RESEARCH PAPER

Persistent Müllerian Duct Syndrome Presenting with Residual Yolk Sac Tumor in Bilateral Undescended Testes: A Rare Case Report

Dr. Divya Karunanithi[1], Dr. Manivannan Rajarathinam[2*], Dr. Kambala Prasanna Kumar[3], Dr. Keshavarajan Gandhirajan[4]

[1] Final Year Postgraduate, Department of General Surgery, Sree Balaji Medical College and Hospital, Tamil Nadu, India; Bharath Institute of Higher Education and Research, India. Email: divya.k6789@gmail.com

[2*] Professor, Department of General Surgery, Sree Balaji Medical College and Hospital, Chennai, India; Bharath Institute of Higher Education and Research, India (Corresponding Author). Email: rjmanivannan64@yahoo.com

[3] Assistant Professor, Department of General Surgery, Sree Balaji Medical College and Hospital, Chennai, India; Bharath Institute of Higher Education and Research, India. Email: drprasannakumarkambala@gmail.com

[4] Consultant Surgical Oncologist, Department of Surgical Oncology, Rela Institute and Medical Centre, Chennai, India. Email: keshav_141@yahoo.co.in

ABSTRACT

Background

Persistent Müllerian duct syndrome (PMDS) is a rare disorder of sexual development characterized by the presence of Müllerian duct derivatives in phenotypically normal males. It results from defects in anti-Müllerian hormone signaling and is commonly associated with cryptorchidism. The occurrence of malignant germ cell tumors in PMDS is uncommon, particularly non-seminomatous tumors in adults.

Case Presentation

A 21-year-old male presented with a progressively enlarging lower abdominal mass and bilateral empty scrotum. Imaging revealed a pelvic mass suggestive of intra-abdominal testicular tumor. Following neoadjuvant chemotherapy, exploratory laparotomy demonstrated a large pelvic tumor (17 × 8 × 5 cm) located between bilateral undescended testes, along with well-formed Müllerian structures including a uterus (6.5 cm) and fallopian tubes. Histopathological examination revealed a residual malignant germ cell tumor with predominant yolk sac tumor component, showing microcystic architecture and Schiller–Duval bodies. Both testes showed features of atrophy with Sertoli cell predominance. Retroperitoneal lymph nodes were reactive without metastasis.

Conclusion

This case highlights a rare presentation of PMDS associated with bilateral cryptorchidism and yolk sac tumor in an adult. Delayed diagnosis of undescended testes significantly increases the risk of malignant transformation. Early recognition and surgical management are essential to prevent complications. Histopathological evaluation remains crucial for definitive diagnosis.

Keywords: Persistent Müllerian duct syndrome; Cryptorchidism; Yolk sac tumor; Germ cell tumor; Disorders of sexual development; Testicular neoplasms; Anti-Müllerian hormone

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Introduction

Persistent Müllerian duct syndrome (PMDS) is a rare disorder of sexual development characterized by the persistence of Müllerian duct derivatives, including the uterus and fallopian tubes, in phenotypically normal males with a 46,XY karyotype [1]. Despite the presence of these internal female reproductive structures, affected individuals typically exhibit normal male external genitalia and secondary sexual characteristics. This paradoxical presentation often leads to delayed diagnosis, with the condition being identified incidentally during surgical procedures.

The underlying pathophysiology of PMDS involves abnormalities in anti-Müllerian hormone (AMH) signaling during embryogenesis [2]. AMH, secreted by Sertoli cells of the fetal testes, is responsible for regression of the Müllerian ducts during the seventh week of gestation. When AMH production is deficient

or when Müllerian duct tissues are insensitive to its action due to receptor defects, these structures persist. Consequently, organs such as the uterus, fallopian tubes, and upper vagina remain alongside normally developed male reproductive organs.

Importantly, androgen production by Leydig cells remains unaffected in PMDS, allowing normal differentiation of Wolffian duct derivatives, including the epididymis, vas deferens, and seminal vesicles [3]. This preservation of androgen function explains the normal male phenotype observed in affected individuals. As a result, PMDS often remains clinically silent and is typically discovered during evaluation for associated conditions such as cryptorchidism or infertility.

The true prevalence of PMDS is not well established due to its rarity and asymptomatic nature, but it is considered an uncommon clinical entity [4]. Most cases are identified incidentally during surgical exploration for undescended testes or inguinal hernia. Cryptorchidism is the most frequent clinical finding in PMDS and is present in the majority of patients. The testes may be located intra-abdominally or within the inguinal canal and are often associated with Müllerian remnants, which can complicate surgical management. Two anatomical variants of PMDS have been described. The more common “male type” involves unilateral cryptorchidism with the contralateral testis descended, often associated with an inguinal hernia containing Müllerian structures. The less common “female type” is characterized by bilateral undescended testes with Müllerian structures located in the pelvis [5]. This variant is clinically significant due to prolonged intra-abdominal retention of both testes, which increases the risk of infertility and malignant transformation.

