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Medical Journal

Breast Cancer

Awareness Month **OCTOBER**

Hysterectomy in a Male!

Rare Stigma of a Case of Persistent Mullerian Duct Syndrome

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BACKGROUND

Disorders of Sex Differentiation (DSD) are very important issues in clinical practice, particularly because of their rarity and difficulty pertaining to their diagnosis and management. Persistent Mullerian Duct Syndrome (PMDS) is a form of disorders of sex differentiation (DSD) caused by a defect in the Mullerian Inhibiting Substance (MIS) system. Patients are genotypically as well as phenotypically male but with the presence of Mullerian duct derivatives, this entity is often misdiagnosed due to lack of familiarity with the condition and requires a high index of suspicion on the operating surgeon's part for its diagnosis. We are reporting such a rare case of persistent Mullerian duct syndrome where late presentation in part of patient resulted in development of testicular malignancy.

CASE REPORT

A 26 year old male presented with abdominal pain and left scrotal swelling in our hospital. On general physical examination, patient had well - developed male facial features and male external genitalia. There was an abdominal mass, the upper limit of which was palpable just above pubic symphysis, and there was a swelling in the scrotum on the left side. But both testicles were found to be absent in scrotal sac. Abdominal USG showed a well-defined smooth large pelvic mass in infraumbilical region measuring 14 × 10.6 × 9.2 cm. CT abdomen with contrast showed a well-defined heterogeneously enhancing mass lesion in pelvis measuring 12.9 × 8.8 × 13.1 cm with few specks of calcifications. Thick pedicle-like attachment is seen extending from lesion to prostate and seminal vesicles. Left testicle could not be visualized in scrotum and inguinal region. FNAC from the abdominal mass reported as teratocarcinoma. These facts indicate a possibility of testicular malignancy from ectopic testicle for which a laparotomy was planned. During surgery, left testes were found to be atrophic and seen in left inguinal region, and the patient had uterus with fallopian tubes. There was 15 × 10 cm tumor occupying the position of right ovary, which was excised along with the uterus and adnexa *(Fig. 1)*. Histopathology report *(Fig. 2)* confirmed the mass as nonseminomatous germ cell tumor (yolk sac tumor) arising from testis. Postoperative tumor markers were made. Serum AFP was grossly elevated (17346 IU/ml), beta HCG was normal (<1.2 mIU/ml) and LDH was marginally increased (384 U/L). Patient received adjuvant chemotherapy with BEP (bleomycin, etoposide and cisplatin) regimen. A karyotype was conducted, and this revealed a 46XY variant *(Fig. 2)*.

Fig. 1 : Laparotomy picture showing uterus, fallopian tube, gonads and external genitalia

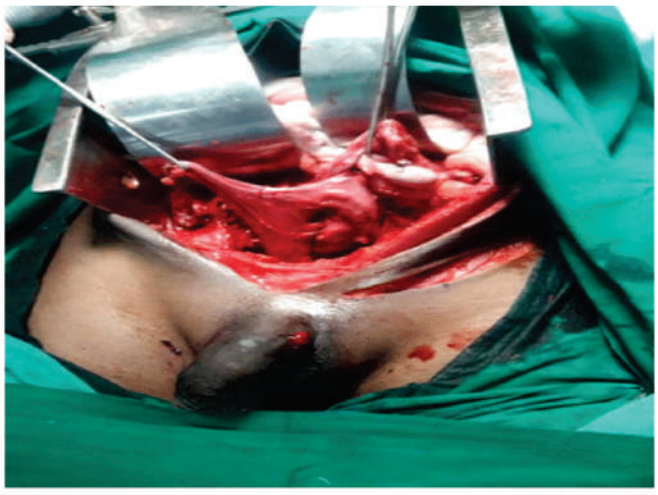
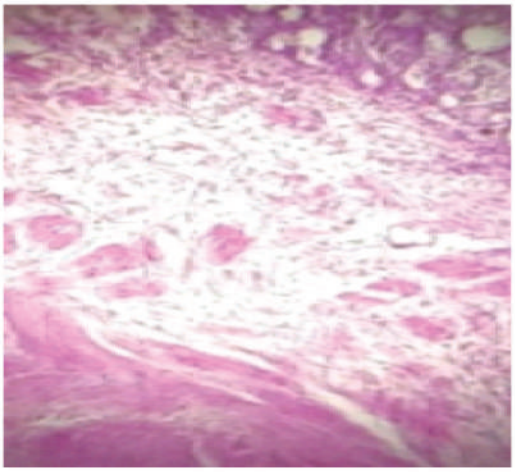


Fig. 2: Histopathology picture showing endometrium and myometrium of uterus



DISCUSSION

Persistent Mullerian duct syndrome (PMDS) is a rare form of male pseudohermaphrodite, in which Mullerian duct derivatives are present in a genotypic (46XY) and phenotypic male. The Mullerian remnants could be present in the form of well-developed or rudimentary uterus, cervix, vagina or fallopian tubes. As already discussed, it is a developmental disorder, the cause of which can be a deficiency of AMH or a defect in the AMH type II receptor (AMHR–II) resulting in persistence of Mullerian structures in a male. About 150 cases have been reported globally, whereas only 20 cases have been documented from Indian literature. Because there should be presence of both testicular and ovarian tissues in the same individual to recognize a case of true hermaphrodite, we cannot label our case as true hermaphrodite. This is owing to the fact that in our case both gonads were found to be histologically proven testicular tissue only. The serum testosterone level in our case was found to be 3.6 ng/ml which is within normal male range.

