Malignant mesothelioma of the tunica vaginalis testis: A case report

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Abstract. The aim of the present study was to report a case of malignant mesothelioma of the tunica vaginalis testis (MMTVT) and to discuss clinicopathological features and therapeutic dilemmas to provide references for individualized management of similar cases. The case of a 57-year-old male patient with MMTVT, admitted in February 2025, was retrospectively analyzed. The patient presented with left scrotal pain and had a 30-year history of vasectomy. Scrotal ultrasound, testicular MRI and serum tumor marker analyses were performed, followed by local resection of the left tunica vaginalis tumor under spinal anesthesia. Diagnosis was confirmed using postoperative pathology and immunohistochemistry. After comprehensive counseling on recurrence and metastasis risks, the patient and their family declined radical orchiectomy and adjuvant chemotherapy, and close surveillance was instituted. Postoperative pathology confirmed biphasic MMTVT. Immunohistochemistry demonstrated positive mesothelial biomarkers: D2-40(+), calretinin (focal+) and cytokeratin 5/6 (focal weak+). Ki-67 was ~10%, with wild-type p53 expression. The tumor was completely excised with negative margins. No recurrence or metastasis was observed at the 12-month follow-up. This case, presenting with scrotal pain as initial presentation, further highlights the clinical heterogeneity of MMTVT. The remote vasectomy history, which is rarely documented, raises an etiological question for investigation. The biphasic subtype with low Ki-67 suggests that prognostic evaluation requires integrating histological subtype and molecular biomarkers. The 12-month recurrence-free survival time following isolated local excision provides preliminary evidence for organ-sparing management, although long-term outcomes require continued surveillance.

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Introduction

Malignant mesothelioma is a rare neoplasm originating from mesothelial cells, typically arising from mesothelial-lined body cavities including the pleura, peritoneum and tunica vaginalis testis (1). Malignant mesothelioma of the tunica vaginalis testis (MMTVT) represents a rare urogenital subtype of malignant mesothelioma. The tunica vaginalis testis is a sac-like structure derived from the peritoneum during testicular embryonic descent, lined by a single layer of mesothelial cells. Accordingly, MMTVT bears close resemblance to peritoneal mesothelioma in terms of both histomorphology and immunophenotype (2-4). Due to its potential to invade the testicular parenchyma, spermatic cord, epididymis and subcutaneous tissues of the penis, MMTVT is also known as paratesticular malignant mesothelioma (5).

MMTVT was first described by Barbera and Rubino (6) in 1957 and accounts for 0.3-5.0% of all mesothelioma cases (7,8). Since the initial report, <300 cases have been documented worldwide. This disease may occur at any age but predominantly affects middle-aged and elderly men aged 55-75 years (7,8). Clinical manifestations are non-specific; scrotal swelling accompanied by hydrocele is one of the most common complaints, rendering preoperative diagnosis challenging. Furthermore, the epidemiological characteristics and risk factors of MMTVT remain controversial (1,2).

The present article reports a case of MMTVT in a 57-year-old male patient with left scrotal pain as the initial manifestation, in which postoperative pathology was used to confirm biphasic MMTVT. Based on the present case report and literature review, the aim of the present study was to explore the atypical clinical presentation of MMTVT, the therapeutic dilemma associated with the biphasic histological subtype and to provide insights into individualized management for patients who decline standard treatment.

Case report

A 57-year-old male patient was admitted to Shijiazhuang People's Hospital Affiliated to Hebei Medical University, Shijiazhuang, China, in February 2025 due to left scrotal pain and discomfort for >20 days. The patient's medical history included a vasectomy 30 years prior and a subcutaneous lipoma excision 4 years ago. The patient denied any long-term