Cryptorchidism is a well-established risk factor for testicular malignancy. Undescended testes are exposed to higher intra-abdominal temperatures, which impair germ cell maturation and predispose to neoplastic transformation [6]. The risk of testicular cancer is significantly higher in individuals with cryptorchidism compared to those with normally descended testes. Germ cell tumors are the most common malignancies associated with this condition, with seminoma being the most frequently reported subtype. However, non-seminomatous germ cell tumors are less commonly encountered in adults.

Yolk sac tumors, also known as endodermal sinus tumors, are aggressive malignant germ cell tumors that are more commonly seen in children but rarely occur in adults [7]. These tumors demonstrate diverse histological patterns, with Schiller–Duval bodies representing a characteristic diagnostic feature. They are associated with elevated serum alpha-fetoprotein levels and exhibit aggressive biological behavior. The occurrence of yolk sac tumor in association with PMDS is exceedingly rare, particularly in adult patients, making such cases noteworthy.

The coexistence of PMDS and malignant germ cell tumors presents diagnostic and therapeutic challenges. The presence of Müllerian structures may alter anatomical relationships, complicating surgical intervention. Additionally, delayed diagnosis due to the asymptomatic nature of PMDS increases the likelihood of malignancy at presentation. Therefore, careful evaluation is essential in patients presenting with undescended testes, especially when associated with abdominal or pelvic masses.

In the present case, a young adult male presented with a pelvic mass and bilateral undescended testes. Surgical findings revealed a tumor located between the testes along with structures resembling a uterus and fallopian tubes. Histopathological examination confirmed a malignant germ cell tumor with predominant yolk sac tumor component, along with testicular atrophy and persistent Müllerian duct derivatives . These findings are consistent with PMDS complicated by malignant transformation.

Although PMDS has been reported in the literature, its association with yolk sac tumor in adults remains extremely uncommon [8]. Most reported malignancies in PMDS involve seminomas or mixed germ cell tumors, with only limited documentation of yolk sac tumors. This highlights the importance of reporting such rare presentations to enhance understanding and guide clinical management.

In conclusion, PMDS is a rare developmental anomaly with significant clinical implications, particularly when associated with cryptorchidism and malignancy. Early diagnosis and timely management are essential to reduce the risk of infertility and malignant transformation. This case underscores the importance of considering disorders of sexual development in patients presenting with undescended testes and pelvic masses.

CASE REPORT

A 21-year-old male presented with complaints of a progressively increasing lower abdominal mass associated with a sense of fullness. There was no history of acute abdominal pain, vomiting, bowel disturbances, or urinary symptoms. The patient had no significant past medical or surgical history. Notably, there was a history of absent testes in the scrotum since

childhood, suggestive of bilateral cryptorchidism, for which no prior intervention had been undertaken.

On general physical examination, the patient was phenotypically male with well-developed secondary sexual characteristics. Local examination of the genitalia revealed an empty scrotum bilaterally. Abdominal examination demonstrated a palpable firm mass in the lower abdomen/pelvic region, non-tender, with limited mobility. No inguinal hernia was detected. Radiological evaluation (ultrasonography and cross-sectional imaging) revealed a heterogeneous pelvic mass with associated structures suggestive of undescended testes. Based on clinical and imaging findings, a provisional diagnosis of intra-abdominal testicular tumor arising in undescended testes was considered. The patient received neoadjuvant chemotherapy prior to surgical intervention due to suspicion of malignancy.

The patient subsequently underwent exploratory laparotomy. Intraoperatively, a large pelvic mass was identified between two intra-abdominal testes. The mass was adherent to surrounding structures and was associated with well-formed tubular structures resembling a uterus and fallopian tubes. Both testes were undescended and located in close proximity to the tumor. Complete excision of the pelvic mass along with bilateral testes, attached Müllerian structures, spermatic cords, and regional lymph nodes was performed.

Gross Findings

The excised specimen consisted of a pelvic mass with attached vascular structures, measuring approximately 17 × 8 × 5 cm . The external surface appeared grey-yellow with friable areas. Two vascular pedicles measuring 9.8 cm and 8.5 cm in length were identified. Two spermatic cords measuring 1.5 cm and 2 cm were also noted.

