Indian J Surg (January–February 2010) 72:16–19
DOI: 10.1007/s12262-010-0003-x

REVIEW ARTICLE

Persistent müllerian duct syndrome: How to deal with the müllerian duct remnants - a review

Manjunath B. G. · Vasanth G. Shenoy · Preetham Raj

Received: 21 May 2009 / Accepted: 25 July 2009

Abstract Persistent müllerian duct syndrome (PMDS) is usually a surprise finding either during orchidopexy or during routine inguinal hernia repair in male patients. Often, the surgeon would face a dilemma about what is to be done with the remnants of müllerian duct, i.e. the fallopian tubes, uterus and proximal vagina. Till recently, it was advised to retain these structures whenever it was felt that the complete excision of these structures may jeopardise the blood supply and integrity of the vas deferens. Recent reports of malignancy in these retained structures would justify more aggressive approach. In our patients with PMDS, we have removed the mucosa of the retained müllerian structures, without compromising the integrity and vascularity of the vas deferens, thus reducing the chances of malignancy.

Keywords Persistent müllerian duct syndrome · Transverse testicular ectopia · Hernia uteri inguinale · Müllerian inhibiting substance

B. G. Manjunath[1] · V. G. Shenoy[2] · P. Raj[3]
[1]Professor of Surgery, Department of General Surgery,
[2]Assistent Professor, Department of Pediatric Surgery,
[3]Registrar, Department of General Surgery,
Dr. B.R. Ambedkar Medical College, Bangalore, India

B. G. Manjunath (✉)
E-mail: dr.bgmanjunath@gmail.com

Introduction

Persistent müllerian duct syndrome (PMDS) is a relatively rare variety of male psuedo-hermaphroditism. Nilson described the condition in 1939 and termed it as hernia uteri inguinale. It is usually an intraoperative surprise during routine orchidopexy or inguinal hernia repair. Patients are phenotypically male and have male (46XY) karyotype. However, they will have müllerian remnants like fallopian tubes, uterus and the proximal vagina, which are in close proximity to the testes and vas deferens. Rudimentary vagina ends by opening into the prostatic utricle.

American National Institute of Health estimates that there are <200,000 cases of PMDS in the US. Exact incidence in India is not known. Review of literature showed about 15 case reports from India, including a report of familial PMDS, other than our cases mentioned here (Fig. 1). PMDS is under-reported, because, significant number of patients with undescended testis do not under go orchidopexy in our country. Many cases of PMDS that are detected accidentally during inguinal hernial repair, are often misdiagnosed due to lack of familiarity with the condition, surgeons often replace müllerian remnants back into the peritoneal cavity and complete the hernial repair. Diagnosis can be missed during initial surgery, leading to re-operations [1].

Aetiology

In a male foetus, masculanisation occurs between 7 and 8 weeks of gestation. The Leydig cells in the testis secrete testosterone which permits the development of Wolffian duct into vas deferens, epididymis and seminal vesicle, while the Sertoli cells in the testis secrete müllerian inhibiting

Fig. 1 Familial PMDS treated at our institute—two brothers standing in the centre had PMDS. Note facial hairs and male type of frontal baldness. Penile length and secondary sexual character were adequate. While one of them had hernia uteri inguinale with TTE, the other had bilateral intra-abdominal testes

substance (MIS), which acts locally and unilaterally to suppress the müllerian duct.

MIS is a member of transforming growth factor-β (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, cause for PMDS is unknown [2].

PMDS can occur sporadically or inherited either as X-linked or autosomal dominant sex-limited trait. Mutation in MIS and MISR-II gene has autosomal recessive transmission [3]. Rarely, PMDS has been reported in association with Klinefelter's syndrome, Turner's syndrome and Mayer-Rokitansky-Kuster-Hauser syndrome.

Diagnosis and management

Clinically, PMDS cases are divided into three categories:

1. Majority (60–70%) with bilateral intra-abdominal testis, in a position analogous to ovaries.
2. Smaller group (20–30%) with one testis in the scrotum, associated with contralateral inguinal hernia whose contents are testis, uterus and tubes (classical presentation of hernia uteri inguinale).
3. Smallest group (10%) where both the testes are located in the same hernial sac along with the müllerian structures (transverse testicular ectopia - TTE). PMDS accounts for 30–50% of all cases of TTE.

