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*Case Report*

# Primary perivascular epithelioid cell neoplasm of thigh bone: a case report and literature review

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**Abstract:** Primary perivascular epithelioid cell tumor neoplasm (PEComa) of bone is extremely rare. To our knowledge, only 11 cases of PEComa primarily arising in bone have been described. Herein, we present one case of primary bone PEComa which occurs in the thigh.

**Keywords:** Primary perivascular epithelioid cell tumor neoplasm, bone, diagnosis, differential diagnosis

## Introduction

Perivascular epithelioid cell tumor neoplasms (PEComas) are rare mesenchymal tumors composed of histologically and immunohistochemically distinctive perivascular epithelioid cells. PEComas other than angiomyolipoma (AML), clear cell "sugar" tumor (CCST) of the lung, lymphangioleiomyomatosis (LAM) are exceedingly rare. To our knowledge, only 11 cases of PEComas occurring in bone have been reported in the published literature. In this report, we describe one additional case of primary PEComa of bone occurring in the right thigh and also review the literature.

## Case report

A 65-year-old man presented to the hospital with a six-month history of progressive right knee pain and swelling in April, 2013. Physical examination showed a swelling, tender mass over the distal end of the right thigh. Magnetic resonance imaging (MRI) of the right knee revealed an expansile lytic lesion involving the distal metaphysis and epiphysis with soft tissue expansion (**Figure 1**). No other mass was found but the right thigh by subsequent systematic examinations including whole body positron emission tomography (PET)/CT. Laboratory tests demonstrated no abnormalities. Surgical excision was recommended and the patient received a wide resection of the distal right thigh and reconstruction of the right knee joint without adjuvant chemotherapy or radiation therapy. After 28-month follow-up, the patient remains disease free.

Grossly, the tumor which emanated from the right thigh, measured 11.5 cm × 8.6 cm × 7.5 cm. The cut surface was gray-tan solitary nodular mass without fibrous capsule. Histologically, the tumor was composed of nests of epithelioid and spindle shaped cells resembling smooth muscle arrayed around thin-walled blood vessels. The tumor cells have clear to granular, lightly eosinophilic cytoplasm, with a moderate degree of nuclear atypia including occasional cells showing nulceomegaly with prominent nucleoli. A few multinucleated giant cells were also observed. Mitoses were present occasionally with mitotic rate under 1/50 high power fields (**Figure 2**). Immunohistochemistry (IHC) revealed the tumor cells were positive for smooth muscle actin (SMA), epithelial membrane antigen (EMA), HMB45 and Melan-A, whereas negative for desmin, S-100 protein, CD34, CD117, Dog-1, CD68, and cytokeratin (AE1/AE3). Ki-67 was positive in 3% of tumor cells (**Figure 3**). Based on pathomorphologic, immunohistochemical features and the clinical findings, the mass on the right thigh was diagnosed as PEComa arising in bone.

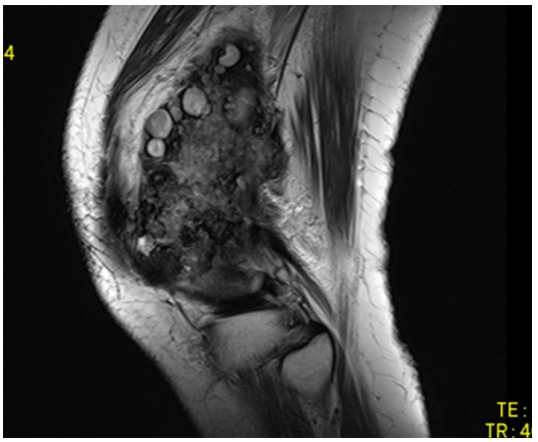


**Figure 1.** Magnetic resonance images showing a large mass in the right knee with cortical destruction and soft tissue expansion.

## Discussion

Primary PEComas of bone are extremely rare tumors. In 2002, Insabato [1] first reported one case of PEComa arising in bone; so far only 11 cases have been reported in the English literature. The clinicopathogical features of the 12 cases including our case are summarized in **Table 1**, including 7 male and 5 female patients, with the mean age of 47.1 years old (range 26~92 years). The primary tumor site includes 3 cases in the right proximal tibia [1, 2], 3 in the right fibula [3-5], 1 in the left femur [6], 1 in the right sixth rib [7], 1 in the seventh thoracic vertebra [2], 1 in the fifth lumbar vertebra [8], 1 in the left acetabulum [5], and 1 in the right thigh (our case). Epithelioid perivascular cells which exhibited characteristic nesting or organoid arrangement were observed in all 2 cases. Of 12 cases, 5 cases were composed of epithelioid cells, 5 were composed of both epithelioid cells and spindle cells, 1 case was composed of both epithelioid cells and clear cells, and 1 was composed of epithelioid cells, spindle cells and clear cells. Furthermore, 3 cases were considered as benign [1, 2, 5], 1 case was considered as malignant potential [7]. The remaining 8 cases including our case were considered as malignant [2, 3, 6, 7, 9, 10]. IHC showed that 5 cases were positive for HMB45 and negative for Melan-A, 1 case positive for Melan-A and negative for HMB45, 9 cases positive for Desmin and SMA, and 2 case positive for SMA and positive for Desmin. Nine cases received surgical excision, whereas 2 cases only underwent adjuvant chemotherapy and radiation therapy without surgical excision due to diffuse metastases of tumor. Two cases died of pelvic and lung metastasis at 12 and 8 months, respectively, after surgical excision. Six cases were free of disease during the 3, 12, 24, 34, 36, and 28 months, respectively, of follow-up. In the other 3 cases, the follow-up was not reported. In the present case, the patient was not treated with chemotherapy or radiation therapy after surgery. He was free of disease at 28 months after surgery, and is undergoing followed-up.