On cut section, two testes were identified within the specimen, measuring 4 × 2.5 × 2 cm and 3 × 2.5 × 1.5 cm respectively. A grey-yellow necrotic tumor measuring approximately 4.5 × 4 × 4 cm was present between the testes. The tumor showed areas of friability and necrosis.

A uterus measuring 6.5 cm in length was identified attached superior to the tumor, along with bilateral fallopian tubes measuring approximately 3.5 cm and 1 cm. The specimen also included epididymis and spermatic cord structures.

Multiple lymph node specimens from para-aortic, inter-aortocaval, and paracaval regions were received, with the largest node measuring 2 × 1 × 1 cm.

Microscopic Findings

Testicular Tissue

Histological examination of both testes revealed seminiferous tubules lined predominantly by Sertoli cells with thickened and hyalinized basement membranes. Several tubules showed intraluminal calcification. The interstitium demonstrated Leydig cell hyperplasia and congested blood vessels, consistent with testicular atrophy secondary to long-standing cryptorchidism .

Tumor

Multiple sections from the tumor showed a malignant neoplasm arranged in sheets, nests, loose reticular, and microcystic patterns enclosing basophilic mucoid material. Tumor cells were polygonal with moderate eosinophilic to clear cytoplasm, pleomorphic hyperchromatic nuclei, and prominent nucleoli. Increased mitotic activity was observed.

Characteristic Schiller–Duval bodies were identified in focal areas, confirming the diagnosis of yolk sac tumor. Extensive areas of necrosis, hyalinization, lymphocytic infiltration, foamy histiocytes, plasma cells, and hemosiderin-laden macrophages were noted, indicating post-chemotherapy changes. Lymphovascular emboli were also identified.

Müllerian Structures

Sections from the uterus revealed well-formed endometrial glands within oedematous stroma and normal myometrial smooth muscle bundles. Fallopian tubes showed attenuated mucosal folds lined by ciliated columnar epithelium, confirming persistent Müllerian duct derivatives.

Other Structures

The epididymis, spermatic cords, and vascular structures showed normal histology.

Lymph Nodes

Examination of para-aortic and inter-aortocaval lymph nodes demonstrated reactive hyperplasia with sinus histiocytosis, with no evidence of metastatic tumor involvement.

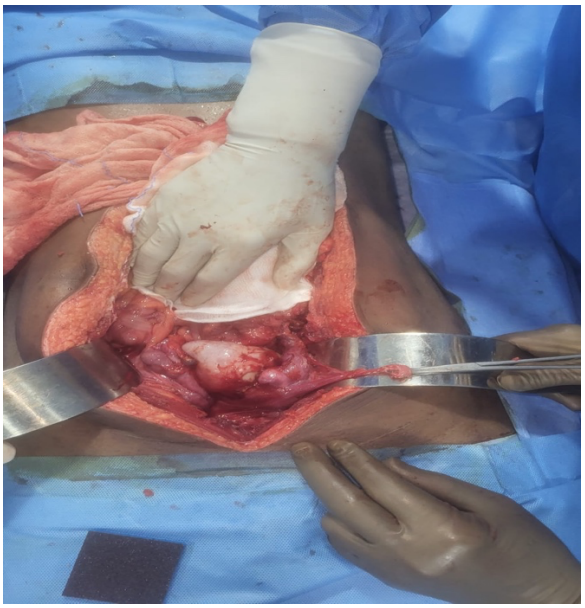

Fig 1 :Intraoperative view of pelvic mass between bilateral undescended testes

Intraoperative photograph showing a large lobulated pelvic mass located between two intra-abdominal undescended testes. The tumor appears solid with areas of hemorrhage and necrosis. Adjacent tubular structures suggestive of Müllerian derivatives are noted.

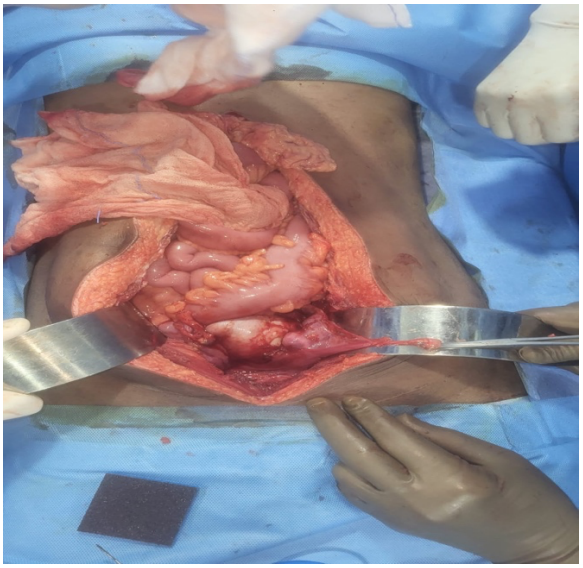

Fig 2 : Intraoperative identification of persistent Müllerian duct structures

Intraoperative image demonstrating a well-formed uterus-like structure with attached tubular components resembling fallopian tubes in a phenotypic male, confirming persistent Müllerian duct derivatives.

