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A Rare Case of Presence of Persistent Mullerian Duct Syndrome in Mixed Non Seminomatous Germ Cell Tumour of Testis

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Abstract: ***Background: Persistent Mullerian duct syndrome (PMDS) is a rare form of internal male pseudohermaphroditism, in which Mullerian duct derivatives (uterus and fallopiantubes) are present in a genotypic (46XY) and phenotypic male. Case Report: A case of 35 – year old male patient presenting with testicular mass along with incidental finding of Persistent Mullerian duct syndrome. The testicular mass turned out to be mixed non seminomatous germ cell tumour comprising post pubertal teratoma and post pubertal Yolk sac tumour of left testis. The other testis (right sided) was dragged to left inguinal region along with mullerian duct remnants appearing as left inguinal hernia. Operative procedure was performed and both the testis along with spermatic cord and persistent Mullerian structures were removed. Conclusion: Though rare, every surgeon operating upon testicular mass with 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 Mullerian duct syndrome, Inguinal hernia, cryptorchidism, non seminomatous germ cell tumour, Mullerian inhibiting substance

1. Introduction

Persistent Mullerian duct syndrome (PMDS) is a rare form of internal male pseudohermaphroditism, in which Mullerian duct derivatives (uterus and fallopian tubes) are present in a genotypic (46XY) and phenotypic male.[1] The syndrome is caused by absence of anti-Mullerian hormone or defective functioning of anti-Mullerian hormone type II receptors.[2] It is familial, probably with a sex-linked autosomal recessive or X-linked recessive inheritance.[3]

2. Case Report

A 35-year old healthy male patient, a father of 2 children, with normal male external genitalia and secondary sexual characteristics presented with left testicular mass noticed since 3 months. On examination he had well-developed left hemiscrotum and palpable testicular mass with irreducible inguinal hernia. His right-sided hemiscrotum was underdeveloped and empty. Local part USG suggested "Large lobulated heterogenous hypoechoic mass" completely involving left testis with internal vascularity and cystic changes suggesting possibility of Testicular mass along with absent right testis locally. Patient was operated for left testicular mass along with exploratory laprotomy for left inguinal hernia. On exploring the left inguinal region, the sac consisted of thick cord like structure adjacent to spermatic cord attached to upper pole of testicular mass along with right undescended testis.

On gross examination of orchidectomy specimen, it measured 15 x 10 x 8 cm in size. Outer surface was partly capsulated and showed capsular breach at base. The spermatic cord was 6 cm long. Cut surface of testicular mass which measured 9 x 9 x 7 cm, was brownish with hemorrhage, necrosis and cystic degeneration (fig 1). Another thick cord like structure adjacent to spermatic cord, attached to upper pole of testicular mass was measuring 6 x 3 cm. Cut surface of this structure showed a slit like lumen. (fig 2) Thick vessels were also adherent to it. Also received a specimen of right undescended testis measuring 2 x 1.5 cm.

Figure 1: Cut surface of testicular mass – brownish with hemorrhage, necrosis and cystic degeneration

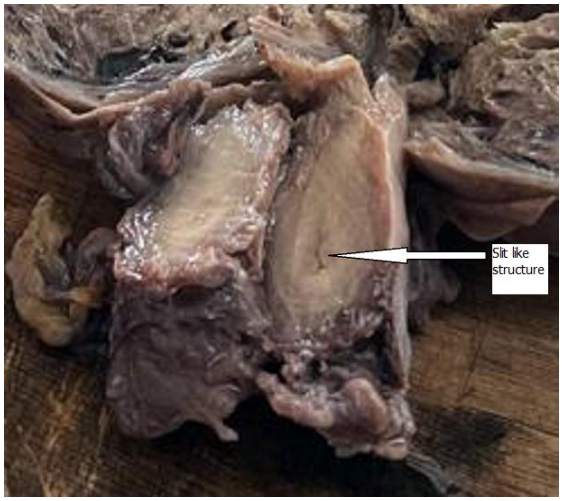

Figure 2: Cut surface of thick cord like structure- showing slit like structure

On microscopic examination, sections from large testicular mass showed histological features of mixed non seminomatous germ cell tumour comprising post pubertal teratoma and post pubertal yolk sac tumour (Fig 3). There were large areas of necrosis and heamorrhage. The teratoma component comprised predominantly of undifferentiated adenocarcinoma (Fig 4). The epididymis and spermatic cord were free of tumour with normal histology. Sections from undescended testis showed atrophic hyalinized tubules and tubules with sertoli cells only without any sign of spermatogenesis. Sections from thick cord like structure adjacent to spermatic cord adherent to upper pole of testicular mass showed endometrial lining and stroma (persistent uterus) (Fig 5). There was no infiltration by tumour. Fig 6 shows microscopy of undescended testis with atrophic hyalinized tubules along with gross of right undescended testis.