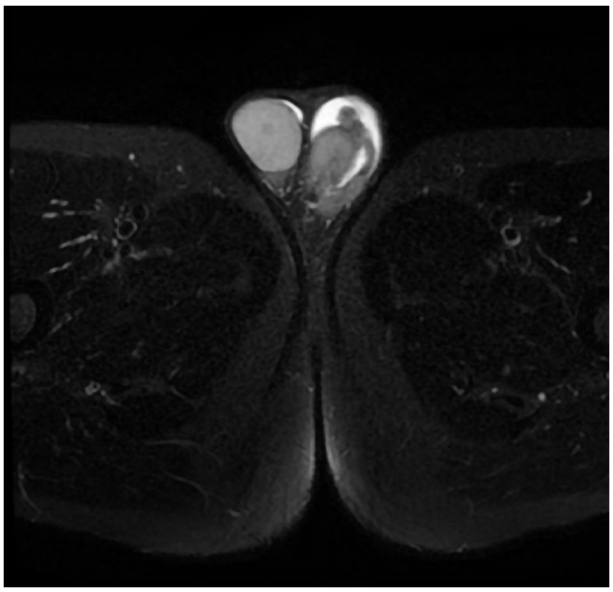

Figure 1. Left testis on 1.5T MRI with diffusion-weighted imaging. A round mass was visible above the left testis, with fluid signal around the testis.

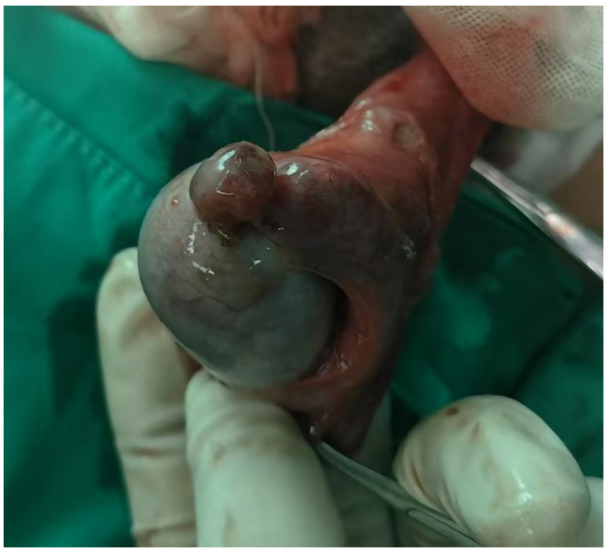

Figure 2. Supratesticular mass. A single papillary projection is observed above the left testis, which is pink, moist and glistening on the surface.

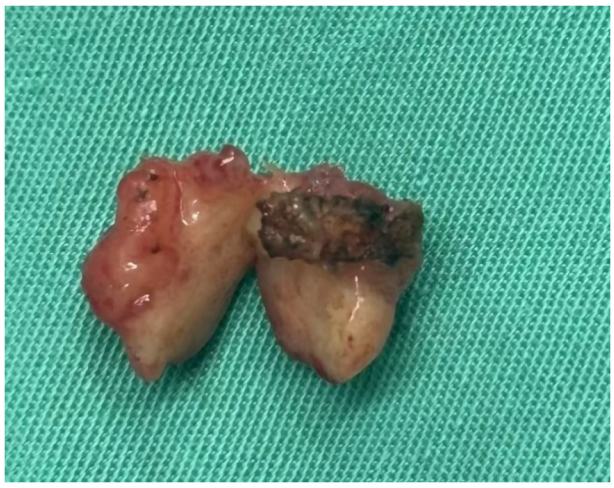

Figure 3. Cross-section of the testicular mass. On sectioning the mass, the cut surface was pale pink and fish-flesh-like in texture, without hemorrhage.

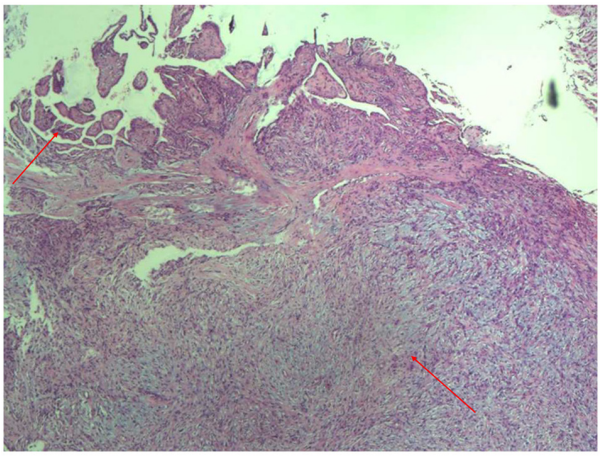

Figure 4. Histopathological features of malignant biphasic mesothelioma of the left tunica vaginalis testis. Microscopically, the tumor exhibited two distinct components: epithelioid tumor cells (right) and spindle-shaped tumor cells (left). Arrows indicate representative epithelioid and spindle-shaped tumor cells.

exposure to asbestos or asbestos products. Physical examination revealed left scrotal enlargement. A hard, mildly tender mass ~1 cm in diameter was palpable between the head of the epididymis and the testis. The right testis and epididymis were unremarkable and no enlarged lymph nodes were palpable in either inguinal region.