As mentioned above, presentation of PEComa of bone is very rare, so the diagnosis of primary PEComa of bone should first rule out the metastasis PEComa, and need to identify with the following tumor: metastatic clear cell carcinoma, metastatic malignant melanoma, epithelioid leiomyosarcoma, clear-cell sarcoma of soft tissue, alveolar soft part sarcoma (ASPS), and epithelioid extra-gastrointesinal stromal tumor (extra-GIST). Metastatic clear cell carcinoma always shows epithelial membrane antigen and keratin positivity except for negative of melanocytic markers. Malignant melanoma usually shows S-100 protein strong positivity and negative of myogenic markers in most cases. In addition to the morphologic differences, epithelioid leiomyosarcoma could be distinguished from PEComa by negative for melanocytic markers. Clear-cell sarcoma of soft tissue exhibits dense fibrous septae rather than the delicate vascular-rich stroma of the PEComa. In addition, Clear-cell sarcoma of soft tissue always shows S-100 protein positivity, which is usually negative in PEComa. The absence of melanocytic markers in ASPS could be helpful for distinguished with PEComa. Epithelioid extra-GIST is easily distinguished from PEComa by positive for CD117, Dog-1, and CD34 and negative for melanocytic markers.

In 2005, Folpe et al. [11] proposed the diagnostic criteria of PEComas which were classified into “benign”, “uncertain malignant potential”, and “malignant”. In that study, the diagnostic criteria of PEComas was mainly based on tumor size greater than 5 cm, infiltrative growth pattern, necrosis, high cellularity, high-nuclear grade, and mitotic activity greater than 1/50 HPF and subsequent aggressive clinical behavior. It was suggested that malignant PEComas

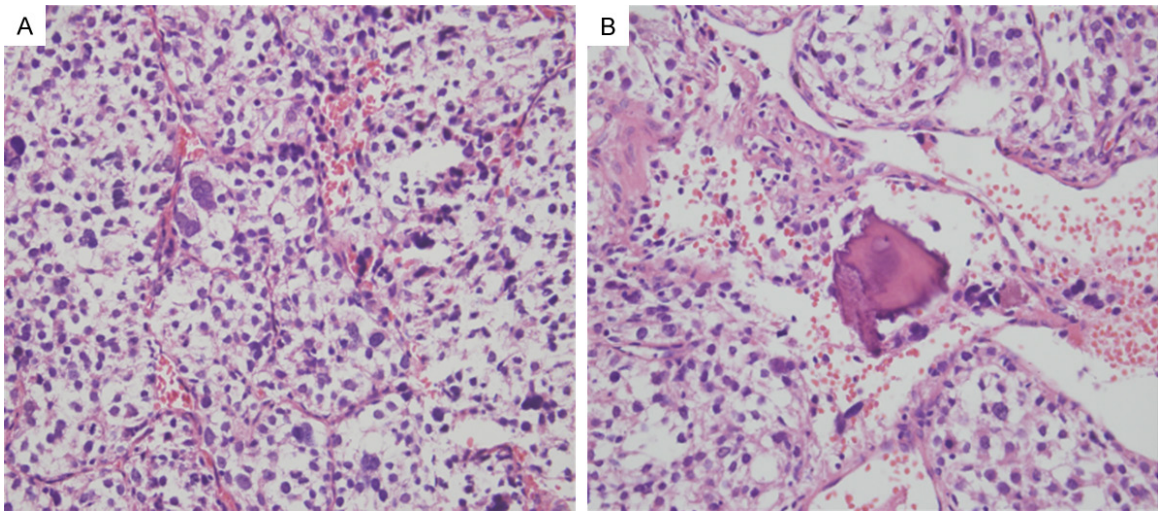


**Figure 2.** Biopsies of Tumor. A. Epithelioid cells arranged in nested architecture with delicate, arborizing capillaries. A few multinucleated giant cells were also observed (hematoxylin and eosin, × 100). B. The lesion shows local invasion of host bone (hematoxylin and eosin, × 100).

