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CASE REPORT

Primary malignant melanoma of the female urethra: a case report and literature review

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Background: *Primary urethral malignant melanoma is an extremely rare malignancy of mucosal origin. Its clinical manifestations are non-specific, often leading to misdiagnosis or delayed diagnosis. Due to its highly aggressive nature and propensity for early metastasis, patient prognosis is generally poor.*

Case description: *This case report describes an 81-year-old Chinese female patient who presented to the Department of Urology at Gansu Provincial Hospital with the chief complaint of "a black mass at the external urethral meatus accompanied by urinary incontinence for two months. Physical examination revealed a dark, protruding mass at the external urethral orifice. Imaging studies showed no evidence of distant metastasis. The patient underwent a "Radical Resection of Urethral Mass." Due to significant urethral shortening following tumor resection, a concurrent "retropubic urethropexy" was performed to preserve postoperative urinary continence. Postoperative pathology and immunohistochemistry confirmed the diagnosis of malignant melanoma. The patient declined adjuvant targeted therapy postoperatively. Short-term follow-up indicated no tumor recurrence, with satisfactory recovery of urinary function.*

Conclusions: *For primary urethral malignant melanoma, radical surgical resection remains the primary treatment modality. In this case, the combination of radical surgery with a concurrent urethropexy procedure achieved complete tumor removal while effectively preventing postoperative urinary incontinence resulting from local anatomical disruption. This approach highlights the importance of individualized, multifunction-preserving treatment strategies for such rare cases. Enhancing clinical awareness of this disease is crucial for facilitating early diagnosis and improving patient prognosis.*

Key Words: Malignant melanoma, female urethral cancer, case report, urethral orifice

Introduction

Malignant melanoma typically originates from embryonic neural crest-derived melanocytes and is characterized as a highly aggressive tumor with a poor prognosis and a strong tendency for metastasis. It is one of the most lethal malignancies worldwide in terms of both incidence and mortality. While it most commonly arises in the skin, it can also occur in other parts of the body, including, albeit rarely, the genitourinary tract.[1,2] Primary malignant melanoma of the female urethra is extremely rare, accounting for only 0.2% of all melanomas.[3] Due to its unclear etiology and non-specific clinical manifestations, it is frequently misdiagnosed as urothelial carcinoma or sarcoma. Currently, there are no established staging guidelines or standardized treatment protocols. Radical surgical excision remains the preferred therapeutic option, often followed by adjuvant chemotherapy or immunotherapy. This article highlights the rarity of this disease from diagnostic and therapeutic perspectives, emphasizes the

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importance of histopathological identification, and aims to raise clinical awareness among physicians.

This study was approved by the Ethics Committee of Gansu Provincial Hospital, with the approval number: 2026-056. This study obtained handwritten informed consent from the patient. Furthermore, it was prepared in accordance with the CARE (Case Report) guidelines,[4] and a corresponding CARE checklist has been provided. For further details, please refer to Supplementary Material S1.

Case Presentations (Table 1)

Patient information

This article reports the case of an 81-year-old female patient who presented to the Department of Urology at Gansu Provincial Hospital with a two-month history of a black mass at the external urethral orifice accompanied by symptoms of urinary incontinence. The patient had no significant past medical history or family history of hereditary diseases. Physical examination revealed no skin rashes, and no palpable lymphadenopathy was detected in the bilateral inguinal regions. Informed consent was obtained from the patient in accordance with the Declaration of Helsinki.

Clinical findings

During examination of the external urethral orifice, a dark black mass measuring approximately 2.0 × 2.0 × 3.0 cm was observed (Figure 1). The mass was notably protruding, moderately mobile, broad-based, with a smooth surface, firm texture, and prone to bleeding. Additionally, chest and abdominal Computed tomography (CT) scans showed no significant abnormalities. Pelvic CT revealed no obvious abnormalities in the bladder, uterus, or bilateral adnexa, and no lymphadenopathy was detected in the pelvic or inguinal regions. Urinalysis indicated red blood cells (+++), while complete blood count and liver and kidney function tests were within normal limits.

Diagnostic evaluation

Based on the physical examination and imaging findings, a preliminary diagnosis of a urethral mass was made. Following multidisciplinary discussion, and considering that the mass was located in the distal urethra with an estimated residual urethral length of only about 2 cm after resection—which could potentially lead to stress urinary incontinence—it was decided to perform "radical resection of the urethral mass" combined with a concurrent "retropubic urethropexy."