Affected individuals have normal male phenotype, normal virilisation, undergo normal male puberty, and may even be fertile if the gonads are placed in the scrotum. Level of circulating MIS is normal for age in MISR-II mutants and usually low or undetectable in MIS gene mutants [2].

In patients with bilateral abdominal testes, both the gonads may be located in a position analogous to ovaries, with a rudimentary uterus in the centre. That may confuse the surgeon regarding the real genetic and gonadal sex of the patient. Loeff et al. performed two-stage procedure, gonadal biopsy was done in stage one, the gonad and müllerian remanants were placed back in the abdomen and then a re-exploration of the patient was done as second stage procedure, several months later [4]. Such a staged procedure is not needed, as the presence of epididymis and the vas deferens would unequivocally reveal that the gonad is a testis. A decision to perform an orchidopexy can be taken during initial exploration itself. However, testicular biopsy may be needed to rule out mixed gonadal dysgenesis or carcinoma *in situ*. Berkman opined that testicular biopsy is not needed as long as the testis is placed at a location where it can be palpated. And impalpable testicular malignancies can be detected through ultrasound [5]. Testicular biopsy would transgress the blood-testes barrier, which may result in the production of antisperm antibodies. Due to the high incidence of malignancy in testes that are located in the abdomen, orchidectomy is indicated in patients when the testes cannot be mobilised to palpable location outside the abdomen [6]. Seminoma, embryonal cell tumours and teratomas have been reported in such testes, even after orchidopexy.

In case of bilateral abdominal testes, müllerian remnants prevent the mobilisation of the testes. Brandli et al. split the müllerian structures in the midline, thus mobilising the testes to reach the scrotum on either sides [7]. Microvascular autotransplantation of the testis is the other alternative [7]. Complete excision of the müllerian duct remnants can result in damage to the integrity or vascularity of the vas deferens. The vas deferens can be particularly in close proximity with the fallopian tubes and the vagina. At times, it can be incorporated into the wall of the vagina [8]. Vandersteen et al. (1997) evaluated the risk of retaining müllerian structure versus risk of injury to the vas deferens during excision of the müllerian remnants and concluded that the müllerian remnants should not be excised, as malignancy had not been reported till then [6]. Berkman (1997) too opined that the removal of remnants was not necessary, since no malignancy was reported [5]. However, since 1997, several cases of malignancies arising from the retained müllerian structures have been reported. Theil et al. (2005) reported death of a 14-year-old boy with PMDS, due to metastasis of adenosarcoma arising from the müllerian remnant [9]. Romereo et al. (2005) reported a 39-year-old man who developed adenocarcinoma of endocervical origin, arising from müllerian remnant [10]. Shinmura et al. (2002) reported clear cell adenocarcinoma a arising from uterus in a 67-year-old man with PMDS [11]. These

recent reports of malignant degeneration of the müllerian remnants warrant a rethink into the management options of the müllerian remnants. In our two cases, we have excised the uterine remnants, which were located away from the vas deferens. The fallopian tubes were layed open and the mucosa was stripped. The proximal vagina which was opening into the prostatic utricle was opened and its mucosa was destroyed with electrocautery, avoiding thermal injury to the vas, which was located very close to the lateral wall of the vagina (Fig. 2). Since reported malignancies of müllerian remnants originate from its mucosa, destruction of the mucosal lining should be sufficient in reducing the risk. Apart from malignancy, retained müllerian remnants which are in connection with the prostatic utricle are known to cause recurrent UTI, stones and voiding disturbances. Destruction of the mucosa of the vaginal remnant will obliterate the cavity due to adhesions, thus reducing the risk of UTI and stone formation.

If a two stages Stephen-Fowler procedure is contemplated for abdominal undescended testes, then, the excision of the müllerian remnant may be hazardous for the collateral circulation of the testes. Excision of the uterus and the fallopian tubes may disrupt the vasal collateral blood supply, which should be retained for the viability of the testis. In such patients, midline splitting of the müllerian remnants and excision of the mucosa would allow the complete mobilisation of both the testes preserving the collateral blood supply from the mesometrium.

