Case Report
Expression of epithelial markers in PEComa of sacral ligament: a potential diagnostic pitfall

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Abstract: Perivascular epithelioid cell neoplasm/tumor (PEComa) was a relatively uncommon lesion of mesenchymal origin characterized by perivascular epithelioid cells with distinctive histological and immunohistochemical features. The occurrence in the sacral ligament was exceptional rare. Cytokeratin and epithelial membrane antigen (EMA) were considered as commonly useful epithelial markers to distinguish epithelial from mesenchymal tumor, but the expression of cytokeratin and EMA had also been seen in some mesenchymal tumor. Here, we presented an unusual case of PEComa of sacral ligament positive for cytokeratin and EMA, which was misdiagnosed as carcinoma. Our case suggested that the epithelial markers (including cytokeratin and EMA) show an overlap with that of PEComa, which represented a diagnostic pitfall for confusing PEComa with carcinoma.

Keywords: PEComa, carcinoma, mesenchymal tumor

Introduction

Cytokeratins are proteins of keratin-containing intermediate filaments which are useful markers for epithelial cells, previous studies have shown that cytokeratin can also been expressed in tumors of mesenchymal origin tumor such as epithelioid sarcoma, epithelioid angiosarcoma [1], mesothelioma, synovial sarcoma [2], osteosarcoma [3], interstitial reticulum cell sarcoma [4] and chordoma [5]. In this paper, we reported a case of CK (pan)-positive PEComa in sacral ligament, which was misdiagnosed as carcinoma of sacral ligament.

Case description

A 52-year-old Chinese woman presented with enlarged mass of sacral ligament without other systemic symptoms for 2 months. Physical examination: the enlarged mass is about 5.5 cm in diameter, with smooth surface, clear boundary and medium texture. The patient had no fever, no night sweat and no rash on body. Serum tumor markers including carbohydrate antigen 125 (CA125), carbohydrate antigen 19-9 (CA19-9) and carcinoembryonic antigen (CEA) were all within the normal range.

Immunohistochemical studies

The biopsy specimen was fixed in 10% buffered formalin solution and embedded in paraffin, sectioned at 4 µm, and stained with hematoxylin and eosin. Immunohistochemical staining was performed by using the streptavidin-peroxidase system (Ultrasensitive, MaiXin Inc, Fuzhou, China) according to the manufacturer’s instruction. Heat-induced epitope retrieval was performed. The following antibodies (MaiXinInc, China, prediluted) were used: Cytokeratin (pan), EMA, S-100, HMB45, MelanA, Desmin, Actin (SMA), CD34, Vimentin and the Ki-67. Positive and negative controls were evaluated appropriately for each procedure.

Pathological findings

The patient was diagnosed as mass of sacral ligament and a sacral ligament mass biopsy was carried out. Hematoxylin and eosin sections showed that the larger more round tumor cells with an ‘empty’ (glycogen-rich) cytoplasm...
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or an eosinophilic, epithelioid appearance. Tumor cells can have large, hyperchromatic nuclei with prominent nucleoli (Figure 1A). Immunohistochemical stainings showed that the tumor cells were positive for cytokeratin (Figure 1B), EMA (Figure 1C), HMB45 (Figure 1D), MelanA (Figure 1E), Desmin and vimentin, but negative for SMA (Figure 1F), p63, S-100 and CD34. The Ki-67 labeling index was about 20%. The tumor cells showed some similar characteristics of carcinoma and expression of epithelial cells marker. Therefore, the patient was initially diagnosed as metastatic carcinoma of sacral ligament and then was referred to the department.

Figure 1. Morphological change and immunohistochemical staining of the tumor (Original magnification ×100). A. The tumor cells are epithelioid with moderate clear cytoplasm and vesicular nuclei. B. The tumor cells were diffuse expression of cytokeratin. C. The tumor cells were diffuse expression of EMA. D. The tumor cells were diffuse and strong expression of HMB45. E. The tumor cells were diffuse and strong expression of MelanA. F. Tumor cells were entirely negative for Actin (SM).
of oncology to search for the origin. