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CASE REPORT

Malignant PEComa of the lumbar vertebra: a rare bone tumour

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Abstract We describe the case of a 26-year-old patient with a perivascular epithelioid cell tumour (PEComa) involving the 5th lumbar vertebra. Radiological findings, pathological features and treatment are presented. We conclude that PEComas should be considered in the differential diagnosis of vertebral lesions.

Introduction

Perivascular epithelioid cell tumours (PEComas) are uncommon mesenchymal tumours composed of distinctive perivascular epithelioid cells [1]. They arise in different soft tissues and visceral organs [2]. PEComas presenting in bone are especially rare [3]. We describe the case of a 26-year-old patient with a PEComa involving the 5th lumbar vertebra.

Case report

An otherwise fit and well 26-year-old gentleman was referred with a 2 month history of progressively worsening lower back pain radiating to his left leg, associated with recent left leg weakness. There were no bowel or bladder symptoms. On examination, there was a tender soft tissue swelling in the left posterior paravertebral region. Muscle power and sensation were reduced in the L5/S1 distribution of the left lower limb.

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MRI demonstrated a large, heterogeneous destructive lesion arising from the left side of the L5 vertebra, which involved the left pedicle and neural exit foramen. The entire L5 vertebra was involved with collapse of the left side of the body and a small extradural extension, which was not causing any significant thecal sac compression (Fig. 1). Anteriorly, the tumour extended to the upper aspect of the left sacroiliac joint laterally and into the retroperitoneum, almost reaching the anterior abdominal wall. Post-contrast CT demonstrated peripheral enhancement and extensive necrosis within the centre of the extra-osseous tumour mass (Fig. 2). The overall features were suggestive of a malignant process.

However, an ultrasound-guided biopsy suggested a tumour with possible nerve sheath differentiation, and although there was cellular atypia, the tumour was not clearly malignant. Therefore, an open biopsy followed by debulking of the posterior paravertebral mass was performed. On histological examination, the tumour was composed of large epithelioid cells with abundant clear and eosinophilic cytoplasm, showing a predominantly nested architecture and delicate arborising capillaries. The tumour showed a permeative growth pattern and entrapped host bone (Fig. 3a). Mitoses were difficult to identify and tumour necrosis was not a feature. Immunohistochemistry showed scattered nests of tumour strongly positive for HMB45 (Fig. 3b), and very focally positive for S100. The other markers tested were all negative, including Melan-A, SMA, desmin, chromogranin, synaptophysin, CD31, CD117, EMA and cytokeratins (MNF116 and AE1–AE3). Based on the morphological features and the immunoprofile, a diagnosis of a malignant perivascular epithelioid cell tumour was proposed. To exclude a clear cell sarcoma and an alveolar soft part sarcoma,

