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### Bladder cancer

#### Case report

# Bladder perivascular epithelioid cell tumors



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#### KEYWORDS

Bladder;  
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cell sarcoma;  
Malignant;  
Cystectomy

#### Abstract

*Introduction:* Perivascular epithelioid cell tumors (PEComas) of the bladder are infrequent localisation of this mesenchymal cancer with uncertain malignant behavior.

*Case report:* We report the case of a 74 years old women who was diagnosed a malignant PEComa of the bladder. She necessitated radical cystectomy with orthotopic ileocaecal pouch reconstruction. Histology and immunohistochemistry confirmed the diagnosis of a malignant PEComa of the bladder. We evaluate the literature cases to adjust the prognosis criteria.

*Conclusion:* Evolution and prognosis evaluation remain hard and could necessitate a radical surgery. Prognosis criteria for the bladder PEComas have to be clarified.

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#### Introduction

Perivascular epithelioid cell sarcomas (PEComas) are a rare type of mesenchymal tumors with an unpredictable evolution. PEComas were introduced by Zamboni et al. [1] for mesenchymatous tumors that include angiomyolipoma, clear cell sugar tumor and lymphangiomyomatosis. These lesions have different clinical characteristics and appeared sporadically or in a Bourneville's tuberous sclerosis syndrome [1–3]. PEComas occur frequently in women between 50 and 60 years old. Soft tissues are the most common local-

ization but bones, lung, liver or urogenital organs can be affected [2–8].

PEComas are composed of epithelioid, fusiform, eosinophil or clear cell that express melanocytic or smooth muscular markers [1].

Despite improvement of diagnosis (histological and immunohistochemical criteria), evolution and prognosis evaluation remain hard. Analysis of literature review is difficult because of a small number of cases reported and the short time of follow-up. Most of the cases are benign but few cases of malignant PEComas have been described.

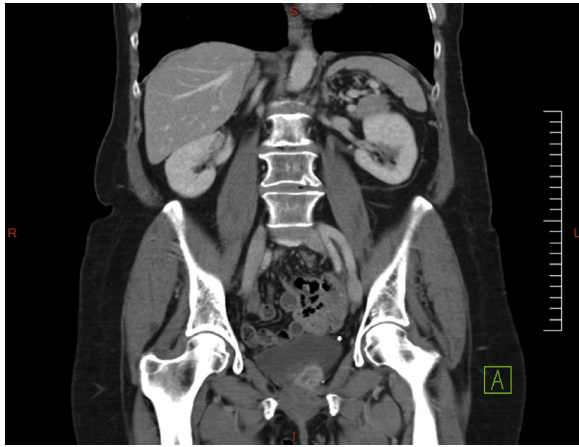
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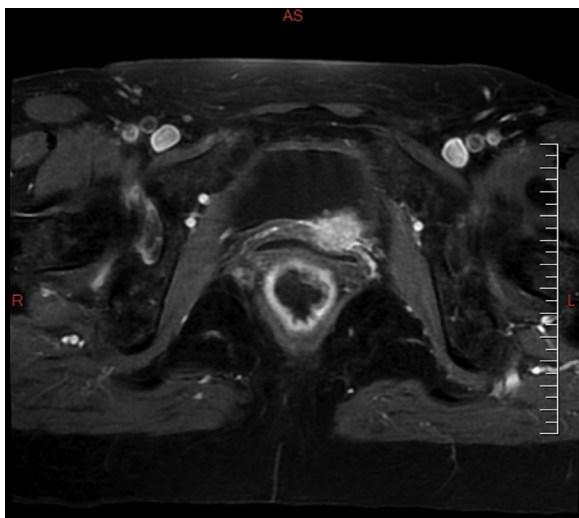
**Figure 1** Mass of the left-postero lateral wall of the bladder on CT-scan.

We report a case of a woman of 74 affected by a malignant PEComa of the bladder which was successfully treated by radical cystectomy.

### Case report

A 74-year-old woman had a single episode of hematuria, the urological tomodensitometry revealed a mass of the left-postero lateral wall of the bladder (Fig. 1). The cystoscopy confirms the presence of the 2-cm tumor, the cytology was normal. Pelvic MRI showed a 3-cm undefined lesion between vagina and bladder (Fig. 2).