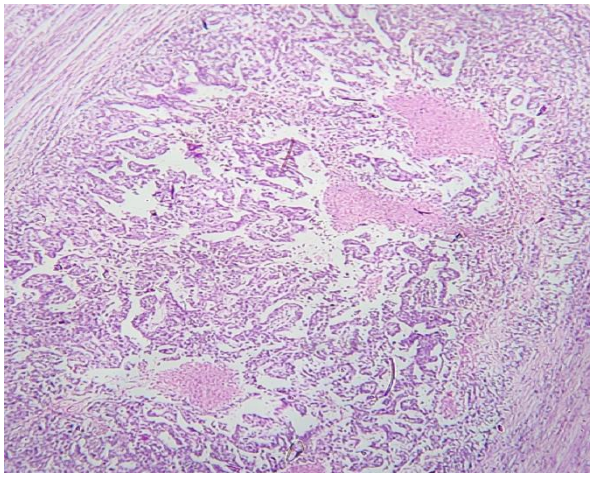

Figure 3: Component of post pubertal Yolk sac tumour

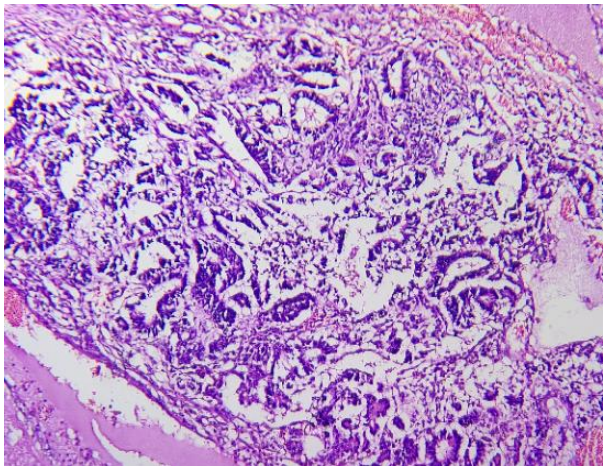

Figure 4: Component of post pubertal teratoma Composed of undifferentiated adenocarcinoma

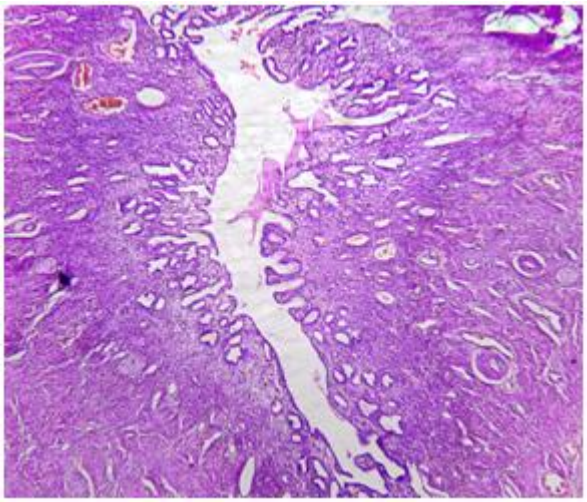

Figure 5: Endometrial lining and stroma

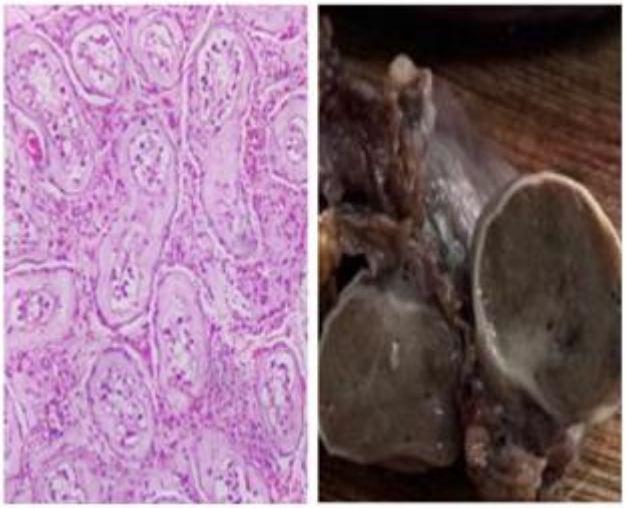

Figure 6: Microscopy of undescended testis showed atrophic hyalinized tubules along with gross of right undescended testis

Final histopathological diagnosis was consistent with **Mixed post pubertal teratoma with yolk sac tumour of left testis in a case of Persistent Mullerian Duct Syndrome with undescended right sided testis.** Additionally, right sided undescended testis present in left inguinal canal was found to be atrophic with complete arrest of spermatogenesis.