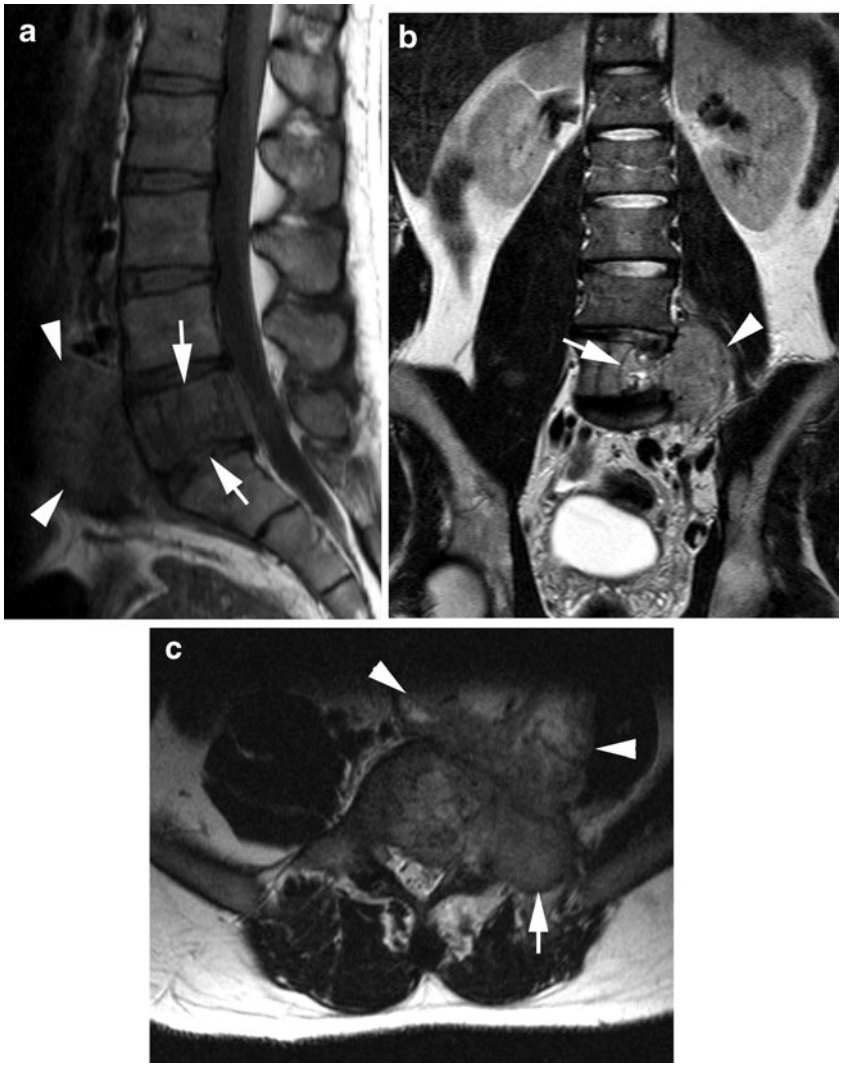

Fig. 1 MRI of the lumbar spine. **a** Sagittal T1W SE MR image showing complete infiltration of the L5 vertebral body (*arrows*), with a small extradural extension and a very large pre-vertebral soft tissue mass (*arrowheads*). **b** Coronal T2W FSE MR image showing collapse of the left half of the vertebral body (*arrow*) with an extra-osseous mass (*arrowhead*) lying deep to the left psoas muscle. **c** Axial T2W FSE MR image showing expansion of the left transverse process (*arrow*) and the large pre-vertebral mass (*arrowheads*)

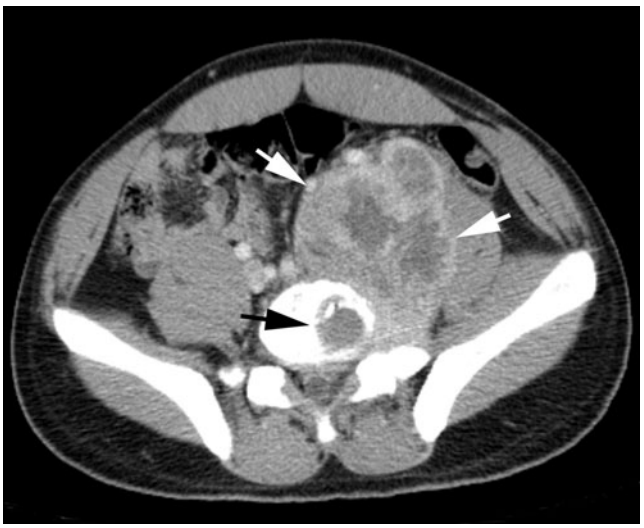

Fig. 2 Axial CT study showing lytic destruction of the left side of L5 (*black arrow*) with a huge anterior extra-osseous mass (*white arrows*) which shows extensive necrosis

molecular assays were performed. In this regard, an *EWSR1* gene rearrangement was not identified on interphase FISH, and no *ASPSCR1-TEF3* hybrid gene was detected by RT-PCR, virtually excluding a clear cell sarcoma and an alveolar soft part sarcoma respectively.