Pathological examination of the bladder's transurethral resection revealed a neoplastic proliferation based on abundant cytoplasmic cells and vesiculous chromatin nucleus without necrosis or angio-invasion. Immunohistochemical studies were performed on formalin-fixed paraffin-embedded tissue using antibodies directed against Melan-A (A103, 1:25, Dako Agilent, Santa Clara, USA), HMB45 (HMB45, Dako, 1:50), smooth muscle  $\alpha$  actin (1A4, 1:50; Dako), desmin (NCL-*DER11*, prediluted, Ventana Roche Medical



**Figure 2** A 3 cm lesion between vagina and bladder on pelvic MRI.

Systems, Tucson, USA), pS-100 (EP-32, 1/400, Clinisciences, Nanterre, France), and TFE3 (MRQ-37, prediluted, Ventana Roche). Appropriate positive and negative controls were employed. This immunohistochemical study was realized on Ventana Roche Benchmark XT with an antigen retrieval process, in a EDTA citrate buffer (pH 8,3) during 30 mn or 60 mn depending of the antibodies (mild or standard cell conditioning, CC1, Ventana Roche), followed by incubation with the different antibody and via the ultraView Universal DAB Detection Kit (Ventana Roche).

These lesion invaded muscle and chorion but bladder mucosa seemed to be respected. Immunohistochemically, the tumor cells demonstrated strong positivity for HMB45 (cytoplasmic), CD68 (cytoplasmic) and TFE3 (nucleus) antibodies, with focal staining by desmin. The neoplastic cells failed to stain with antibodies against vimentin, Melan-A, PS100, smooth muscle actin and epithelial markers: diagnosis of PEComa with uncertain malignant potential was suggested (Fig. 3).

Radical cystectomy with orthotopic ileocaecal pouch reconstruction was performed without any complication and patient was discharged on day 10. Pathological examination confirmed PEComa diagnosis with positivity for HMB45 and TFE3 and negativity for Melan-A and Desmin. Mitotic rate (3/50 HPF) with abnormal mitotic figures, high nuclear grade and hyper cellularity were in favor of a malignant potential of this PEComa (Fig. 4).

### Discussion

The World Health Organization defines PEComas as mesenchymal tumors composed of histologically and immunohistochemically distinctive perivascular epithelioid cells [2]. Main differential diagnosis are renal carcinoma metastasis, adrenocortical carcinoma and epithelioid sarcomas.

While PEComas have been described many times in gynecologic tract, retroperitoneum, gastrointestinal tract, pancreas, liver, gallbladder, bones and soft tissues, oro-nasopharyngeal tract, pericardium, few publications reported it for urologic localization.

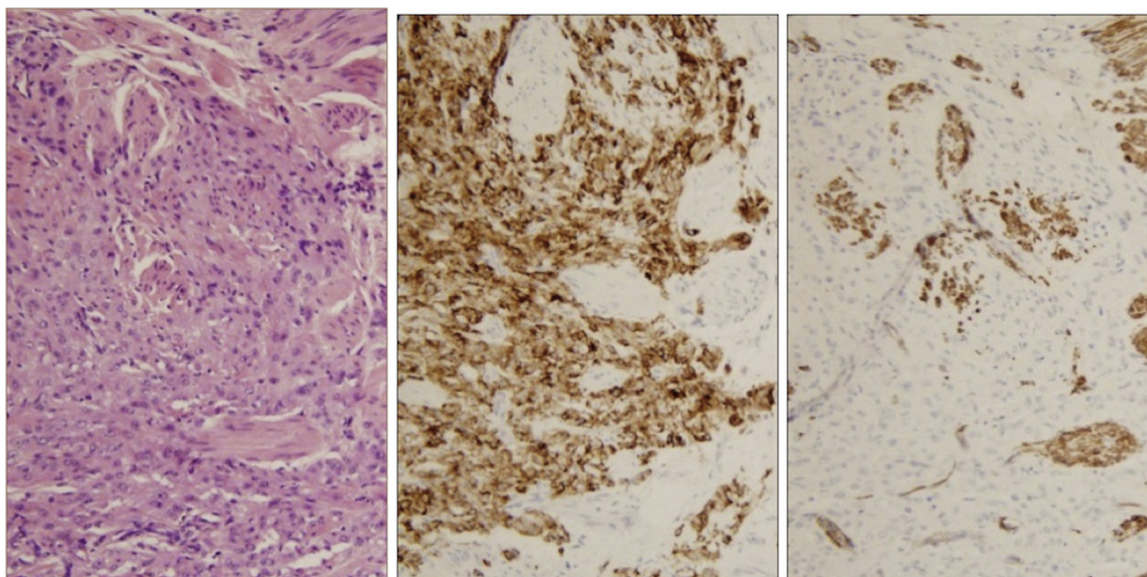
In the genitourinary tract, PEComas have been described in the kidney [9–13], bladder [7,13–25] (Table 1), prostate [7,25]. Clinical presentation of bladder PEComas are variable in the literature from abdominal pain to hematuria mimicking an urothelial carcinoma. Due to the lack of evidence proof and limited follow-up, it's hard to assess the prognosis of the bladder PEComa. While majority of the reported cases seemed to have benign behavior, some of them were aggressive tumors leading to local recurrences, metastasis and death of the patient, attesting the necessity of an accurate identification and therapeutic strategy.

