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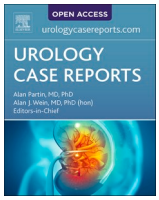

Oncology

Perivascular epithelioid cell neoplasm (PEComa) of the urinary bladder presenting as urinary tract infection in a young woman

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ABSTRACT

PEComa is a rare mesenchymal tumor with unique features, sometimes manifesting in younger patients and can exhibit malignant transformation. We present a 24-year-old woman with urinary symptoms and hematuria. Imagining revealed a protruding mass in the bladder dome, raising suspicion for adenocarcinoma due to its location and vascular appearance. Pathology revealed PEComa. Clinicians should inquire about macroscopic hematuria and assess the entire urinary tract even in young patients with apparent urinary tract infection. Practitioners should be mindful of PEComa tumors, especially in cases involving young patients with tumors concerning the bladder dome. A variety of immunohistochemical techniques facilitate the diagnosis.

1. Introduction

Perivascular epithelioid cell tumors (PEComas) are rare mesenchymal neoplasms which arise from perivascular epithelioid cells and exhibit a variety of distinct histological and immunohistochemical features. While renal angiomyolipoma (AML) is the most common form of PEComa, these tumors may manifest in a wide range of sites including lung, liver, gynecologic, bone and soft tissue. Bladder PEComas, though infrequent, merit attention due to their potential for malignant transformation, tendency to present at relative young age and variable treatment responses. Immunohistochemical methods including HMB-45, actin, desmin, melan-A, pan-cytokeratin staining are very useful to establish or rule out PEComa. This case report underscores the importance of inquiring about macroscopic hematuria and investigating it thoroughly even in young adults presenting with irritative urinary symptoms. In addition, it highlights the atypical manifestation of bladder PEComa.

2. Case study

A 24-year-old female, with medical history notable for aplastic anemia followed by hematopoietic stem cell transplantation seven years prior, presented to the Emergency Department with symptoms of irritative voiding and abdominal discomfort persisting over several days. When asked directly about hematuria, the patient recollected one incident of macroscopic hematuria. Laboratory tests were notable for mild leukocytosis and a slightly elevated *C*-reactive protein level. Urinalysis demonstrated positive findings for erythrocytes, leukocytes and nitrites. The patient's working diagnosis was urinary tract infection. She was discharged home with antibiotic therapy and ambulatory urinary tract ultrasonography (US).

Four days later her symptoms had resolved. The US detected a bladder anterosuperior hypoechoic mass measuring 48mm × 18mm (Fig. 1- A). Computer tomography (CT) revealed a hyperdense solid mass with contrast uptake compressing the upper bladder wall with likely involvement of the urachus (Fig. 1- B). Cystoscopy revealed a round prominent penetrating mass measuring five on 5 cm protruding from the bladder dome (Fig. 1- C). Considering the patient's age, the size and location of the tumor, and considering the possibility of adenocarcinoma involving the urachus, it was decided to proceed to partial cystectomy.

The patient underwent an open partial cystectomy. Complete excision of the mass along with the superior bladder wall was performed (Fig. 1-D). The patient's postoperative recovery was uneventful.

The pathological examination revealed a mesenchymal lesion characterized by clear to eosinophilic epithelioid cells, alongside mildly spindle pleomorphic cells arranged within a delicate vascular stroma interspersed among tumor cell nests (Fig. 2). Notably, no mitotic

