a structure with a macroscopically similar to uterus localized posterior to the bladder tractioned next to the left internal inguinal ring – Figure 3. The uterine horns were continued with two tubular structures similar to Fallopian tubes.

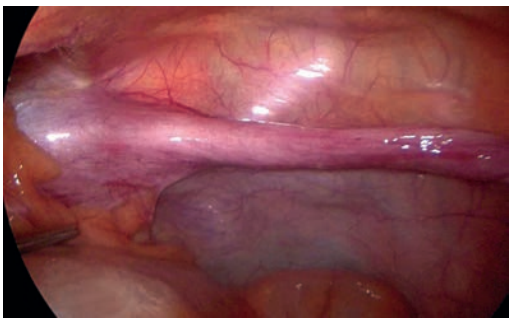


Fig. 3. Intraoperative aspect, with the uterus tractioned to the left internal inguinal ring, and a canalicular structure beginning from the right uterine horn and heading for the right internal inguinal ring, with suggestive aspect for Fallopian tube.

After incision of the anterior parietal peritoneum, the utero-vesical space was dissected and posterior dissection was performed until the identification of the prostate. We then sectioned the two tubular structures, with the preservation of an artery localized lateral on the left on the structure that entered the left internal inguinal ring. Then the inferior part of the structure was sectioned close to the prostate - Figure 4. We inserted a small drainage for 24 h and discharged the patient after 48 h postoperative.

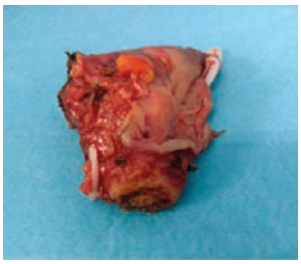


Fig. 4. Aspect of the resected structure, we can notice in the inferior pole a small opening, probably of the cervical canal.

Results

The pathology examination of the structure found a microscopically uterine structure, with a walled formed of muscular fibers, small caliber vessels with a thick wall and endometrium with simple glandular hyperplasia and edema. Also, on each side of the uterus, structures composed of concentric muscular fibers and connective tissue, with a central papillary glandular aspect, compatible with the histological structure of the vas deferens.

The patient was evaluated at 3 months and 6 months postoperatively, with clinical and ultrasound evaluation performed, patient reporting the lack of pain, while scrotal ultrasound reported the same aspect as preoperative.

Discussions

Persistent Müllerian duct syndrome (PMDS) is a rare form of male internal pseudohermaphroditism, caused by a deficiency of MIH or anomaly of MIH receptor. Hence müllerian derivatives (i.e. uterus, upper vagina and fallopian tubes) are encountered in a normal genotypically and phenotypically male, with normal development of the external genitalia.

The Müllerian and Wolffian ducts are both present at 7 weeks of gestation, testis differentiating by the end of the 7th week of gestation. Three hormones are involved in the normal sexual differentiation. MIH is secreted by Sertoli cells and leads to regression of the müllerian ducts, testosterone has a direct effect on the wolffian ducts and promotes their differentiation into epididymis, vas deferens and seminal vesicles, while dihydrotestosterone induces male differentiation of external genitalia. PMDS patients have both Wolffian and Müllerian duct structures due to a deficiency of MIF [10,11].

PMDS was classified into three groups by Hutson et al. [12]. Group A also called a female type is characterized by the presence of the testes in the position of the normal ovaries. Group B and C are both a male type, in group B one testicle is found in a hernia sac or in the scrotum along with the uterus and tubes also being called hernia uteri inguinale, while on group C, both testes are found in the same hernia sac, hence a transverse testicular ectopia. On review of the procedure our patient seems to be of group B male type.

Even though PMDS can occur sporadically, most commonly, it occurs as autosomal recessive trait due to mutation in AMH or AMHR-II [13]. Patients with type I PMDS have a defect in AMH gene located at 19p13, which was seen in 45 % cases. Patients with type II PMDS have defective AMH receptor (AMHR-II), located at 12q13 [14], seen in 40 % cases, while in 16 % of cases the cause is unknown [15].

Regarding therapeutic management of a patient with PMDS the biggest debate comes on the surgical conduit in relation with the müllerian derivatives. Undescended testes, frequently present in PMDS, have a considerable risk of malignancy compared to a normal descended testis [16], 16 cases of testicular tumors associated with PMDS have been reported [17], the real incidence being hard to determine, with some studies reporting an overall incidence of 5-18% [18].

As mentioned before there isn't a consensus in regard to the surgical management of müllerian derivatives. Some authors support preservation of the structures [8,19-21], aiming to maintain fertility, but most of the patients are infertile with absence of spermatozoa seen at semen analysis, however there have been a few reported cases of fertility, although without absolute proof of paternity [10]. Other authors suggest that in type A patients with bilateral cryptorchidism the uterus should be divided to assist in orchidopexy thus achieving adequate length for the testis to reach the scrotum [22]. While other authors support the excision of the remnants [9-11,23]. One must also consider the risk of malignancy, with 11 cases reported in the literature ranging from 4 to 68 years old, in some cases presenting metastatic spread and leading to the death of the patient [18]. Manjunath et al. support that the malignant potential comes from the mucosa, hence they support a technique that involves dividing of the structures, with resection of the mucosa and orchidopexy [14,24].

Laparoscopy has showed to have benefits in the diagnostic and treatment of the condition [14]. Many authors have described different approaches for PMDS, while Shorasaki et al. described laparoscopic excision and orchidopexy [25], Turaga et al. described a personalized approach based on an algorithm depending on intraoperative findings [26]. Other authors suggested splitting the remnants in the midline to achieve ade-

quate mobility for the testis to reach the scrotum [14], while other authors suggested stripping the mucosa of the remnants following splitting o the structures, to avoid malignancy. In our case we decided to perform hysterectomy thus avoiding the malignancy risk arising from the müllerian remnants, taking into account that the patient had descended testes, but associated primary infertility and testicular hypoplasia.

Conclusions

Persistent müllerian duct syndrome is a rare type of male pseudohermaphroditism, determined by a mutation of the AMH gene or its receptor, all in an otherwise differentiated male patient with a 46XY karyotype.

It usually associates unilateral or bilateral cryptorchidism, it is recommended to perform orchidopexy as soon as possible to preserve sexual function and fertility, and also to avoid the long term higher risk of malignancy that undescended testicles predispose to.

Regarding the müllerian derivatives, consensus on the correct surgical treatment has yet to be meet. Some authors suggest preserving the structures so that testicular vascularization isn't damaged during excision, while others suggest removing them to avoid the malignancy risk. We decided for the later, performing the intervention laparoscopically, which is a safe technique, without major postoperative complications and with a fast recovery after surgery.

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