Diagnosis of bladder PEComas is rare and may be underestimated because of a lack of awareness of both urologist and pathologist community. We think that this pathology has to be known as a differential diagnosis of urothelial carcinoma to allow a much more accurate treatment for the patient.

Patients' follow-up remains critical even after complete resection or benign tumor. In our opinion, bi-annual examination and thoracic-abdominal-pelvic computed tomography scan, associated with annual fibroscopy in case of conservative treatment, should be

**Table 1** Review of bladder PECOMA publications.

	Author	Title	Journal	Year	Number of patients	Type of publication
[7]	Pan CC	Clear cell myomelanocytic tumor of the urinary bladder.	Am J Surg Pathol	2003	1	Case report
[25]	Kalyanasundaram K	Perivascular epithelioid tumor of urinary bladder and vagina.	Ann Diagn Pathol	2005	1	Case report
[20]	Parfitt JR	Primary PEComa of the bladder treated with primary excision and adjuvant interferon-alpha immunotherapy: a case report.	BMC Urol	2006	1	Case report
[24]	Weinreb I	Perivascular epithelioid cell neoplasms (PEComas): four malignant cases expanding the histopathological spectrum and a description of a unique finding.	Virchows Arch Int J Pathol	2007	1	Case report
[21]	Sukov WR	Perivascular epithelioid cell tumor (PEComa) of the urinary bladder: report of 3 cases and review of the literature.	Am J Surg Pathol	2009	3	Case series
[13]	Wang G	Perivascular epithelioid cell tumor of urinary system: a clinicopathologic analysis of 21 cases.	Chinese Journal of Pathology	2012	1	Case report
[18]	Yin L	Perivascular epithelioid cell neoplasm of the urinary bladder in an adolescent: a case report and review of the literature.	Diagn Pathol	2012	1	Case report
[19]	Kyrou D	Bladder perivascular epithelioid cell tumor: a novel rare neoplasm.	Urol Int	2012	1	Case report
[23]	Shringarpure SS	PEComa of the urinary bladder.	Saudi J Kidney Dis Transplant	2012	1	Case report
[16]	Abou Ghaida R	Bladder perivascular epithelioid cell tumors.	BMJ Case Rep	2013	1	Case report
[17]	Williamson SR	Malignant perivascular epithelioid cell neoplasm (PEComa) of the urinary bladder with TFE3 gene rearrangement: clinicopathologic, immunohistochemical, and molecular features.	Am J Surg Pathol	2013	1	Case report
[22]	Sendo H	A case of gallbladder metastasis from a malignant perivascular epithelioid cell tumor of the bladder.	Jpn J Gastro-Enterol	2013	1	Case report
[14]	Tarplin S	Perivascular epithelioid cell tumor of the bladder.	BMJ Case Rep	2014	1	Case report
[15]	Russell CM	Perivascular epithelioid cell tumor (PEComa) of the urinary bladder associated with Xp11 translocation.	Ann Clin Lab Sci	2014	1	Case report