Later on, Karyotyping was done by G-Banding technique of peripheral blood which revealed normal male karyotype i.e. 46XY.

3. Discussion

In true hermaphrodites, both ovarian and testicular tissue is present in one or both gonads [4]. As stated by Stern ON et al, in pseudo-hermaphrodite females, although the gonads are ovaries, male tendencies are seen in the organ of reproduction [5]. Conversely, in male pseudo-hermaphroditism, the gonads are testes but the external genitalia are not completely virilized. Michiels et al have stated that it is possible for pseudo-hermaphroditism to be undetected until puberty [6]. Persistent Mullerian Duct Syndrome is a rare form of internal male pseudo-hermaphroditism in which Mullerian duct derivatives are seen in men. It was first described by Nilson in 1939 [7]. A familial association has been found in some cases as seen in the case published by Prakash N et al [8]. The exact cause of PMDS is not known, however it is thought to result from a defect of the synthesis or release of MIF, or from defects in the MIF receptor that may lead to the persistence of uterus and fallopian tube in males. It is likely that remnant Mullerian structures lead to cryptorchidism by hindering the normal testicular descent mechanism [8]. Derivatives of the Mullerian duct, that is, the fallopiantubes, uterus and the upper part of the vagina, are present in a normal genotypically and phenotypically male individual. Patients with PMDS usually have normal development of external genitalia and secondary sexual characteristics [10] As described by Renu Det al, there are two anatomic variants of PMDS: male and female. The male form is encountered in 80% to 90% of cases, characterized by unilateral cryptorchidism with contralateral inguinal hernia, and can be one of two types: the first type is hernia uteri inguinalis, which is characterized by one descended testis and herniation of the ipsilateral corner of uterus and fallopian tube into the inguinal canal. The second type is crossed testicular ectopia, which is characterized by herniation of both testes and the entire uterus with both fallopian tubes [10]. The female form, seen in 10% to 20% of cases, is characterized by bilateral cryptorchidism. The gonads are fixed within the pelvis, with the testes fixed within the round ligament in the ovarian position with respect to the uterus [10]. PMDS is usually coincidently detected during surgical operation, as in our patient's case. However pre-operative ultrasonography, computerized tomography and MRI allow possible pre-operative diagnosis [9].

The differentiating factor in the current case is that this patient presented primarily with testicular mass which showed features of mixed non seminomatous germ cell tumour and presence of persistent Mullerian duct syndrome was an incidental finding. No such case of testicular tumour in properly descended testis along with associated PMDS has been noted till now. So there is no direct association of PMDS with testicular tumour in our case. However, every surgeon operating upon testicular mass with inguinal hernia or undescended testes needs to know about the possibility of presence of the uterus in a phenotypic male patient at any age. High degree of suspicion and awareness is needed to diagnose this condition. There have been case reports of embryonal carcinoma, seminoma, yolk sac tumor and teratoma in patients with PMDS, whereas tumors of the Mullerian duct derivatives are very rare [8, 10]. Though a case of clear cell adenocarcinoma has been reported in a patient who had persistent Mullerian duct structures in mullerian duct syndrome, these tumours may derive from mesothelium by the process of Mullerian neo metaplasia, from Mullerian remnants or from mucinous epithelium of teratoma (11). So, early treatment is needed to maintain fertility and to prevent the occurrence of malignancy in remnant müllerian structures [12].

As described by Yuskel Bet al, the prognosis of PMDS depends upon the integrity of the testicular tissue and successful correction of cryptorchidism, which is often complicated by the close anatomical relationship between the vas deferens and the Mullerian derivatives [9].The risk of malignancy in an ectopic testis in a case of PMDS is similar to that in a healthy male, with the incidence being 15%. [10].

4. Conclusion

PMDS is a rare form of male pseudo-hermaphroditism, the patient is usually assigned to the male sex at birth without hesitation but may have unilateral or bilateral cryptorchidism. Since patients are phenotypically male, the diagnosis is usually not suspected until surgery is performed for cryptorchidism or hernia repair. Hernia uteri inguinalis is type I of the male form of PMDS and in order to prevent further complications such as infertility and malignant change, the surgeon should be aware of PMDS while dealing with patients who present with unilateral orbilateral cryptorchidism.

Thus, in cases of unilateral or bilateral cryptorchidism associated with hernia, the possibility of PMDS should be kept in mind.

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