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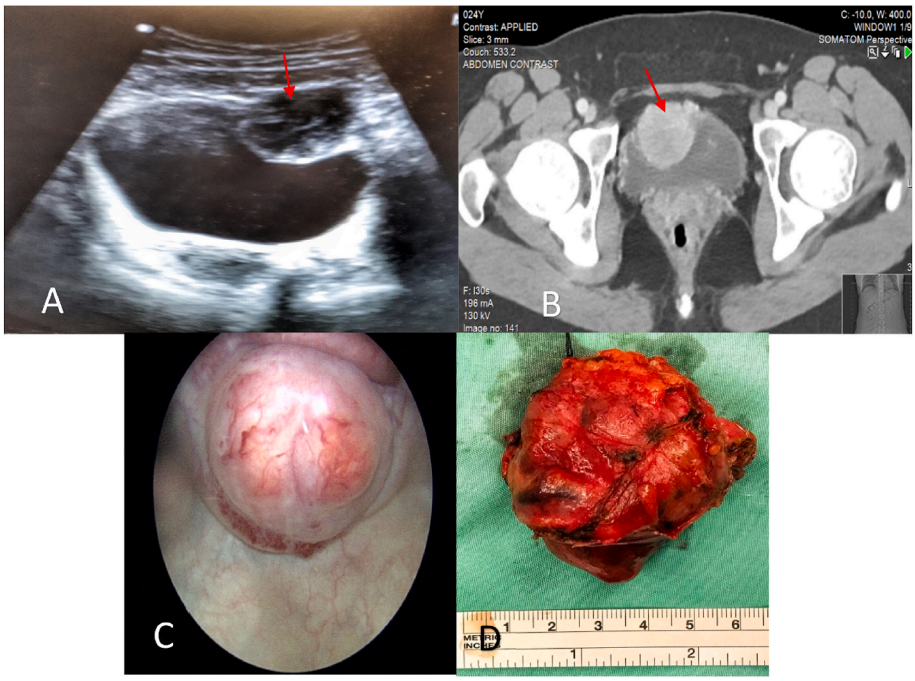

Fig. 1. (A) patient's US reveals a hypoechoic mass (red arrow) in the anterosuperior region of the urinary bladder. (B) CT reveals a hyperdense mass (red arrow) located on the anterior bladder wall. (C) Cystoscopic image of a bulging five-centimeter bladder dome mass. (D) The excised mass and adjacent bladder wall. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

features, necrosis, or vascular invasion were identified. Immunohistochemical analysis demonstrated positivity for HMB-45 and actin, while desmin, melan-A, and pan-cytokeratin staining were negative. Surgical margins were free of tumor cells. These histopathological features are in line with a diagnosis of PEComa.[4] A follow-up CT scan conducted one year later exhibited no signs of recurrence.

3. Discussion

Several types of benign masses can develop in the urinary bladder, representing 1–5% of all bladder tumors.[1,2] PEComas, which are usually benign,[3] are a rare subgroup of mesenchymal neoplasms that derive their name from their characteristic perivascular localization and the distinctive epithelioid appearance of their constituent cells.[4]

Bladder PEComas were first described in the early 1990s and have since earned attention due to their distinctive histological and immunohistochemical features. Bladder PEComas predominantly affect individuals in the younger and middle-aged demographics, with an average age of onset of approximately thirty-nine years and a male-to-female ratio of approximately 1:1.3.[5]

PEComas are believed to originate from smooth muscle and melanocytic cells which are known as perivascular epithelioid cells (PECs). Histological features are notable for clear to eosinophilic epithelioid cells and a delicate vascular stroma. Immunohistochemical markers such as HMB-45 and actin are key to establishing the diagnosis and are highly useful in distinguishing them from other mesenchymal neoplasms,[4] such as fibromas, sarcomas, lipomas, leiomyomas, rhabdomyoma, hemangiomas, lymphangiomas, etc.[6] Emerging research continues to add to the genetic profiling of these tumors which greatly facilitates differential diagnosis. In a recent genetic study of 35 PEComa specimens, Seeber et al. discovered a wide variety of underlying genetic mutations.[7]

Imaging studies often reveal PEComa-characteristic features. US commonly reveals an oval or nodular solid mass with hypoechoic or isoechoic features, delineated from surrounding tissues by a distinct margin. Color Doppler flow imaging typically demonstrates abundant blood flow within and surrounding the lesion. Unenhanced CT typically depicts a solid, nodular, or irregular mass with well-defined margins and soft tissue density. Contrast imaging is notable for heterogenous enhancement of the mass, with occasional identification of spotted vessel signs at the periphery during the arterial phase, further accentuating the vascular nature of the lesion. Preoperative cystoscopic biopsy plays a pivotal role in the diagnostic workup of bladder PEComa, facilitating accurate histopathological confirmation and guiding subsequent treatment.[6]

Staging is based on the Schoolmeester criteria (Table 1) which is based on histopathological features. When a PEComa displays more than two high-risk features, it is designated as malignant.[8]

