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PERSISTENT MULLERIAN DUCT SYNDROME – A RARE CASE REPORT

Pediatrics

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ABSTRACT

4 years old male child was reported with the complain of Pain abdomen with protruded umbilicus, Pain, dribbling and burning sensation while micturition there were no history of fever, blood in urine or stool. Physical examination at presentation revealed an impalpable gonad on the right side with otherwise normal masculine external genitalia and normal penile length. All the features including morphologically male genitalia and testis with uterus (no vagina / no evident ovaries) suggestive of PMDS. Anti-mullerian hormone levels was done which below the normal level (1 .0 ng /ml normal level between 1.5 to 4.0 further supported our diagnosis.

KEYWORDS

INTRODUCTION

Persistent Mullerian duct syndrome (PMDS) is a rare syndrome and sometimes the cause of a common problem in pediatrics and surgical practice, namely undescended testes, in most cases without any underlying pathology.[1] There is a defect in anti-Mullerian hormone secretion or receptor activity resulting in persistence of Mullerian structures such as a uterus or fallopian tubes with otherwise normal virilisation.[2] Nelson in 1939 first described this association in a man with inguinal hernia as hernia uteri inguinale and About 150 cases of PMDS have been reported in literature.[3] It is however important to recognize and determine the definite diagnosis of PMDS, which may decrease future medical and social problems for the patient.

CASE REPORT

4 years old male child was presented to pediatric OPD with the complain of Pain abdomen with protruded umbilicus, Pain, dribbling and burning sensation while micturition there were no history of fever, blood in urine or stool. He was born at term after an uncomplicated pregnancy and no perinatal complications occurred. Blood pressure (96/62 mm of hg which was between 50 – 90th) and other vital were within the normal rage for child's age. Physical examination revealed Umbilical hernia with Infra-umbilical abdominal wall defect and a non-palpable testis on the right side with normal male genitalia. Other than the umbilical hernia and unilateral cryptorchidism, the boy was healthy and had a normal development. Family and social history revealed no remarkable insights. Physical examination at presentation revealed an impalpable gonad on the right side with otherwise normal masculine external genitalia and normal penile length.

INVESTIGATIONS

While investigating the child all the report including complete blood count, urine routine microscopic findings and culture and Renal function test were normal except the imaging studies.

An ultrasound showed abdominal wall defect at umbilical region with omental herniation. A globular uterus-like organ behind bladder with thin endometrium simulating lining, thickened bowel loops, thickened mesentery and mesenteric lymphadenopathy were also noted. Notably, fallopian tubes and vagina was absent. The prostate was present and unremarkable. A normal descended and size testis on the left side; on the right, no testis could be visualized in the scrotum or inguinal region without any inguinal defect. A CT abdomen and pelvis with contrast confirmed the USG findings and demonstrated small enhanching omphalocele with surrounding fat stranding which was suggestive of omphalitis without any urachal cyst/patent urachus and patent vitello-intestinal duct. It showed a well-formed uterus alongside the urinary bladder and extending into the right inguinal region.

All the features including morphologically male genitalia and testis with uterus (no vagina / no evident ovaries) suggestive of PMDS. Anti-mullerian hormone levels was done which below the normal level (1 .0 ng /ml normal level between 1.5 to 4.0 further supported our diagnosis. Karyotyping, Exploratory laparotomy/excision were planned for the patient subsequently. However the patient refused for further intervention.

DISCUSSION

PMDS is a rare form of internal male pseudohermaphroditism caused by a deficiency of MIF.[4,5] Derivatives of the Mullerian duct (i.e., fallopian tubes, uterus, and the upper part of the vagina) are present in a normal genotypically and phenotypically male. PMDS patients have normal development of external genitalia and secondary sexual characteristics.