As far as other differential diagnosis are concerned, Swyer's syndrome and testicular feminization syndrome can be considered for a case of XY pseudohermaphrodite. In case of Swyer's syndrome, there are streak gonads, with the presence of Mullerian structures. However, in contrast to persistent Mullerian duct syndrome (PMDS) external genitalia for these cases represent female phenotypic variety.

These patients generally present in adolescence with delayed puberty and amenorrhea due to the fact that the gonads have no hormonal or reproductive potential.

Similarly, although the karyotype for testicular feminization syndrome is XY type with the presence of normal male range serum testosterone level, these patients are characterized by the absence of uterus and other Mullerian structures due to the effect of Mullerian inhibiting substance secreted normally from Sertoli cells of testes, and again these patients are phenotypically females.

According to the position of the testes and uterus, these patients can be grouped into following three categories: (1) In 60 - 70% of patients, the bilateral testes and epididymis are connected to the fallopian tubes in the abdomen, the bilateral testes are in analogue positions to the ovaries and their inguinal sacs remain empty (the female type); (2) in 20 - 30% of patients, there is a presence of a testes in the hernia sac, or a scrotal testis with a contra lateral testis located in the abdomen (the uteri inguinale type); and (3) in~10% of patients, the two testes are present in the same hernia sac along with the uterus and uterine tubes (the transverse testicular ectopia).

Familial cases of persistent Mullerian duct syndrome (PMDS) have been reported and are associated with autosomal recessive mode of inheritance. Presentations may vary and include undescended testes, inguinal hernia or infertility. Very rarely as in our case patient may present with tumor arising from the ectopic gonads. Sometimes, the diagnosis is made incidentally during surgical exploration for cryptorchidism or herniorrhaphy. Gonadal biopsy should be performed to rule out the possibility of any malignancy.

These patients seem to have a slightly higher potential for gonadal malignancies like seminoma and dysgerminoma. The risk is more in the 46 XY genotype and under masculinization. In our case, the patient was unfortunate in the fact that he presented late for bilateral undescended testes culminating in development of nonseminomatous germ cell tumor (yolk sac tumor) of testicular origin.

Ultrasound, MRI and laparoscopy may be helpful in diagnosing patients with DSD and in the planning of corrective surgery.

Management of these cases must be individualized. If malignant transformation has already occurred, along with surgical removal of the testes, adjuvant radiation therapy and/or chemotherapy must be a part of management. The overall incidence of malignant transformation is 15%. Patients presenting with cryptorchidism can have a better future fertility if they can be managed before puberty. Treatment of the remnants of Mullerian duct remains controversial. Although previous studies have demonstrated that children with PMDS require removal of Mullerian duct remnants due to malignant tumors identified in Müllerian remnants and the Mullerian duct being connected with the seminal vesicle causing urinary tract infections, periodic hematuria, stones and urination disorders. Some other studies refute this fact have suggested to retain Müllerian remnants for preventing damage to the vas deferens and disruption of collateral blood supply to the testes. However, in our case the patient was already developed with malignancy which was infiltrating into the serosal surface of uterus, thus forcing us to remove the gonads as well as Mullerian remnants.

CONCLUSION

Persistent Mullerian duct syndrome (PMDS) has an autosomal recessive inheritance. Screening of siblings and second-degree relatives is necessary. Early presentation and early diagnosis are the cornerstone in the management of these cases. On the other hand, late presentations can have various detrimental effects starting from problems of infertility to development of malignancy. Management may vary from individual to individual basis. Those patients presenting before puberty can be managed with a better outcome.

- Compliance with Ethical Standards.
- Conflict of interest.
- All authors declare that they have no conflict of interest.
- Human and Animals Rights.
- All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 1975 Declaration of Helsinki, as revised in 2008.
- Informed Consent.
- Informed consent was obtained from the patients before publication of this case report.

2018 Nobel Prize in Medicine Awarded to Two Cancer Immunotherapy Researchers


James P.Allison


Tasuku Honjo

The Nobel Prize in Physiology or Medicine was awarded on 1st October 2018 to James P. Allison, Professor of the University of Texas, MD Anderson Cancer Center, Houston of the United States and Tasuku Honjo, Professor of Kyoto University of Japan for their work on a protein called CTLA - 4 that inhibits a person's immune system by putting the brakes on the actions of Tumor cells. They realized that if we could release that "brake," the immune system would wreak havoc on tumors.. Their success has brought immunotherapy out from decades of skepticism.

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