Treatment

Intraoperatively, the lesion and a 3 cm margin of surrounding tissue were completely excised. A synthetic mesh was subsequently placed to reinforce the anterior vaginal wall, providing support to the residual urethra and bladder neck to reduce the risk of postoperative stress urinary incontinence. The urinary catheter was removed one week after surgery, and the patient was able to void spontaneously with a favorable recovery.

Follow-up and outcomes

Histopathological examination of the postoperative specimen revealed marked nuclear atypia, with the tumor being predominantly composed of epithelioid cells along with the presence of spindle cells and small pigmented cells. The tumor cells exhibited pleomorphism, characterized by large, hyperchromatic nuclei, prominent nucleoli, cytoplasmic melanin granules, and observable pathological mitotic figures. Immunohistochemical staining revealed positivity for S-100(S-100 Protein), HMB-45(Human Melanoma Black-45), Ki-67(red, +40%) (Kiel-67), while CKP(Cytokeratin Pan), EMA(Epithelial Membrane Antigen), CK7(Cytokeratin 7), P63(Tumor Protein 63), P53(Tumor Protein 53), and GATA3(GATA Binding Protein 3) were negative (Figure 2). These pathological findings indicate high proliferative activity and are consistent with the typical histopathological features of malignant melanoma. Therefore, postoperative sentinel lymph node biopsy was recommended to delineate staging and guide subsequent therapeutic decisions (such as lymph node dissection or adjuvant radiotherapy/chemotherapy), thus potentially improving prognosis. After thorough explanation, the patient's family, considering the patient's advanced age and satisfaction with the current surgical outcome, decided to forego further interventions at this time. Follow-up examination conducted one month postoperatively demonstrated a well-healed surgical incision, normal voiding function, and an otherwise unremarkable clinical status.

Discussion

Primary malignant melanoma of the urethra is a rare mucosal-origin malignancy that predominantly affects middle-aged and elderly women between the ages of 50 and 70, with a higher incidence observed in

TABLE 1. **Timeline of diagnosis and treatment**

Time point	Key event	Clinical summary
2 Months Prior to Presentation	Symptom Onset	A black mass at the external urethral orifice was noted, accompanied by urinary incontinence.
Initial Visit	Admission & Diagnostic Workup	A protruding, firm, dark black mass (~2.0 × 2.0 × 3.0 cm^3) was observed at the urethral orifice. Imaging showed no metastasis. Preliminary diagnosis: urethral mass.
Preoperative Phase	Multidisciplinary Discussion & Treatment Planning	Decision for radical urethral mass resection with concurrent retropubic urethropexy to reduce postoperative incontinence risk.
Operative Day	Surgical Procedure	Complete excision of the mass with 3-cm margins. Placement of a synthetic mesh for urethral and bladder neck support.
Postoperative Week 1	Early Recovery	Urinary catheter removed. Patient voiding spontaneously with good recovery.
Postoperative (Pathology)	Histopathological Diagnosis	Final pathology confirmed malignant melanoma (S-100+, HMB-45+, Ki-67 ~40%). Sentinel lymph node biopsy was recommended for staging.
1 Month Post-Op	First Follow-Up	Surgical site well-healed. Normal voiding function. No remarkable clinical findings.
Decision Point	Family Decision	Given the patient's age and satisfactory surgical outcome, the family declined further intervention.

Note. S-100+: S-100 Protein(+); HMB-45+: Human Melanoma Black-45 (+); Ki-67: Kiel-67.