In PMDS patients with TTE, mobilisation of the testis is usually easier. PMDS accounts for nearly 50% of all cases of TTE. Trans-septal orchidopexy is the treatment of choice, along with excision of the müllerian remnants, as mentioned earlier. Lima et al. recommended that all cases of TTE should undergo abdominal exploration to rule out PMDS [12]. Martin et al. documented spermatogenesis in a patient with TTE [13]. One of our patients of PMDS, who had TTE, had oligospermia (Fig. 3). Other patient with bilateral abdominal testes had azoospermia. 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 [14].

Laparoscopy has huge benefits in the diagnosis as well as the treatment of PMDS [8]. Shirasaki et al. described laparoscopic excision of the uterus followed by orchiopexy in 1-year-old child with PMDS [15]. Turaga et al. described an algorithm-based approach for hernia uteri inguinale, depending on laparoscopic findings [16]. Ng et al. described one stage orchiopexy for intra-abdominal testes in PMDS with division of the testicular vessles, with careful preservation of the collateral blood supply around the müllerian remnants [17]. El-Gohary et al. described laparoscopic orchidopexy in PMDS by splitting the müllerian remnants in the midline and thus achieving adequate length for the testes to reach the scrotum [1]. Our technique of stripping the mucosa of the müllerian remnant can be used during such a procedure, so as to reduce the risk of malignancy. We believe that removing/destroying the mucosa can be achieved laparoscopically, though we have not attempted the procedure through laparoscope. Laparoscopy has the advantage of improved access to proximal vagina which is located deep in the pelvis where it opens into the prostatic utricle.

Screening of the siblings and second degree relatives is necessary, as PMDS has autosomal recessive inheritance. Ultrasonography and MRI have been reported to be of value in locating the müllerian remnants [18, 19]. But we feel that all the siblings with undescended testis should be subjected to diagnostic laparoscopy.

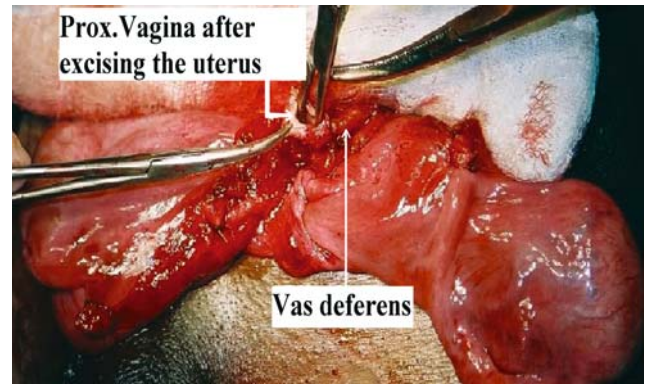

Fig. 2 Proximal vagina after the excision of the uterine remnant. The vagina opens into the prostatic utricle. This vagina could not be excised due to its close association with vas deferens, hence, its mucosa was partly stripped and rest was destroyed with electrocautery, avoiding thermal injury to the vas

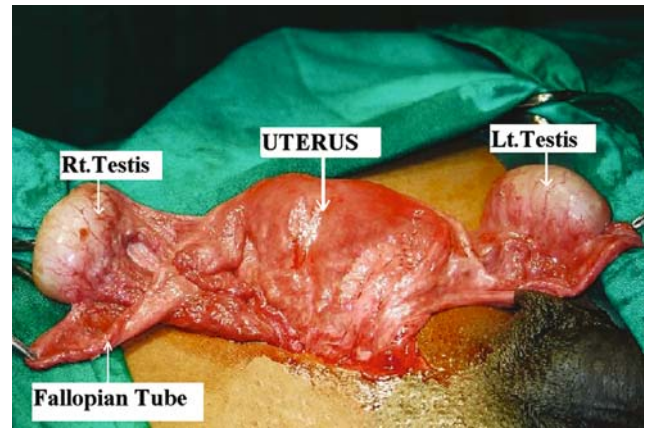

Fig. 3 Hernia uteri inguinale with transverse testicular ectopia. The uterus and both the testes are coming out of the abdomen through left internal inguinal ring and the testes are located at a site analogous to ovaries

Conclusion

Previous reports have advocated retaining müllerian remnants to prevent damage to the vas deferens. However, recent reports of malignancy in the retained remnants of müllerian structures warrant a rethink. Our approach of stripping/destroying the mucosa of the retained müllerian remnants will reduce the risk of malignancy, simultaneously preventing damage to the vas deferens and disruption of collateral blood supply to the testes. Laparoscopy has distinctive advantage in diagnosing PMDS and in the excision of müllerian remnants deep in the pelvis. Familiarity of the surgeon with this disease condition would increase the chances of correctly diagnosing and appropriately dealing with the müllerian remnants.