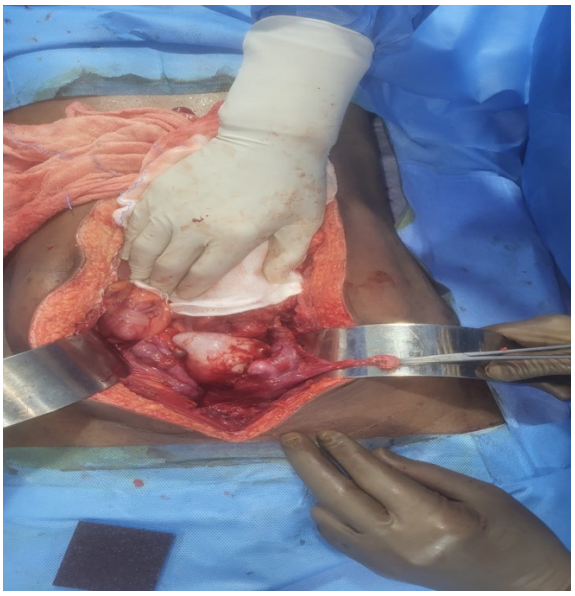

Fig 3 : Close-up view of tumor with adjacent undescended testicular tissue

Closer intraoperative view showing the pelvic tumor in relation to adjacent undescended testis. The mass appears irregular with necrotic areas, consistent with malignant germ cell tumor.

Final Diagnosis

Histopathological examination of the post-neoadjuvant chemotherapy pelvic mass excision specimen revealed a residual malignant germ cell tumor with predominant yolk sac tumor component, characterized by microcystic and reticular architectural patterns with identification of Schiller–Duval bodies, along with areas of necrosis, hyalinization, and inflammatory infiltrate consistent with post-chemotherapy changes. Foci of lymphovascular invasion were also identified.

Both testes were undescended and demonstrated features of testicular atrophy, including seminiferous tubules lined predominantly by Sertoli cells, thickened and hyalinized basement membranes, intraluminal calcification, and interstitial Leydig cell prominence.

Sections from the attached structures showed well-formed Müllerian duct derivatives, including a uterus with normal endometrial glands and myometrium, and fallopian tubes lined by ciliated columnar epithelium with attenuated mucosal folds, consistent with persistent Müllerian duct syndrome.

Examination of para-aortic and inter-aortocaval lymph nodes showed reactive hyperplasia with sinus histiocytosis, with no evidence of metastatic involvement.

Overall, the findings are diagnostic of persistent Müllerian duct syndrome associated with bilateral cryptorchidism and residual yolk sac tumor following neoadjuvant chemotherapy, without nodal metastasis.

Discussion

Persistent Müllerian duct syndrome (PMDS) is an exceptionally rare disorder, with fewer than 300 cases reported globally. Population-level data summarized by the Centers for Disease Control and Prevention indicate that congenital anomalies of the reproductive system contribute to a small but significant proportion of developmental disorders, often remaining undetected due to subtle presentation [8]. PMDS exemplifies this, as affected individuals typically present with normal male phenotype, leading to delayed diagnosis.

Anatomical variation plays a key role in clinical presentation. Telli O et al. described transverse testicular ectopia with PMDS, where both testes were located on one side, and reported testicular sizes of approximately 3–4 cm, with associated Müllerian remnants identified intraoperatively [9]. In contrast, our case demonstrated bilateral intra-abdominal testes measuring 4 × 2.5 × 2 cm and 3 × 2.5 × 1.5 cm, both reduced in size, indicating significant atrophy. Unlike the unilateral ectopia described by Telli et al., our case represents the female-type variant, which is less common but carries a higher oncogenic risk due to bilateral cryptorchidism.

Radiological findings described by Renu D et al. highlighted that Müllerian structures in PMDS are often small and may measure 2–4 cm, frequently missed on imaging [10]. In comparison, our case demonstrated a well-developed uterus measuring 6.5 cm and fallopian tubes measuring 3.5 cm and 1 cm, indicating more pronounced persistence of Müllerian derivatives. Additionally, the pelvic mass in our patient measured 17 × 8 × 5 cm, which is considerably larger than the 3–10 cm range typically reported for intra-abdominal testicular tumors, suggesting delayed clinical presentation.