On the basis of these findings, a staging CT scan was performed which demonstrated bilateral pulmonary nodules in keeping with metastases. A subsequent bone scan showed increased activity related to the left side of the L5 vertebra which was in keeping with the primary abnormality. A further focus of increased activity was identified in the left anterior superior iliac spine and was suspicious for bony metastasis.

Due to the extensive anterior disease, and the presence of metastases, a curative surgical procedure was not an option. Therefore, the patient underwent posterior lumbar decompression and stabilisation with cement augmentation of the L5 vertebra.

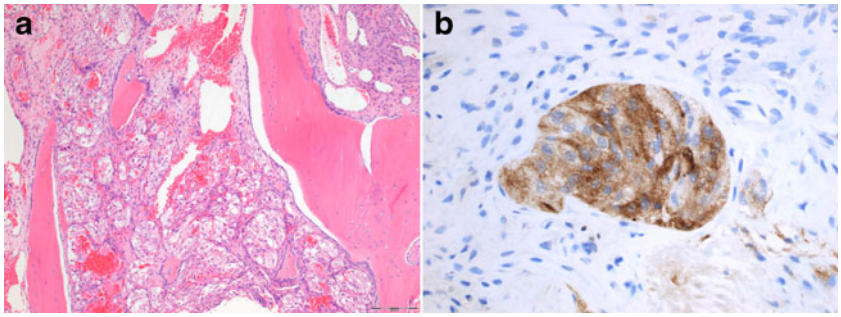

Fig. 3 Histology. **a** Haematoxylin and eosin section (×40 total magnification) showing a tumour composed of nests of polygonal cells infiltrating bone. **b** A nest of tumour cells immunoreactive for the melanocytic marker HMB-45

Discussion

Malignant perivascular epithelioid cell tumour (PEComa) is a very rare entity which predominantly affects young adults and female individuals [4]. It is composed of distinctive perivascular epithelioid cells with variable immunoreactivity for melanocytic and muscle markers [5]. PEComas include clear cell "sugar" tumour of the lung and extrapulmonary sites, angiomyolipoma, clear cell myomelanocytic tumour of the falciform ligament/ligamentum teres and rare lymphangioleiomyomatosis-like tumours [6].

At present, this neoplasm does not have a known normal cellular counterpart, and the natural history is often unpredictable [7]. Treatment modalities are still controversial, particularly in advanced conditions. Surgical resection, however, represents the most curative approach for primary PEComa at presentation as well as for local recurrence and metastasis, as chemotherapy and radiotherapy have not demonstrated significant benefits [8, 9]. Only recently, limited clinical studies have reported encouraging results in terms of therapeutic response after oral administration of mTOR inhibitor in patients with metastatic PEComa [10].

PEComas have been identified at multiple anatomic sites and are considered ubiquitous tumours. Different organs such as the liver [7], uterus [11], vulva [12], rectum [13], heart [14], breast [15], urinary bladder [16], abdominal wall [17], pancreas [18] and cheek [19] have been involved, and the disease has been associated with few, if any symptoms, though abdominal pain and bleeding have been reported [4, 20, 21]. PEComas might often be misdiagnosed with hepatocellular carcinoma, haemangioma, focal nodular hyperplasia, gastrointestinal stromal tumours, melanoma, clear cell sarcoma and leiomyosarcoma [22]. A well-defined pre-operative diagnosis is difficult to make because of non-specific radiological features, and CT is uninformative regarding any tumour characteristics. Pre-operative needle biopsy might overcome this limitation, but the data from current clinical practice suggest that the diagnosis of PEComa is usually confirmed after surgery [4]. The biological behaviour of PEComa is variable, with some patients developing metastases or local recurrence. The mortality rate from the tumour is high [23].