**Figure 3** Neoplastic cells positives to HMB45 markers and negatives for Caldesmon markers ( $\times 40$ ).

**Table 2** Folpe's classification of PEComas [27].

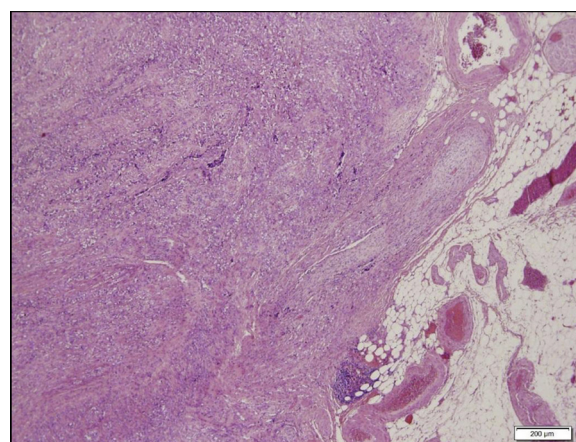
	Criteria	Percentage fulfilling criteria with aggressive behavior	Comment
Benign	No worrisome features ( $< 5$ cm, non-infiltrative, non-high nuclear grade and cellularity, mitotic rate $\leq 1/50$ HPF, no necrosis, no vascular invasion)	0 of 22 (22%)	
Uncertain malignant potential	1) Nuclear pleomorphism/multinucleated giant cells only or	1) 0 of 6 (0%)	1) "Symplastic" PEComa-probably benign, but few reported cases 2) Large tumors should be extensively sampled to exclude areas with other worrisome features
	2) Size $> 5$ cm only	2) 2 of 17 (12%)	
Malignant	Two or more worrisome features ( $> 5$ cm, infiltrative, high nuclear grade and cellularity, mitotic rate $\geq 1/50$ HPF, necrosis, vascular invasion)	12 of 17 (71%)	

provided during 5 years. However, pelvic MRI and bone scan should be reserved for elective suspicious cases.

Prognosis criteria proposed by Eken et al. [26] were based on soft tissues and gynecologic tract PEComas: size, infiltrative status, cellularity, mitotic rate, necrosis and vascular invasion (Table 2).

This classification seems to be inappropriate for bladder PEComas because of the risk of sub-staging. Despite a few number of reported case about aggressive PEComas, we think that the clinical presentation is a very important feature to presume of the behavior of the tumor: hematuria or indirect sign of fistula (digestive or gynecologic) may be a sign of aggressive trend (Table 3).

According to our experience and the literature, a size of tumor less than 5 cm does not presume of the benign behavior especially as hematuria was present. We believe that treatment of bladder PEComas have to be radical (partial or total cystectomy depending on tumor size) anytime behavior remains unclear, transurethral resec-



**Figure 4** Neoplastic infiltration into muscle and superficial perivesical fat, with perineural invasion ( $\times 40$ ).

**Table 3** Review of characteristics of aggressive bladder PEComas.

	Russel et al. [15]	Williamson et al. [17]	Parfitt et al. [20]	Our case
Clinical presentation	Hematuria	Hematuria	Enterovesical fistula	Hematuria
Size	4,2 cm	5 cm	3 cm	3 cm
Infiltrative status	+	+	+	+
Hyper-cellularity	+	+	—	+
Mitotic rate	3/50	2/10	Rare	1/50
Necrosis	—	+	+	+
Vascular infiltration	—	+	—	+

tion should be reserved for benign behavior (without any worrisome features).

### Conclusion

Perivascular epithelioid cell sarcomas constituted a heterogeneous family of tumors located in all the body. During the last 10 years, only 20 bladder PEComas were reported.

Evolution and prognosis evaluation remain hard and could necessitate a radical surgery.

Prognosis criteria for the bladder PEComas have to be clarified to adjust the treatment for this specific localization. Long time follow-up has to be reported to define the surveillance modalities.

### Conflict of interest

None.

### Authors' contributions

T. Tricard [ttricard@msn.com]: inception, write-up, structure, image collation, literature review, sub-mission.

S. Lopez [drsantiagolopez@gmail.com]: write-up, structure.

V. Lindner [veronique.lindner@chru-strasbourg.fr]: patient case report and management.

J-L. Jung [jeanluc.jung@ch-colmar.fr]: supervision and review.

### Consent from the patient

Attained.

### Source of funding

None.

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