Pre-admission scrotal ultrasound demonstrated a 12x12 mm solid lesion superior to the left testis, left testicular hydrocele (14 mm) and left varicocele (2.6 mm). A 1.5T testicular MRI with diffusion-weighted imaging indicated slight enlargement of the left epididymis and left testicular hydrocele (Fig. 1). Tumor markers, including α-fetoprotein (6.10 ng/ml; reference range, 0.00-7.00 ng/ml) and β-human chorionic gonadotropin (<0.20 mIU/ml; reference range, 0.0-2.6 mIU/ml), were within normal limits.

Preoperative evaluation, including electrocardiography, coagulation profile, echocardiography, and cardiopulmonary assessment, showed no significant abnormalities, confirmed no notable surgical contraindications. The patient received left testicular mass resection under spinal anesthesia 4 days after admission at the same hospital. Intraoperatively, a mass measuring ~1.5x2.0x1.0 cm was identified superior to the left testis. The surface demonstrated a single papillary nodule with regular borders. The testicular appendage was not involved (Fig. 2). The mass was completely excised at its base and appeared pale pink and firm, with a moist and glossy surface. Sectioning revealed a fish-flesh-like, pale pink cut surface without obvious hemorrhage, erosion or necrosis (Fig. 3).

The surgical specimens were fixed in 10% neutral buffered formalin at room temperature for ~24 h, embedded in paraffin and sectioned at 4-5 μm. Sections were stained with H&E at room temperature (hematoxylin for 10 min, eosin for 3 min). Immunohistochemical staining was performed on a fully automated Ventana BenchMark ULTRA immunostainer

(Ventana Medical Systems, Inc.) using the UltraView Universal DAB Detection kit. After automated deparaffinization, washing with UltraWash (Reaction Buffer; Ventana Medical Systems, Inc.) and rehydration, Heat-induced epitope retrieval was carried out with ULTRA Cell Conditioning 1 buffer at 95˚C for 36 min (mild conditioning). Endogenous peroxidase was blocked with the kit's inhibitor reagent. The slides were then incubated with commercially available ready-to-use (prediluted) primary antibodies against cytokeratin (CK), CK8/18, CK7, Calretinin, D2-40, smooth muscle actin (SMA), CD34, CK5/6, Desmin, S-100, p16, p53, Bcl-2, STAT6 and Ki-67 (Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.) at 37˚C for 24 min. Subsequently, the sections were incubated with the UltraView Universal HRP Multimer (ready-to-use) at 37˚C for 8 min, and the signal was visualized with the UltraView DAB chromogen. Finally, sections were counterstained with hematoxylin II for 8 min at 37˚C. Microscopic observation was performed using an Olympus CX41 light microscope. The postoperative pathological images revealed epithelioid tumor cells of cuboidal or flat morphology in the upper-left area, while dense spindle-shaped tumor cells were noted in the right region. Pathological examination confirmed a malignant biphasic mesothelioma arising from the mesothelium of the left tunica vaginalis testis (Fig. 4). The immunohistochemical staining results were as follows: CK(+), CK8/18(+), CK7(+), Calretinin (partial+), D2-40(+), SMA(+), CD34 (vascular+), CK5/6 (focal weak+), Desmin (focal+), S-100(-), p16 (scattered+), p53 (wild-type), Bcl-2(-) and Ki67 (~10%) (Fig. S1).

The patient recovered smoothly postoperatively with good wound healing. The right testis and epididymis remained normal. As of February 2026, the patient showed no signs of local recurrence or distant metastasis.