PMDS are otherwise normally differentiated 46XY male. Embryologically, in a human fetus the Mullerian and Wolffian ducts are both present at 7 weeks of gestation. In a male fetus, the testis differentiates by the end of the 7th gestational week. Normal sex differentiation is controlled by testosterone, dihydrotestosterone, and MIF. Sertoli cells secrete MIF, which leads to regression of the Mullerian ducts. Testosterone has a direct effect on the Wolffian ducts, and promotes their differentiation into the epididymis, vas deferens, and seminal vesicles.[5] Dihydrotestosterone induces male differentiation of external genitalia. PMDS patients have both Wolffian and Mullerian duct structures due to a deficiency of MIF.[5] Anti-Mullerian hormone (AMH) secreted by the fetal Sertoli cells causes degeneration of the Mullerian ducts.[6-8] In cases of PMDS there is a defect in either AMH secretion or in the AMH receptor, which leads to a failure of normal regression of the Mullerian structures resulting in normal masculine virilisation with the presence of Mullerian derivates like a uterus or fallopian tubes.[6,9]

It is inherited as an autosomal recessive or X-linked recessive mutation of short arm of chromosome 19.[12] Exact pathogenesis is known in about 85% of cases. Type I PMDS (male type) (45%) is due to AMH deficiency and type II PMDS (female type) (40%) is due to receptor defects and in the remaining 15% the exact cause is unknown.[13]

Two anatomic variants of PMDS have been described, the male type and the female type. The most common variant is the male form, encountered in 80-90% of cases and characterized by unilateral cryptorchidism with a contralateral inguinal hernia. The male form of PMDS can be of two types. The first type is hernia uteri inguinalis, which is usually characterized by a descended testis and herniation of the ipsilateral corner of the uterus and the ipsilateral fallopian tube into

the inguinal canal.[5,10] The second type is crossed testicular ectopia, which is characterized by herniation of both testes and the entire uterus and both fallopian tubes.[5,10]

The second anatomic variant of PMDS, the female form, is 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.[5,11] The gonads are fixed within the pelvis.[10] The mobility of Mullerian structures is an important factor that determines the clinical presentation.[5,10] If the uterus and fallopian tubes are mobile, they may descend into the inguinal canal during testicular descent. On the other hand, if the Mullerian structures are relatively immobile, testicular descent may be impeded.[5,10]

Normal testicular descent is impeded by the close association of the testis and vasa to broad ligament. This mechanical effect of PMD structures prevents testicular descent or leads both testes to descend towards the same hemiscrotum.[12] As the androgen levels are normal, penile development is not affected and testicular histology is not affected apart from lesions due to UDT.[14] Awareness of this phenomenon is essential to avoid labeling these boys as vanishing testis syndrome.[12]

Overall incidence of testicular tumors in PMDS is about 18%, which is comparable to that of individuals with UDT.[13] There are no reports of malignancy arising from retained MD structures.[12]

In our case there was omphalitis with unilateral cryptorchidism and unambiguous male genitalia with normal penile length. However the Mullerian structures were mobile and were intra-abdominal without inguinal herniation. in view of the mobile Mullerian structures, it probably falls into the first category or the male type of PMDS. Considering the differentials, congenital adrenal hyperplasia (CAH) can present with the similar feature but with ambiguous genitalia which is more characteristic in female and in male often missed due lack of specific feature. In our case as the child is with the unilateral cryptorchidism and unambiguous male genitalia with normal penile length ruled out the diagnosis CAH.

Mixed gonadal dysgenesis (MGD) can be the other differential diagnosis. In MGD there is presence of ambiguous genitalia, unilateral testis, and contralateral streak gonad. In addition mullerian structures are normally present and gender assignment is female, with XO/XY mosaic karyotyping.[12] In contrast PMDS show normal virilisation of male external genitalia, 46XY karyotype and gonadal biopsy is suggestive of testis.

Management of child with PMDS requires multidisciplinary approach including parental counseling, medical and surgical management.

Optimal surgical management includes orchiopexy but the uterus and fallopian tube (if present) are left in place. Orchiectomy is indicated if testis cannot be brought into the scrotum. Careful identification of the vas deferens with meticulous dissection of the mullrian structures facilitate intra scrotal placement of the testis. However surgical management of the patients with PMDS is controversial because there is potential morbidity with either retention or removal of mullrian structures. Surgical excision of PMD structures may results in ischemic and/or traumatic damage to the vas deferens and testis. However the case of a boy with PMDS as like ours an uterine adenosarcoma raises question about the advisability of leaving mullrian structure in place.[15]

CONCLUSION

Awareness between the pediatrician and pediatric surgeon about the possible forms of PMDS helps to plan the proper line of management of this, which is encountered incidentally. Management is by simple scrotal orchidopexy with preservation of vascularity of testis. Risk of testicular tumor and infertility has to be addressed. Parents should be genetically counseled.

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