The cornerstone of PEComa treatment is surgical resection. A seminal study by Folpe et al.,[9] involving 26 patients, underscored the significance of tumor size and specific pathological characteristics, such as necrosis and a high mitotic count, in predicting the likelihood of recurrence. Additionally, factors like infiltrative margins, high-grade nuclear atypia, and vascular invasion were considered when assessing the tumor's malignant potential. Treatment of metastatic PEComas may also include adjuvant radiation therapy, tyrosine kinase inhibitors (TKIs) and mammalian target of rapamycin (mTOR) inhibitors and yields variable response rates.[10]

As this case illustrates well, it is imperative to probe for macroscopic hematuria during patient history-taking. Whenever the patient confirms an event of macroscopic hematuria, it is critical to obtain imaging studies of the upper and lower urinary tract, even in younger patients, notwithstanding the rarity of bladder tumors in this demographic. Tumors involving the bladder dome and urachal area should always raise suspicion of uncommon bladder neoplasms. Diagnosis relies on histopathology and a number of stains facilitate the diagnosis which is key to determining further management.

Concent of the patient

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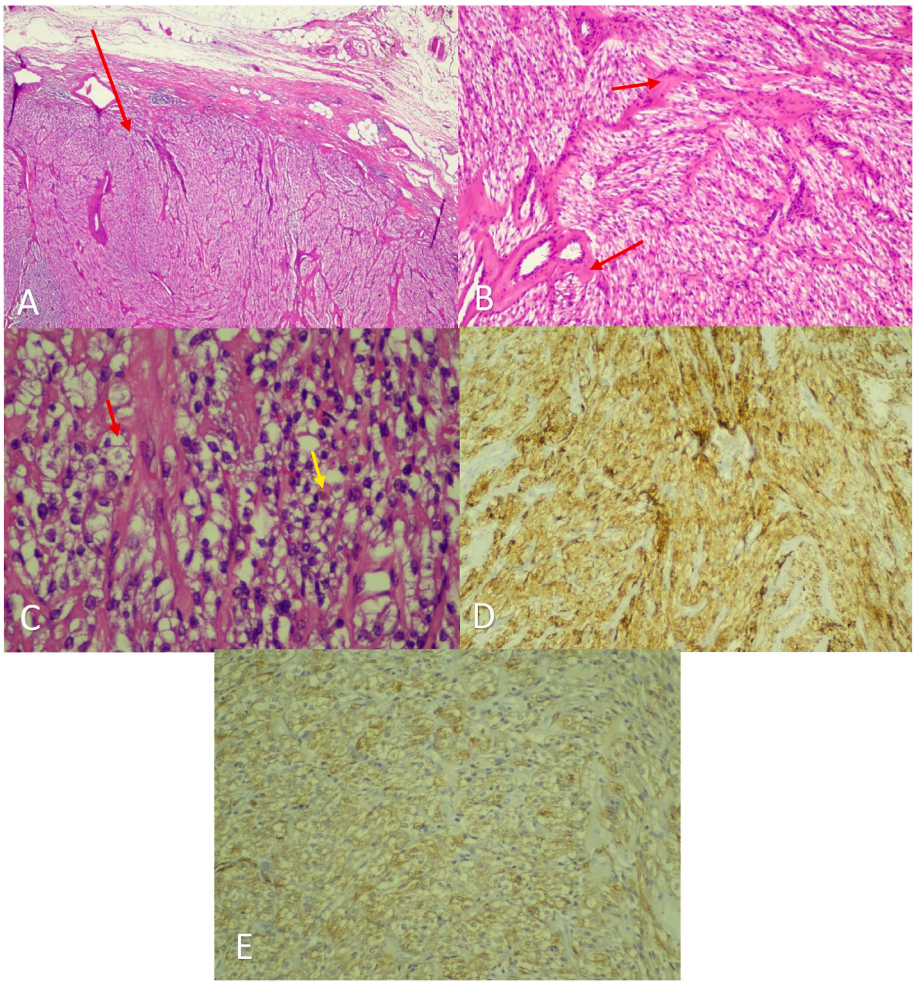

Fig. 2. (A) The tumor (red arrow), surrounded by fatty tissue. Note the well demarcated tumor boundary. (B) The tumor showing hyalinized stroma (red arrows). (C) Tumor cells are noncohesive epithelioid cells with clear to eosinophilic granular cytoplasm (red arrow), slightly atypical nucleolus, but almost no mitotic figures. Melanin pigment can be observed (yellow arrow). (D) The tumor with a positive HMB-45 stain. (E) The tumor with a positive actin stain.

