Persistent Mullerian duct syndrome with testicular seminoma: A report of two cases

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ABSTRACT

Persistent Mullerian duct syndrome is a rare form of male pseudohermaphroditism, characterized by the presence of the Mullerian duct structures in an otherwise phenotypically as well as genotypically normal male. We report two cases of males with cryptorchidism, and seminoma in the undescended abdominal testis along with Mullerian duct derivatives (uterus and fallopian tube).

Key words: Cryptorchidism, Mullerian inhibiting factor, persistent Mullerian duct syndrome

INTRODUCTION

Persistent Mullerian duct syndrome (PDMS) is a rare form of male pseudohermaphroditism with the presence of Mullerian duct derivatives in an otherwise phenotypical male.¹ These patients have unilateral or bilateral cryptorchidism and are genetically 46XY. PMDS results from the failure of synthesis or release of Mullerian inhibiting factor (MIF), the failure of end organ to respond to MIF, or a defect in timing of the release of MIF.

CASE REPORTS

Case 1
A 25-year-old male, from the farming community, presented with a lump in the abdomen since 3 years, which was gradually increasing in size but with a rapid increase in size since 4 months. The patient was married with two children and there was no history of erectile dysfunction. Clinical examination showed fullness of abdomen in umbilical, right iliac, and left lumbar regions, both the testes were absent in the scrotum. An ultrasound examination revealed a large mixed echogenic mass measuring 15 × 10 cm located in the right side of the pelvis. The clinical diagnosis was a tumor in the undescended abdominal testis. Serum levels of human chorionic gonadotropin and alpha-fetoprotein were normal.

Per-operatively there was a large mass in the right side of the pelvis adherent to the pelvic organs along with a rudimentary uterus and one side gonad. The specimens were sent to the department of Pathology.

Gross examination showed a rudimentary uterus of size 6 × 2 × 1 cm with one side gonad of 2.5 × 1.5 cm, which was gray brown and soft to cut, along with two tubular structures. The other side mass was 17 × 13 × 5 cm, cut section of which revealed a tumor that was predominantly solid with dark brown and gray white areas [Figure 1].

Microscopic examination of the uterus showed well-developed endocervical tissue with thinned out ectocervix, endometrial glands in primitive stroma, and normal myometrial tissue. The gonad with two tubular structures showed histologic picture of a prepubertal testis with no spermatogenesis, a fallopian tube, and epididymis.

The tumor was composed of groups of cells with clear cytoplasm, centrally placed hyperchromatic nucleus, and prominent nucleoli. These groups of cells were separated by thin fibrous septae with lymphocytic infiltrates and also large areas of necrosis. Focal areas showed syncytiotrophoblast type of giant cells. The histologic picture was that of a
classical seminoma [Figure 1]. Internal iliac lymph nodes and omentum showed secondary deposits.

**Case 2**

A 35-year-old male presented with a lump in the abdomen since 6 months. The patient was married with two children. Clinical examination revealed a left-sided abdominal mass, and the scrotal sacs were empty.

Per-operatively a tumor was present in the retroperitoneum adherent to the posterior wall. Uterus and fallopian tubes were identified. Paraortic lymph nodes were also seen. Gross examination showed a specimen of uterus with cervix of size 8 × 4 × 3 cm with bilateral masses. Left mass was 11 × 9 × 8 cm with an attached tube-like structure and a smaller gray brown mass of size 2 × 1 cm. The cut section of the large mass was gray white with necrotic areas. The right side mass was 3 × 3 × 2 cm gray brown in color, lobulated, and resembled testicular tissue. The attached smaller mass was gray brown of size 1.5 cm. Microscopic examination revealed a primitive uterus with well-formed endocervical glands, thinned out ectocervix, atrophic endometrium, and myometrium [Figure 2].

The left side mass showed the picture of a classical seminoma with necrosis and infiltration into the smaller mass attached to it, which had a microscopic appearance of both epididymis and fallopian tube side by side. The right side mass showed a prepubertal testis with no spermatogenesis but with Leydig cell hyperplasia [Figure 3]. Attached to this mass was the other epididymis.

**DISCUSSION**

PMDS is a rare form of male pseudohermaphroditism. It is an intersex condition in a 46XY phenotypic male characterized by persistent Mullerian duct structures and a cryptorchid testis or testes. It may be discovered in infants, children, or adults. PMDS is thought to result from the synthesis or release of MIF or from the MIF receptor defect. The MIF gene has been located to the short arm of chromosome 19. MIF released from the sertoli cells of the fetal testis from 7 weeks of gestation onward is responsible for the regression of Mullerian duct. The defect of MIF gene leads to persistence of the uterus and fallopian tube in the male. It is likely that these remnant Mullerian structures produce cryptorchidism by hindering the normal testicular descent mechanism. Two clinical variants of PMDS are described: hernia uteri inguinalis and transverse testicular ectopia. In the more common hernia uteri inguinalis, there is unilateral cryptorchidism and contralateral inguinal hernial sac with uterus. In transverse testicular ectopia both the testes are located on one inguinal side and the opposite inguinal canal and scrotum are empty. Similar to other undescended testes, the gonads of these patients are at an increased risk for malignant transformation. Embryonal carcinoma, seminoma, yolk sac tumor, and
teratomas have been seen in patients having PMDS.\[1\] The overall incidence of malignant change is 15%.\[2\] In both our cases, a testicular seminoma was found unilaterally with the other testis showing no neoplasm or spermatogenesis. Infertility is common in PMDS; however, there have been a few reported cases of fertility. In both our cases the patients fathered two children. However, chromosomal analysis or DNA studies were not done. The possible explanation could be that there was spermatogenesis in the gonads probably before the initialization of the tumor.

The main therapeutic importance in identifying PMDS is the potential for fertility and prevention of malignant change. Surgical management for preserving fertility is orchiopexy for repositioning of testis into the scrotum, herniorrhaphy with hysterectomy, and bilateral salpingectomy. Vas deferens is retained to preserve fertility. Orchidectomy is indicated for testes that cannot be mobilized or have undergone malignant change.\[5\] The management of seminoma depends on the clinical stage and status of lymph nodes with two lines of treatment: (1) surgery to remove the tumor, with or without radiation therapy to lymph nodes in the abdomen after the surgery, with lifelong follow-up or (2) surgery to remove the tumor, followed by chemotherapy and lifelong follow-up. To conclude, clinicians and pathologists should be aware of this entity of PMDS, when handling cryptorchidism. This would help to prevent complications, such as malignancy and infertility.

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