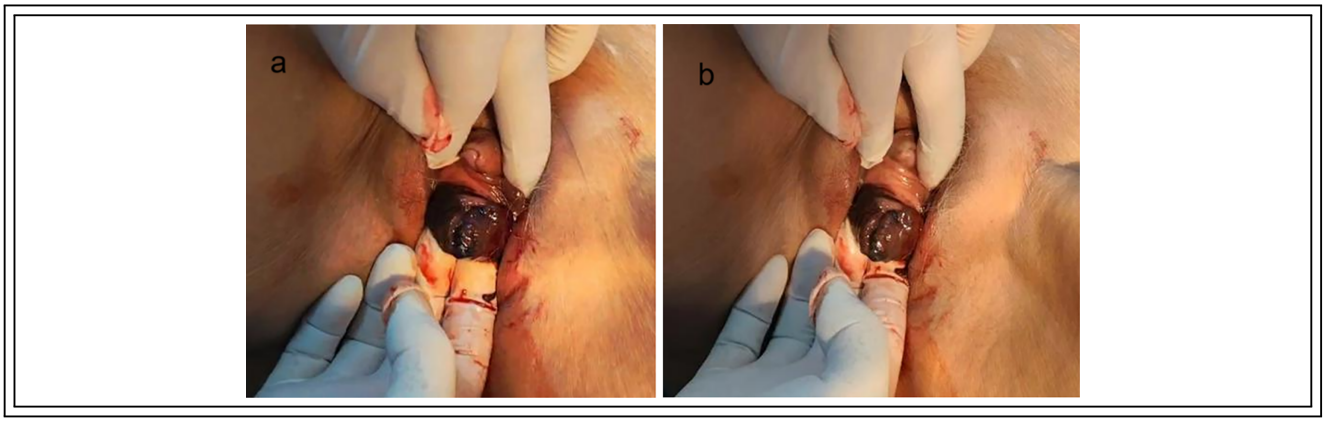

FIGURE 1. (a, b) The black mass at the external urethral orifice protruded into the vulva

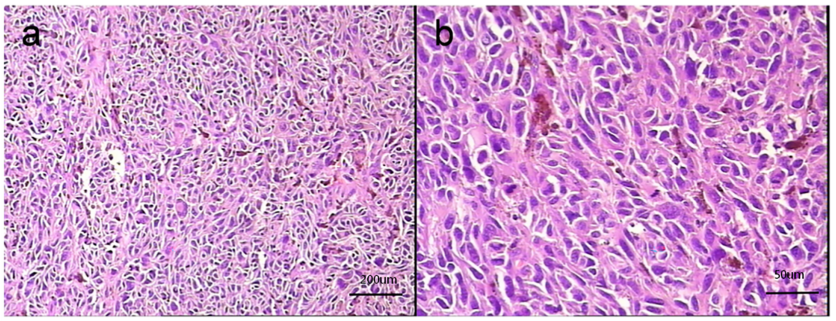

FIGURE 2. Pathological section (Hematoxylin and Eosin [H&E] staining). (a) The tumor cells exhibit marked nuclear atypia, with enlarged hyperchromatic nuclei, prominent nucleoli, and visible mitotic figures (×10 magnification). (b) The melanocytes show significant cellular heterogeneity, predominantly composed of epithelioid and spindle-shaped cells, with melanin pigmentation observed in some cells (×20 magnification)

White females[2]. It accounts for only 0.2% of all malignant melanomas but represents approximately 4% of malignant urethral tumors in women.[3] The tumor exhibits a distinct anatomical distribution, with over 90% of cases occurring in the distal urethra, although it may also involve the proximal urethra and adjacent tissues such as the anterior vaginal wall.

The clinical manifestations are closely associated with the tumor's location. Lesions located in the proximal or mid-urethra often present with painless gross hematuria, dysuria, or a weakened urinary stream. In contrast, tumors involving the distal urethra or external urethral orifice typically manifest as ulcerative lesions, palpable firm masses, or vaginal bleeding.[5,6] Histologically, urethral melanomas can be classified into pigmented and amelanotic subtypes.[7] Most lesions exhibit melanin pigmentation and a tendency to bleed easily; however, approximately 25% of urethral melanomas are amelanotic, lacking visible melanin deposits and appearing black, brown, pink, or blue.[8,9] These tumors often exhibit a polypoid or mass-like growth pattern and are frequently misdiagnosed as urethral caruncles, mucosal prolapse, or urothelial tumors.[10]

From a growth pattern perspective, malignant melanomas are categorized into vertical and radial growth types, with the radial growth pattern being more common in primary urethral melanoma.[11] In the early stages, the tumor can metastasize through superficial lymphatic channels to the vulva and vagina, and through deeper lymphatic vessels to the inguinal lymph nodes; in some cases, hematogenous spread to distant organs may also occur. The tumor's growth pattern, extent of local invasion, and lymph node involvement are key prognostic factors.[12,13] Studies indicate that the 5-year survival rate for primary urethral malignant melanoma is only about 3%, significantly lower than the approximately 80% 5-year survival rate for cutaneous melanoma.[10] This poor prognosis is largely attributed to the tumor's aggressive nature, high local recurrence rate, and early metastatic potential.

