

Primary perivascular epithelioid cell tumour (PEComa) of the prostate

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Abstract

Perivascular epithelioid cell tumours (PEComas) are a family of rare mesenchymal tumours arising in various anatomic locations. PEComas are defined by the presence of perivascular epithelioid cells that coexpress muscle and melanotic markers, especially HMB-45. They have unpredictable biological behaviour and are mostly benign, but some tumours can become unresectable or metastatic. Surgical resection, when possible, is the best treatment option. Radiation therapy, cytotoxic chemotherapy or immunotherapy have been reported as treatment options, either alone or in combination therapy. Prostatic PEComa is extremely rare, with only 1 malignant case reported. We report the first case of prostatic PEComa, which was benign and treated with transurethral resection.

Introduction

The World Health Organization defines PEComas as mesenchymal tumours composed of histologically and immunohistochemically distinctive perivascular epithelioid cells (PECs).¹ PEComas are rare mesenchymal neoplasms, chiefly composed of HMB-45–positive epithelioid cells with clear to granular eosinophilic cytoplasm and a round-to-oval centrally located nucleus. PEComas show immunoreactivity for both melanocytic (HMB-45 and/or melan-A) and myoid (actin and/or desmin) markers and negative for epithelial markers.^{1,2} In recent decades, these tumours have been described in virtually all body sites. We describe a prostatic PEComa in a 36-year-old male.

Case report

A 36 year-old-male came to the urology clinic with a 2-month history of frequent urination, hesitancy and drib-

bling without hematuria or dysuria. His general physical examination was unremarkable. His hemogram, urine and blood biochemical analyses were within normal ranges. The rectal examination revealed prostatic enlargement of grade 3/4. The International Prostate Symptom Score (IPSS) score was 27 and uroflowmetry showed an 11 mL/sn average flow rate, 16 mL/sn maximum flow rate (Qmax), and 80 mL residual urine. Ultrasound demonstrated prostatic enlargement (60 cc). Cystoscopy demonstrated only left prostatic lobe enlargement with increased vascularization, which was closing the urethral lumen. Subsequently, the patient underwent laser prostatectomy. The operation was completed with transurethral resection because the bleeding could not be controlled with laser coagulation.

Histopathologic examination revealed a neoplasm that had diffusely invaded the lamina propria and muscularis propria (Fig. 1, Fig. 2). The tumour was composed of mainly epithelioid and spindle cells with abundant clear-to-eosinophilic granular cytoplasm, distinct cell borders, and round nuclei with occasional nucleoli (Fig. 3). The spindle cells, resembling smooth muscle cells, had abundant clear cytoplasm and were arranged in a storiform pattern. The epithelioid cells, with abundantly clear eosinophilic cytoplasm and apparent nucleoli, were mostly arranged as small nests commonly related to variably sized vessels. A thin vascular stroma was present among the tumour nests. Mitotic activity, vascular invasion and necrosis were not identified. An accompanying conventional prostatic carcinoma was not observed. Malignant melanoma, clear cell sarcoma, clear cell carcinoma, paraganglioma and prostatic tumours were included in the differential diagnosis and an immunohistochemical panel was performed for this purpose.

The immunohistochemical analysis was carried out on paraffin sections by using Ventana-Benchmark XT (Ventana Medical Systems, Inc., Tucson, AZ) technique. The primary antibodies used included HMB45, Melan-A, S-100 protein, smooth muscle actin (SMA), CD68, synaptophysin (Syn), chromogranin-A, pancytokeratin, PSA and vimentin. Tumour

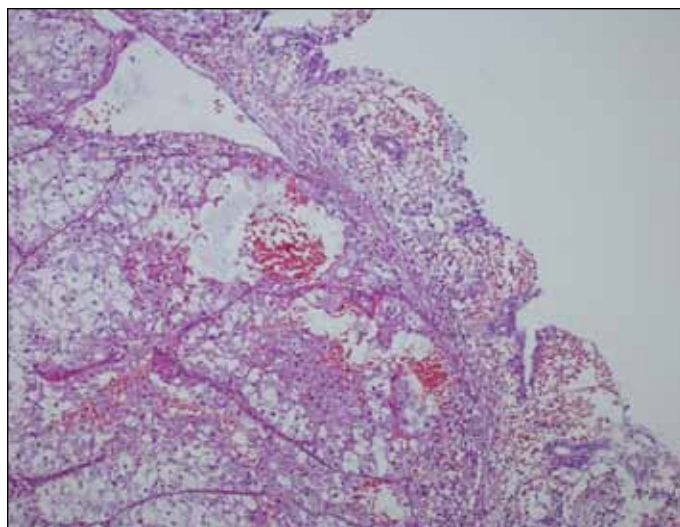


Fig. 1. Tumour under the epithelium of prostatic urethra (hematoxylin and eosin stain $\times 40$).