In 1992, Bonetti proposed the concept of perivascular epithelioid cells (PECs), and the term PEComa was first introduced by Zamboni in 1996 [20]. Only in 2003, after initial scepticism, the World Health Organization defined PEComas as mesenchymal tumours [24]. One hypothesis is that the neoplasm derives from undifferentiated cells of the neural crest with smooth muscle and melanocytic phenotype; a second hypothesis is that PEComa has a myoblastic, smooth muscle origin, while a third suggests a pericytic origin [21].

Immunohistochemistry-supported histology techniques are required to make the correct diagnosis. Recently, Folpe and colleagues have suggested criteria for malignancy, including a size greater than 5 cm, mitotic count of more than 1 per 50 high-power fields and necrosis [24]. In some conditions, PEComas can show pronounced muscle features, and in others they can exhibit more epithelioid morphology with strong positivity for HMB45 and weak or focal expression for SMA [7]. CD31 positivity in the cellular membrane of PECs has been documented in a subset of malignant PEComas, termed "PEComas not otherwise-specified" [8]. PEComa of the liver is extremely unusual, and there are about 10 cases in the literature [25]. The right lobe of the liver is the most common site, and all cases occurred adjacent to the ligamentum teres and falciform ligament [4].

PEComa involving the bones is rare. There are in total six cases reported [3], two in the tibia and one each in a thoracic vertebra, the scapula and femur. The sixth case was reported in the humerus, but it was not certain whether it was a primary lesion of the bone or a secondary deposit from a uterine PEComa.

To our knowledge, this is the first case report in the literature of a PEComa involving the lumbar vertebra and the second case involving the vertebral column. Although rare, PEComas should be considered in the differential diagnosis of vertebral lesions.

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Conflict of interest The authors declare that they have no conflict of interest.