Due to its highly aggressive biological behavior and propensity for early metastasis, coupled with the non-specific nature of its clinical symptoms, primary malignant melanoma of the urethra is often associated with delayed diagnosis and poor prognosis. Therefore, a comprehensive clinical assessment of the primary lesion, surrounding involved tissues, and regional lymph node metastasis is crucial. Imaging modalities such as inguinal lymph node ultrasonography, chest CT, contrast-enhanced CT of the abdomen and pelvis, and cystoscopy can be employed for this purpose. CT scans and sentinel lymph node biopsy are valuable for evaluating distant metastasis, staging, and therapeutic response in malignant melanoma.[14,15] In patients with confirmed lymphatic or distant metastases, enhanced MRI of the brain may also be considered to detect intracranial involvement.[16] In the present case, chest, abdominal, and pelvic CT scans revealed no evidence of distant metastasis, suggesting that the disease was still in an early or localized stage.

Histopathological examination remains the gold standard for confirming the diagnosis of urethral malignant melanoma. However, its variable morphology necessitates differential diagnosis from high-grade or poorly differentiated urothelial carcinoma, sarcoma, and metastatic cutaneous melanoma. Immunohistochemical (IHC) staining is instrumental in identifying

mucosal, hypopigmented, or amelanotic variants of melanoma.[5] Common melanocytic markers include S-100 protein, HMB-45, Melan A, and tyrosinase.[17] Among these, S-100 protein demonstrates high sensitivity but relatively low specificity. In contrast, markers such as HMB-45, Melan A, and tyrosinase have higher specificity, although their sensitivity may vary. Given the heterogeneity of melanocytic tumors, it is recommended to use a panel of 2–3 highly specific markers in conjunction with S-100 protein to enhance diagnostic accuracy.[18] In amelanotic urethral melanoma, the strong specificity of HMB-45 makes it a key diagnostic marker.[19] Therefore, in clinical practice, combining multiple immunohistochemical markers with histopathological features is essential to improve the accuracy and reliability of diagnosis.

Mucosal melanoma is typically diagnosed at an advanced stage and is associated with a poor prognosis. The standard treatment for most mucosal melanomas involves wide local excision and lymph node dissection, followed by chemotherapy or immunotherapy.[20] For primary malignant melanoma of the urethra, there are currently no standardized staging guidelines or established treatment protocols. Surgical resection remains the primary treatment modality. Common surgical options include partial urethrectomy, radical urethrectomy, and total urethrectomy, often combined with inguinal lymphadenectomy.[21] Radical urethrectomy is generally indicated for tumors with deep invasion and extensive involvement, requiring resection of the entire urethra and bladder neck, along with the anterior vaginal wall to achieve negative surgical margins.[10] In contrast, partial urethrectomy is suitable for tumors located in the distal urethra that are small, superficially located, and without regional lymph node or distant metastasis, with a recommended surgical margin of approximately 3 cm from the tumor. However, the optimal margin for negative resection remains controversial. Some researchers advocate for wider surgical margins to reduce the risk of local recurrence, minimize surgical trauma, and improve cure rates.[22–24] Studies have shown that for mucosal melanomas with a Breslow thickness $\geq$2 mm, a 3 cm margin is more effective in reducing local recurrence than a 1 cm margin.[25] On the other hand, some believe that in certain cases of mucosal melanoma, narrower surgical margins may be acceptable if supplemented with adjuvant therapy. A meta-analysis indicated that postoperative adjuvant radiotherapy can reduce the risk of local recurrence, although it does not affect the risk of distant metastasis.[26] Furthermore, the choice of adjuvant therapy should be individualized based on specific clinical factors. For example, in patients with negative surgical margins but other high-risk features, adjuvant external beam radiotherapy may be considered.[27] For patients with advanced or recurrent disease, chemotherapy or immunotherapy serves as the mainstay of treatment.[28] Immune checkpoint inhibitors, such as anti-PD-1 or anti-CTLA-4 antibodies, have demonstrated some efficacy in metastatic melanoma, although the response rate in mucosal melanoma remains relatively low.[29]