References

1. El-Gohary MA (2003) Laparoscopic management of persistent müllerian duct syndrome. Pediatr Surg Int 19(7): 533–536
2. Josso N, Belville C, di Clemente N, et al. (2005) AMH and AMH receptor defects in persistent müllerian duct syndrome. Hum Reprod Update 11(4):351–356
3. Hoshiya M, Christian BP, Cromie WJ, et al. (2003) Persistent müllerian duct syndrome caused by both a 27-bp deletion and a novel splice mutation in the MIS type II receptor gene. Birth Defects Res A Clin Mol Teratol 67(10):868–874
4. Loeff DS, Imbeaud S, Reyes HM, et al. (1994) Surgical and genetic aspects of persistent müllerian duct syndrome. J Pediatr Surg 29(1):61–65
5. Berkman F (1997) Persistent müllerian duct syndrome with or without transverse testicular ectopia and testis tumours. Br J Urol 79(1):122–126
6. Vandersteen DR, Chaumeton AK, Ireland K, et al. (1997) Surgical management of persistent müllerian duct syndrome. Urology 49(6):941–945
7. Brandli DW, Akbal C, Eugsster E, et al. (2005) Persistent müllerian duct syndrome with bilateral abdominal testis: Surgical approach and review of the literature. J Pediatr Urol 1(6):423–427
8. Lima M, Morabito A, Libri M, et al. (2000) Laparoscopic removal of persistent müllerian duct in a male: Case report. Eur J Pedtr Surg 10(4):265–269
9. Thiel DD, Erhard MJ (2005) Uterine adenosarcoma in a boy with persistent müllerian duct syndrome: first reported case. J Pedtr Surg 40(9):e29–31
10. Romereo FR, Fucs M, Castro MG, et al. (2005) Adenocarcinoma of persistent müllerian duct remnants, case report and differential diagnosis. Urology 66(1):194–195
11. Shinmura Y, Yokoi T, Tsutsui Y (2002) A case of clear cell adenocarcinoma of the müllerian duct in persistent müllerian duct syndrome: The first reported case. Am J Surg Pathol 26(9):1231–1234
12. Lima M, Domini M, Libri M (1997) Persistent müllerian duct syndrome associated with transverse testicular ectopia: A case report. Eur J Pedtr Surg 7(1):60–62
13. Martin EL, Benette AH, Cromie WJ (1992) Persistent müllerian duct syndrome with transverse testicular ectopia and spermatogenesis. J Urol 147(6):1615–1617
14. Imbeaud S, Rey R, Berta P, et al. (1995) Testicular degeneration in three patients with the persistent müllerian duct syndrome. Eur J Pediatr 154(3):187–190
15. Shirasaki Y, Nagai A, Nasu Y, et al. (2003) Laparoscopic removal of müllerian structures and orchiopexy for persistent müllerian duct syndrome. Urology 62(6):1121
16. Turaga KK, St Peter SD, Calkins CM, et al. (2006) Hernia uterus inguinale: a proposed algorithm using laparoscopic approach. Surg Laparosc Endosc Percutan Tech 16(5): 366–367
17. Ng JW, Koh GH (1997) Laparoscopic orchidopexy for persistent müllerian duct syndrome. Pediatr Surg Int 12(7):522–525
18. Otsuka T, Nakasono T, Matsuo Y, et al. (2003) Persistent müllerian duct syndrome suggested by magnetic resonance imaging. Radiat Med 21(6):277–299
19. Di Cesare E, Di Bartolo, DeVincentiis, et al. (1998) US and MRI in a case of persistent müllerian duct syndrome. Pediatr Radiol 28(11):865-867