cells were positive only for HMB45, and the staining pattern was diffuse (Fig. 4). The tumour tested negatively for all other antibodies. The patient was diagnosed with prostatic PEComa, on the basis of the above histopathological and immunohistochemical features.

Subsequent transurethral resection was performed 2 weeks later and the last pathological examination revealed coagulative necrosis and granulation without perivascular epithelioid cells. Routine follow-up procedures included rectal examination, computed tomography of the pelvis and cystoscopy. There was no recurrence. The patient was clinically free of disease 30 months after surgery.

Discussion

PEComas with perivascular epithelioid cell differentiation are in a family of related mesenchymal neoplasms, which includes angiomyolipoma, lymphangiomyomatosis, clear cell "sugar" tumour of the lung, clear-cell myomelanocytic tumour of the falciiform ligament/ligamentum teres and a group of immunopheno-typically similar lesions arising in a variety of visceral and soft tissue sites.^{1,2} Bonetti and colleagues first proposed a cellular link among these mesenchymal lesions, solidifying acceptance of the concept of the perivascular epithelioid cell (PEC).²

These tumours all include epithelioid to spindle cells with a clear to granular cytoplasm, a round to oval, centrally located nucleus, and an inconspicuous nucleolus. Immunohistochemically, coexpression of melanocytic (HMB45, Melan-A, tyrosinase) and myoid (smooth muscle actin, desmin) markers.³ Our case showed strong and diffuse staining for only HMB-45 in the spindle and epithelioid cell components.

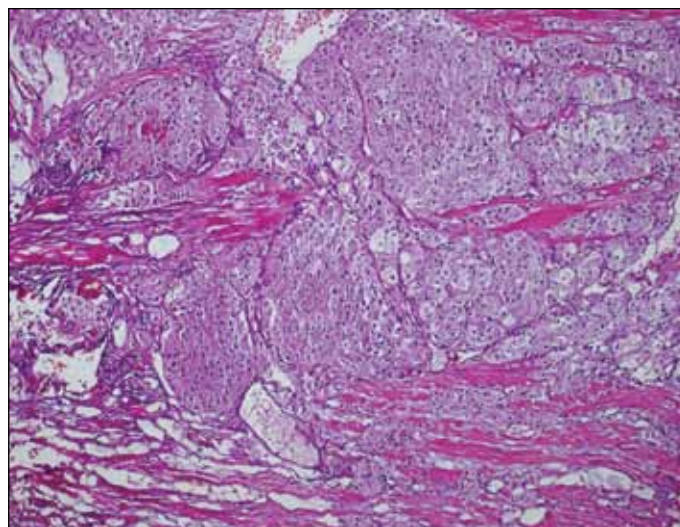


Fig. 2. Tumour diffusely invaded the muscularis propria, showing solid nested growth (hematoxylin and eosin stain $\times 100$)

Pathologically, the main differential diagnoses includes clear cell sarcoma of soft parts (CCSSP), paraganglioma, melanoma, metastatic carcinoma (especially from the kidney or adrenal gland), other epithelial tumours with clear cell morphologic features, and epithelioid smooth muscle tumours.⁴ The vascular stroma and perivascular arrangement of epithelioid cells in PEComa are not common features of clear cell sarcoma of soft parts, and nearly all CCSSPs are positive for S100 protein.^{3,4} In our case, the absence of expression of epithelial markers and the positive expression of HMB-45 meant that we excluded carcinoma and smooth muscle tumour from the diagnosis.