In this case, despite the absence of a definitive preoperative diagnosis, a radical urethrectomy (without lymph node dissection) was performed, which is consistent with the fundamental surgical principles for urethral melanoma.[3,8,30] Following mass resection, the residual functional urethral length was approximately 2.0 cm, indicating significant urethral shortening. Postoperatively, the patient exhibited signs of stress urinary incontinence (urine leakage upon gentle suprapubic pressure). To improve urinary continence, a retropubic urethropexy was subsequently performed. The surgical procedure was as follows: After urethral catheterization, approximately 100 mL of normal saline was injected into the submucosal plane of the anterior vaginal wall to create a hydrodissection layer. A midline longitudinal incision of about 3 cm was made in the anterior vaginal wall, starting approximately 1.5 cm distal to the external urethral orifice. Using a finger, the surgeon bluntly dissected the plane between the anterior vaginal wall and the urethra in a retropubic direction along the descending ramus of the pubis. A puncture needle was introduced vertically at a point approximately 0.5 cm lateral to the junction of the middle and lower third of the left descending pubic ramus, entering the previously dissected space. After confirming the absence of gross hematuria (ruling out bladder injury) and the integrity of the lateral vaginal wall, the right arm of the sling was guided from inside to outside. The same procedure was repeated on the contralateral side for sling placement. Cystoscopy was performed intraoperatively to confirm that the sling did not penetrate the bladder wall. Finally, the sling was positioned flat beneath the posterior segment of the urethra and bladder neck, ensuring a tension-free state. This procedure reinforced the support of the anterior vaginal wall to the urethra and bladder neck, improved urinary continence, and reduced the risk of postoperative incontinence.

The principal strength of this case lies in the achievement of tumor resection and immediate preservation of voiding function through a single-stage operation. However, the treatment strategy

failed to complete the full standard diagnostic-therapeutic pathway. Although preoperative imaging revealed no distant metastasis, the patient and family—citing advanced age and satisfaction with the surgical outcome—declined the recommended postoperative sentinel lymph node biopsy and did not proceed with any adjuvant therapy. Consequently, accurate pathological staging of the tumor could not be determined. Furthermore, for this mucosal melanoma with high-risk features such as deep invasion and a Ki-67 index of 40%, adjuvant treatment (e.g., targeted therapy, immunotherapy, or radiotherapy) plays a crucial role in reducing the risk of recurrence and metastasis and improving long-term survival. Relying solely on surgery without consolidated multimodal treatment introduces significant uncertainty regarding long-term oncologic outcomes. Thus, while this case demonstrates technical feasibility and short-term benefits, its long-term oncologic efficacy remains uncertain. Highlighting these limitations is not to negate the value of the surgical attempt, but rather to emphasize that in managing similar rare cases in the future, every effort should be made to complete standardized staging evaluation. Through multidisciplinary discussion, comprehensive communication with the patient regarding integrated treatment plans—including adjuvant therapy—should be pursued to strike an optimal balance between personalized care and evidence-based principles.

Conclusions

Primary malignant melanoma of the urethra is extremely rare, and its pathogenesis remains poorly understood. The clinical presentation is often non-specific, making delayed diagnosis or misdiagnosis common in clinical practice. Due to the variability in tissue morphology and immunophenotype, diagnosis primarily relies on histopathological examination and must be differentiated from urothelial carcinoma, sarcoma, and metastatic cutaneous melanoma. Immunohistochemical staining plays a crucial role in identifying histological variants. Currently, there is no standardized treatment protocol for this disease. Radical urethrectomy remains the preferred treatment approach, but achieving negative surgical margins is essential to improve survival rates and reduce the risk of postoperative recurrence. In summary, future research should aim to elucidate the molecular mechanisms underlying the disease, optimize therapeutic strategies, and develop more effective biomarkers and targeted therapies to enhance cure rates and overall survival.

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Author Contributions

Jianlin Xie and Qingwei Zhang: manuscript writing and data analysis. Jingde Wu: data collection and data analysis. Yingjun Ma: data analysis. Yujie Yan: literature search and reference collection. Xiande Huang: supervision and guidance. All authors reviewed and approved the final version of the manuscript.

Availability of Data and Materials

All data supporting the conclusions of this article are included within the article and its supplementary figures. Additional information can be obtained by reasonable request to the corresponding author.

Ethics Approval

This study was approved by the Ethics Committee of Gansu Provincial Hospital (Approval No. 2026-056). Written informed consent was obtained from the patient prior to the commencement of the study.

Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Materials

The supplementary material is available online at https://www.techscience.com/doi/10.32604/cju.2026.076571/s1.

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