Table 1
Schoolmeester criteria.

MALIGNANT PROFILE	CHARACTERISTICS
Benign	<5 cm in diameter Non-infiltrative Non-high nuclear grade and Cellularity Mitotic rate ≤1/50 HPF No necrosis No vascular invasion
Uncertain malignant potential	One or both of the following features: Nuclear pleomorphism/multinucleated giant cells >5 cm in diameter
Malignant	Two or more of the following features: >5 cm in diameter Infiltrative High nuclear grade and cellularity Mitotic rate ≥1/50 HPF Necrosis Vascular invasion

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Dana Greenberg: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Yoav Avidor:** Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Rami Mattar:** Conceptualization, Data curation, Investigation. **Muhammad Majdoub:** Conceptualization, Data curation, Methodology, Project administration. **Alona Meir:** Data curation, Investigation, Resources. **Ronen Rub:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Jakus D, Jurić I, Šitum M. Benign urinary bladder masses: rare entities. Internet *Afr J Urol.* 2023;29(1). https://doi.org/10.1186/s12301-023-00382-2.
2. Gómez Vegas A, Silmi Moyano A, Fernández Lucas C, et al. Leiomyoma of the lower urinary tract. Internet *Arch Esp Urol.* 1991;44(7):795–798 [cited 2024 Mar 20] https://pubmed.ncbi.nlm.nih.gov/1953060/.
3. Padmehr R, Arasteh S, Aminimoghaddam S, et al. PEComa-A rare uterine neoplasm: a case report. Internet *J Reproduction Infertil.* 2022;23(3):224. https://doi.org/10.18502/jri.v23i3.10015 [cited 2024 Mar 20].
4. *Pathology and Genetics of Tumours of Soft Tissue and Bone.* London, England: Oxford University Press; 2002. CHANGE TO ONE).
5. Wu Y-L, Lang L, Ma Q, et al. Perivascular epithelioid cell tumor of urinary bladder. *Am J Clin Pathol [Internet].* 2021;156(1):56–71. https://doi.org/10.1093/ajcp/aqaa204.
6. Bansal A, Goyal S, Goyal A, Jana M. WHO classification of soft tissue tumours 2020: an update and simplified approach for radiologists. *Eur J Radiol [Internet].* 2021;143 (109937). https://doi.org/10.1016/j.ejrad.2021.109937, 109937.
7. Seeber A, Holzer L, Elliott A, et al. Deciphering the molecular landscape and the tumor microenvironment of perivascular epitheloid cell neoplasma (PEComa). Internet *J Clin Oncol.* 2021;39(15_suppl):11539. https://doi.org/10.1200/jco.2021.39.15_suppl.11539.
8. Schoolmeester JK, Dao LN, Sukov WR, et al. TFE3 translocation-associated perivascular epithelioid cell neoplasm (PEComa) of the gynecologic tract: morphology, immunophenotype, differential diagnosis: morphology, immunophenotype, differential diagnosis. Internet *Am J Surg Pathol.* 2015;39(3): 394–404. https://doi.org/10.1097/PAS.0000000000000349.
9. Folpe AL, Goodman ZD, Ishak KG, et al. Clear cell myomelanocytic tumor of the falciform ligament/ligamentum teres: a novel member of the perivascular epithelioid clear cell family of tumors with a predilection for children and young adults. Internet *Am J Surg Pathol.* 2000;24(9):1239–1246. https://doi.org/10.1097/00000478-200009000-00007.
10. Czarnecka AM, Skoczylas J, Bartnik E, Świtaj T, Rutkowski P. Management strategies for adults with locally advanced, unresectable or metastatic malignant perivascular epithelioid cell tumor (PEComa): challenges and solutions. *Cancer Manag Res [Internet].* 2023;15:615–623. https://doi.org/10.2147/CMAR.S351284.