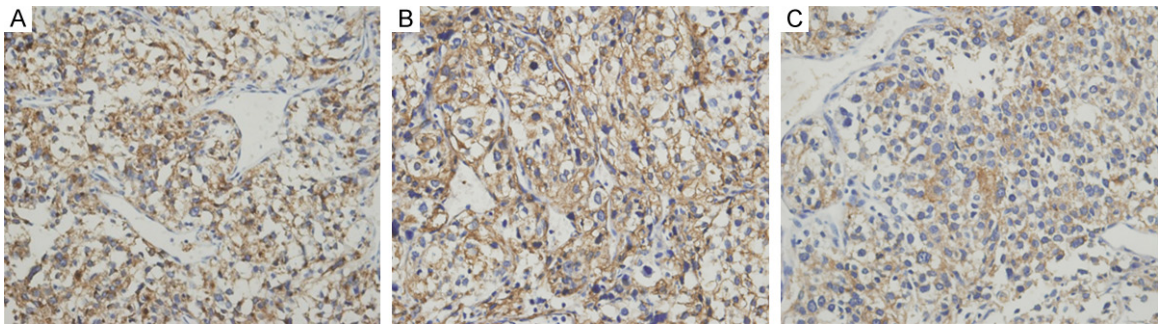


**Figure 3.** IHC assay. A. Neoplasm cells are positive for HMB45 (EnVision × 100). B. Neoplasm cells are positive for SMA (EnVision × 100). C. Neoplasm cells are positive for EMA (EnVision × 100).

should include 2 or more these worrisome features mentioned above. According to the above diagnostic criteria, it seems that our case should be considered as a malignant PEComa arising in the thigh.

However, of 12 cases, 2 cases with benign histologic features occurred metastasis [2, 5]. One case with very small tumor displayed malignant biological behavior [2]. One case only received a local resection which displayed malignant morphological, was free of disease at 12 months after surgery [1]. In our case, fulfilled the morphological criteria for malignancy proposed by Folpe et al. The patient only received a wide resection of the distal right thigh without adjuvant chemotherapy or radiation therapy. After 28 months of follow-up, the patient remains disease free. Since PEComas is extremely rare, its biological behavior remains largely unknown. As mentioned above, primary PEComas of bone with a benign appearance could present metastasis, while those with a malignant morphology could free of disease long time. We suggest that a long-term follow-up should be carried out for patients with primary PEComas of bone, even if when the lesion shows a “benign morphology”. Identification of the accurate assessment of biological behavior criteria of this disease must be determined on the basis of more patient cases accumulation.

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**Table 1.** Clinicopathogical features of 12 cases of primary bone PEComa

| Reference | Age (y)/Sex | Site | Size (cm) | Histology | IHC | Treatment | Follow-up |
|---|---|---|---|---|---|---|---|
| 1 | 30/M | Right proximal tibia | 2 | Epithelioid | HMB-45 | Local resection | 12-months well |
| 3 | 52/F | Right midshaft fibula | 6.3 | Epithelioid | HMB-45, CyclinD1 | Wide excision | 3-months well |
| 7 | 28/M | Right 6th rib | 2 | Epithelioid, Clear cells, Spindle cells | HMB-45, SMA | Complete resection | Not reported |
| 4 | 92/F | Right fibula | Not reported | Epithelioid | HMB45, CD10, TFE3 | Local resection | Not reported |
| 2 | 35/M | 7th thoracic vertebra | 1.8 | Epithelioid, Spindle cells | HMB45, Melan-A, SMA | Chemo-radiotherapy | 12-months pelvic bone metastases |
| 2 | 39/F | Right proximal tibia | 6.5 | Epithelioid, Spindle cells | HMB45, Melan-A, SMA | Local resection, radiotherapy | 34-months well |
| 2 | 48/F | Right distal tibia | Very small | Epithelioid, Spindle cells | HMB45, Melan-A, SMA | Excisional biopsy, amputation | Recurred 3 times in three years |
| 5 | 29/M | Left acetabulum | 5 | Epithelioid, Spindle cells | Melan-A, Desmin, Vimentin | Left hemipelvectomy, temsirolimus | 8-months died, Lung metastases |
| 5 | 93/F | Right distal fibula | Not reported | Epithelioid | HMB45 | Local resction | 24-months well |
| 8 | 26/M | 5th lumbar vertebra | Large | Epithelioid | HMB45, S-100 | Conservative | Not reported |
| 6 | 47/M | Left femur | 5.2 | Epithelioid, Clear cells | HMB45, PNL, TEF32 | Curettage, Chemo-radiotherapy | 42-months lung metastases |
| Our case | 65/M | Right distal thigh | 11.5 | Epithelioid, Spindle cells | HMB45, Melan-A, SMA | Wide excision | 28-months well |

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## Disclosure of conflict of interest

None.

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