About 15 cases of lower urinary tract PEComas have been described.⁵ In 2003, Pan and colleagues⁶ reported the first prostatic PEComa. The tumour was composed of a variable percentage of epithelioid and spindle cells with clear to granular cytoplasm arranged in nests separated by a vascular stroma. Immunohistochemically, the tumour was typically positive for HMB-45 and negative for epithelial markers, vimentin and S100 protein. The prostatic tumour showed low mitotic activity, coagulative necrosis and malignant behavior. On the contrary, in our benign case, the tumour did not show mitotic activity, coagulative necrosis, or vascular invasion. The tumour in our case was evidently benign according to the malignant criteria described by Folpe and colleagues.⁴

The optimal treatment for PEComas is not known at this time. Primary excision, the main treatment, is usually curative.⁷ However, locally advanced or metastatic disease portends a poor prognosis, and strategies incorporating chemotherapy (dacarbazine, vincristine and imatinib mesylate), radiation and immunotherapy have been reported.^{4,8,9} Since PEComa can be aggressive, careful follow-up is recommend-

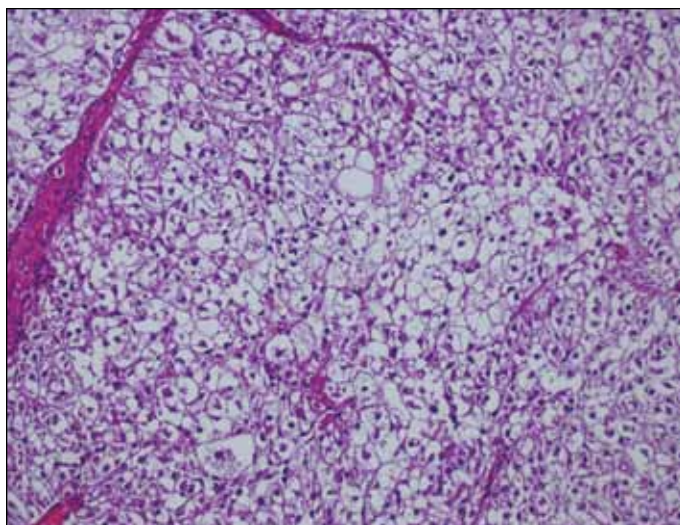


Fig. 3. Tumour cells with distinct bordered clear cytoplasm and santral nuclei (hematoxylin and eosin stain $\times 200$).

ed. In the future, new targeted therapies may emerge as definitive treatments for localized aggressive and metastatic PEComa. We have demonstrated the second case of PEComa of the prostate, but it is also the first one of its kind to display benign behaviour.

Conclusion

We report the first case of benign prostatic PEComa with long-term follow-up. Most of the lesions were benign, although some tumours revealed malignant morphology with an aggressive clinical course, including distant metastases. No effective medical treatment has been reported for patients with advanced disease. Further studies on additional cases with longer term follow-up periods are necessary to accurately predict the biologic behaviour and optimal treatment of these tumours.

Competing interests: Dr. Eken and Dr. Saglican declare no competing financial or personal interests.

This paper has been peer-reviewed.

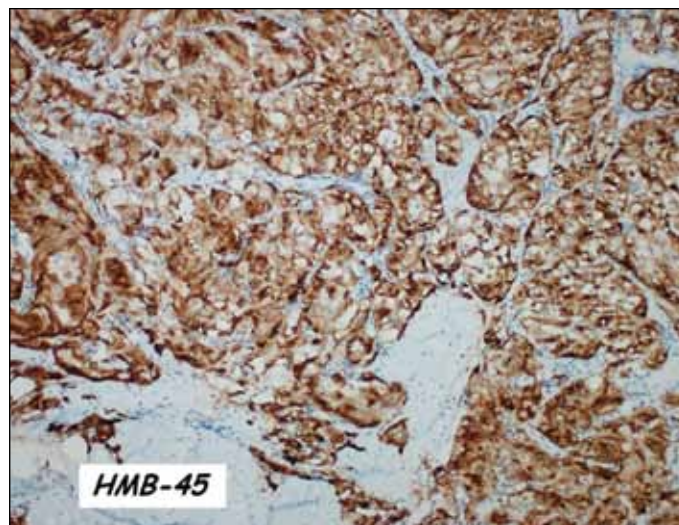


Fig. 4. Diffuse positivity with HMB-45 in tumour cells ($\times 200$).

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