References

1. Folpe AL. Neoplasms with perivascular epithelioid cell differentiation (PEComas). In: Flectcher CDM, editor. World Health Organization classification of tumours: pathology and genetics of soft tissue and bone. Lyon: IARC Press; 2002. p. 221–2.
2. Pea M, Bonetti F, Martignoni G, et al. Apparent renal cell carcinomas in tuberous sclerosis are heterogeneous: the identification of malignant epithelioid angiomyolipoma. Am J Surg Pathol. 1998;22:180–7.
3. Yamashita K, Fletcher CD. PEComa presenting in bone: clinicopathologic analysis of 6 cases and literature review. Am J Surg Pathol. 2010;34(11):1622–9.
4. Priola AM, Priola SM, Cataldi A, Marci V, Fava C. Acute abdomen as an unusual presentation of hepatic PEComa. A case report. Tumori. 2009;95:123–8.
5. Martignoni G, Bonetti F, Chilosi M, Brunelli M, Segala D, Amin MB, Argani P, Eble JN, Gobbo S, Pea M. Cathepsin K expression in the spectrum of perivascular epithelioid cell (PEC) lesions of the kidney. Mod Pathol. 2011;25:100–11.
6. Martignoni G, Pea M, Reghellin D, Gobbo S, Zamboni G, Chilosi M, Bonetti F. Molecular pathology of lymphangioleiomyomatosis and other perivascular epithelioid cell tumors. Arch Pathol Lab Med. 2010;134:33–40.
7. Selvaggi F, Risio D, Claudi R, Cianci R, Angelucci D, Pulcini D, D'Aulerio A, Legnini M, Cotellese R, Innocenti P. Malignant PEComa: a case report with emphasis on clinical and morphological criteria. BMC Surg. 2011;11:3.
8. Armah HB, Parwani AV. Perivascular epithelioid cell tumor. Arch Pathol Lab Med. 2009;133:648–54.
9. Hornick JL, Fletcher CDM. PEComa: what do we know so far? Histopathology. 2006;48:75–82.
10. Wagner AJ, Malinowska-Kolodziej I, Morgan JA, Qin W, Fletcher CDM, Vena N, Ligon AH, Antonescu CR, Ramaiya NH, Demetri GD, Kwiatkowski DJ, Maki RG. Clinical activity of mTOR inhibition with sirolimus in malignant perivascular epithelioid cell tumors: targeting the pathogenic activation of mTORC1 in tumors. J Clin Oncol. 2010;28(5):835–40.
11. Yamada Y, Yamamoto H, Ohishi Y, Nishiyama K, Fukuhara M, Saitou T, Tsuneyoshi M, Oda Y. Sclerosing variant of perivascular epithelioid cell tumor in the female genital organs. Pathol Int. 2011;61:768–72.
12. Mentzel T, Reisshauer S, Rütten A, Hantschke M, de Almeida LM Soares, Kutzner H. Cutaneous clear cell myomelanocytic tumour: a new member of the growing family of perivascular epithelioid cell tumours (PEComas). Clinicopathological and immunohistochemical analysis of seven cases. Histopathology. 2005;46(5):498–504.
13. Ryan P, Nguyen VH, Gholoum S, Carpineta L, Abish S, Ahmed NN, Laberge JM, Riddell RH. Polypoid PEComa in the rectum of a 15-year-old girl: case report and review of PEComa in the gastrointestinal tract. Am J Surg Pathol. 2009;33(3):475–82.
14. Tai Y, Wei L, Shi H. Perivascular epithelioid cell tumor of the heart in a child. Pediatr Dev Pathol. 2010;13(5):412–4.
15. Govender D, Sabaratnam RM, Essa AS. Clear cell 'sugar' tumor of the breast: another extrapulmonary site and review of the literature. Am J Surg Pathol. 2002;26(5):670–5.
16. Chan AW, Chan CK, Chiu Y, Yip SK, Lai FM, To KF. Primary perivascular epithelioid cell tumour (PEComa) of the urinary bladder. Pathology. 2011;43(7):746–9.
17. Luo DL, Liu YH, Zhuang HG, Luo XL. Tumors showing perivascular epithelioid cell differentiation: a clinicopathologic study of 39 cases. Zhonghua Yi Xue Za Zhi. 2007;87(41):2909–13.
18. Nagata S, Yuki M, Tomoeda M, Kubo C, Yoshizawa H, Kitamura M, Uehara H, Katayama K, Nakayama H, Okamoto Y, Hanaki H, Kido S, Ichiki T, Tomita Y. Perivascular epithelioid cell neoplasm (PEComa) originating from the pancreas and metastasizing to the liver. Pancreas. 2011;40(7):1155–7.
19. Ghazali N, Cascarini L, Norris P, Barrett AW, Lavery KM. Perivascular epithelioid cell tumor (PEComa) of the cheek. Oral Surg Oral Med Oral Pathol Oral Radiol Endodontol. 2010;110(1):e26–31.
20. Baek JH, Chung MG, Jung DH, Oh JH. Perivascular epithelioid cell tumor (PEComa) in the transverse colon of an adolescent: a case report. Tumori. 2007;93:106–8.
21. Martignoni G, Pea M, Reghellin D, Zamboni G, Bonetti F. PEComas: the past, the present and the future. Virchows Arch. 2008;452:119–32.
22. Genevay M, Mc Kee T, Zimmer G, Cathomas G, Guillou L. Digestive PEComas: a solution when the diagnosis fails to “fit”. Ann Diagn Pathol. 2004;8:367–72.
23. Peng J, Yu B, Wang J, Hong X, Xu Y, Cai S. An unresectable malignant perivascular epithelioid cell tumor resistant to multiple combined chemotherapies: a unique case report. J Pediatr Hematol Oncol. 2010;32(4):136–8.
24. Folpe AL, Kwiatkowski DJ. Perivascular epithelioid cell neoplasms: pathology and pathogenesis. Hum Pathol. 2010;41:1–15.
25. Parfitt JR, Bella AJ, Izawa JI, Wehrli BM. Malignant neoplasm of perivascular epithelioid cells of the liver. Arch Pathol Lab Med. 2006;130:1219–22.