At the molecular level, Nathalie Josso et al. reported that AMH or AMHR2 mutations result in complete or partial failure of Müllerian duct regression, with persistence of fully formed structures in severe cases [11]. The presence of a structurally normal uterus and fallopian tubes in our case suggests a complete defect in AMH signaling, consistent with severe phenotypic expression.

Complex associations of PMDS have been described in literature. Rehman et al. reported a rare combination of PMDS with transverse testicular ectopia and mosaic Klinefelter syndrome, where testicular volumes were markedly reduced and infertility was a major presentation [12]. While our patient did not demonstrate chromosomal anomalies, both testes showed marked atrophy with Sertoli cell-only pattern, similar to findings in syndromic cases, indicating chronic impairment of spermatogenesis.

Histopathological findings in PMDS have been well documented. Prakash et al. reported normal uterine histology with well-preserved endometrial glands and myometrium in PMDS cases [13]. Our findings closely mirror this, with normal endometrial glands and smooth muscle bundles, confirming Müllerian origin. Similarly, Gujar et al. described Müllerian structures measuring 3–5 cm in hernia uteri inguinalis cases [14], whereas our case demonstrated larger and more well-developed structures, further emphasizing its rarity.

The role of cryptorchidism in malignancy is well established. Patil et al. reported PMDS cases without malignancy, highlighting that early orchiopexy significantly reduces cancer risk [15]. However, untreated cryptorchidism increases the risk of malignancy by approximately 3–8 fold. In our case, absence of prior surgical correction likely contributed to malignant transformation. Histologically, features such as basement membrane thickening, calcification, and Sertoli cell predominance indicate long-standing testicular damage.

Malignancies associated with PMDS are rare, with seminoma being the most commonly reported tumor. Kovachev et al. described a case of seminoma in PMDS, with tumor size around 5 cm, and even reported coexistence with Müllerian leiomyoma [16]. In contrast, our case demonstrated a non-seminomatous germ cell tumor with predominant yolk sac component, which is significantly rarer. Yolk sac tumors account for <5% of adult testicular tumors, compared to up to 80% in pediatric populations, underscoring the unusual nature of this finding.

The tumor in our case measured 4.5 × 4 × 4 cm, comparable to reported sizes of germ cell tumors; however, its occurrence in the setting of PMDS is extremely uncommon. Histologically, it exhibited classical features including microcystic and reticular patterns with Schiller–Duval bodies. Additionally, extensive necrosis and hyalinization were observed, consistent with post-chemotherapy changes. The presence of lymphovascular emboli indicates aggressive tumor biology, although absence of metastasis in 2 para-aortic and 3 inter-aortocaval lymph nodes suggests localized disease.

The importance of structured reporting in rare cases has been emphasized by RA Agha et al., who recommend detailed documentation to improve understanding of rare clinical entities [17]. Our case adheres to these recommendations by providing comprehensive clinicopathological correlation.

More recently, Yang et al. reported PMDS cases associated with infertility and transverse testicular ectopia, with smaller Müllerian structures and absence of malignancy [18]. Compared to their findings, our case is distinguished by multiple high-risk features: bilateral cryptorchidism, large pelvic mass (17 cm), well-developed Müllerian structures, and adult-onset yolk sac tumor with post-chemotherapy changes, making it exceptionally rare.

In summary, this case highlights the interplay between delayed diagnosis, bilateral cryptorchidism, and embryological abnormalities in promoting malignant transformation. The presence of a yolk sac tumor in an adult patient with PMDS, along with well-developed Müllerian structures and absence of nodal metastasis, represents a unique and rare clinical entity. Early detection and timely surgical management of cryptorchidism remain critical in preventing such outcomes and improving prognosis.

Conclusion

Persistent Müllerian duct syndrome is a rare disorder of sexual development that often remains undiagnosed until adulthood due to normal male phenotype. This case highlights an unusual association of bilateral cryptorchidism with a residual yolk sac tumor, emphasizing the significant risk of malignant transformation in undescended testes. The presence of well-developed Müllerian structures further supports underlying defects in anti-Müllerian hormone signaling. Early diagnosis and timely surgical management of cryptorchidism are crucial to prevent infertility and malignancy. This case underscores the importance of considering disorders of sexual development in males presenting with pelvic masses and demonstrates the essential role of histopathology in definitive diagnosis.

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