Discussion

The clinical manifestations of MMTVT are typically non-specific, with patients most commonly presenting with a scrotal mass and/or hydrocele (9). This typically necessitates differentiation from benign conditions such as chronic epididymitis or simple hydrocele. The preoperative diagnostic rate is low; most cases are discovered incidentally during surgery for hydrocele or excision of a scrotal mass (9-12). A detailed history, physical examination, imaging studies, laboratory tests and ultimately pathological findings are essential for establishing the diagnosis. The present case report describes a 57-year-old male patient who presented with left scrotal pain and discomfort, in contrast to the more commonly reported painless scrotal swelling or hydrocele in the literature. This atypical symptom presentation expands the known clinical heterogeneity of MMTVT and reminds clinicians that the absence of typically painless manifestations does not rule out this rare malignancy. In the present report, preoperative imaging suggested a solid mass and subsequent pathology confirmed a mesothelial tumor of the tunica vaginalis origin, consistent with the typical clinical course of this disease.

Long-term asbestos exposure is a well-established major risk factor for mesothelioma (9,12). However, as reported by Radovanovic *et al* (3), only 30-40% of MMTVT cases are associated with asbestos exposure. Other reported risk factors include radiotherapy, chromosomal abnormalities, trauma, chronic epididymitis and chronic orchitis (3,13). Supporting the link to radiotherapy, Drevinskaite *et al* (11) reported the cases of two patients with malignant prostate tumors who were confirmed to have MMTVT 3 or 8 years after receiving radiation therapy. The patient in the present study had a history of vasectomy 30 years ago. Although the causal relationship between vasectomy and tumorigenesis remains unclear and lacks robust epidemiological evidence, this finding may provide a clue for future research and warrants further investigation with additional case accumulation.

Given the rarity of MMTVT, no definitive treatment guidelines have been established. Radical orchiectomy remains the mainstay of treatment for paratesticular malignant mesothelioma (9,14-16). For localized, small-volume tumors with negative margins confirmed using intraoperative frozen section, some physicians consider simple tumor excision to be an option (17). In the present report, the patient was diagnosed with a scrotal mass preoperatively and pathology confirmed MMTVT postoperatively. The overall recurrence rate of MMTVT is ~50%, and radical orchiectomy decreases the local recurrence rate to 11% (18,19). In the present case, the necessity of radical orchiectomy was fully explained to the patient and their family, but the patient explicitly declined to undergo a second surgical procedure. In the context of shared decision-making, after carefully weighing the potential survival benefit against the patient's strong preference and concerns regarding surgical trauma, a conservative surveillance strategy was adopted following multidisciplinary discussion. It must be acknowledged that this represents a deviation from the standard treatment, and the favorable short-term outcome in the present case should not be misinterpreted as justification for omitting radical surgery. Therefore, close long-term follow-up was of paramount importance in this scenario.

Given the aggressive biological behavior and high risk of recurrence associated with MMTVT (20), adjuvant therapy is often considered for patients with positive surgical margins, a high Ki-67 index or lymph node metastasis. The current standard adjuvant regimen for MMTVT is primarily chemotherapy with pemetrexed combined with a platinum agent (21). In the present case, the tumor was completely resected with negative margins, there was no lymph node metastasis and the resected tissue had a low Ki-67 index, indicating a relatively early stage. However, given its biphasic histological subtype, adjuvant chemotherapy with cisplatin plus pemetrexed was considered by the senior physician to reduce the risk of long-term recurrence. After being informed of the potential benefits, risks and considerations associated with chemotherapy (22), the patient and their family chose to decline adjuvant chemotherapy due to concerns about side effects and personal preference. Therefore, a strict follow-up protocol was established: Every 3-6 months for the first 2 years, every 6-12 months for the subsequent 3 years and at least annually thereafter. The aim of this follow-up regimen is to detect and manage any potential recurrence as early as possible.

Pathological examination remains the gold standard for diagnosing MMTVT. Microscopic evaluation revealed a mixture of two components: The upper left area was composed of cuboidal or flattened epithelioid tumor cells arranged in glandular, tubular and papillary structures, and the right showed densely packed spindle-shaped tumor cells

arranged in fascicles or a storiform pattern, exhibiting mild to moderate atypia. Immunohistochemical findings indicated a typical mesothelial origin. The tumor cells were positive for CK5/6, D2-40 and calretinin, which are consistent with a mesothelial origin (2,20). According to the Guidelines for Pathologic Diagnosis of Malignant Mesothelioma: 2017 Update of the Consensus Statement From the International Mesothelioma Interest Group, , BRCA1-associated protein 1 (BAP1) is a molecular marker for the differential diagnosis of mesothelioma, and previous literature supports Wilms' tumor 1 (WT-1) in this setting (2,20). Loss of nuclear BAP1 expression is a specific feature to distinguish malignant mesothelioma from benign mesothelial hyperplasia; 40-60% of malignant mesotheliomas carry BAP1 inactivating mutations that cause this protein loss, and positivity for WT-1 is a marker supporting mesothelial origin (2,20). Due to technical limitations, BAP1 and WT-1 testing were not performed in the present case, which represents a significant limitation of this report. It is recommended that these two immunohistochemical stains be routinely performed in future similar cases to further improve diagnostic accuracy. The Ki-67 proliferation index in the present case was ~10%, p53 demonstrated a wild-type expression pattern and p16 was focally positive, suggesting relatively low proliferative activity of the tumor. However, the aggressiveness of the biphasic subtype of MMTVT is generally higher than that of the epithelioid subtype (23). This discrepancy between the low proliferation index demonstrated by immunohistochemistry and the more aggressive biphasic morphology subtype indicates that the prognosis of MMTVT cannot be assessed using a single parameter. Instead, a comprehensive evaluation combining histological subtype, immunophenotype and molecular markers is required. This is why long-term close follow-up for the patient was arranged. The prognosis of MMTVT is poor, with 5-year overall survival rating from 30 to 49% (9,24). Death often occurs within 2-3 years after diagnosis, typically due to local recurrence or distant metastasis to the pleura or lungs (11). Poor prognostic factors include large tumor size, positive surgical margins, lymph node metastasis and high Ki-67 expression. The patient in the present report showed no recurrence or metastasis after 12 months of follow-up, indicating a favorable outcome so far. However, given the potential for late recurrence, long-term follow-up is essential.

This present study has several limitations. First, as a single-case report, the generalizability of the conclusions is limited. Second, the absence of BAP1 and WT-1 immunohistochemical staining may compromise the accuracy of diagnostic stratification. Third, the follow-up duration was only 12 months, and the long-term prognostic outcome remains unclear. Fourth, the patient's refusal of standard treatment further limits the reliability of the therapeutic conclusions. Fifth, due to the retrospective nature of the present case study, the exact clone numbers and suppliers of the individual antibodies could not be fully verified. Nevertheless, all immunohistochemical procedures were strictly performed in accordance with the standard operating protocols of the Department of Pathology, Shijiazhuang People's Hospital.

In conclusion, the present case indicates that clinicians should remain vigilant for this rare malignancy in patients presenting with scrotal pain, rather than the typical painless swelling. The biphasic histological subtype exhibits greater invasive potential than the epithelioid subtype, and its recurrence risk should not be underestimated even with a low proliferation index. Prognostic evaluation should integrate histological subtypes and molecular markers rather than relying on a single indicator. Furthermore, the potential association between prior vasectomy and MMTVT deserves attention and requires validation in larger-scale case series. In summary, the diagnosis and management of MMTVT remain challenging. Strengthening clinical awareness, optimizing preoperative imaging evaluation and implementing multidisciplinary individualized treatment strategies are critical for improving patient prognosis. Long-term regular follow-up is essential for the early detection of tumor recurrence.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

ZL and AH performed case data collection, manuscript drafting and study conception. SL and JZ analyzed, interpreted and discussed the data. CS and YG performed the experiments and confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

This study was approved by the Medical Ethics Committee of Shijiazhuang People's Hospital (approval no. 2026-136).

Patient consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying clinical data.

Competing interests

The authors declare that they have no competing interests.

Use of artificial intelligence tools

During the preparation of this work, artificial intelligence tools were used to improve the readability and language of the manuscript, and subsequently, the authors revised and edited the content produced by the artificial intelligence tools as necessary, taking full responsibility for the ultimate content of the present manuscript.

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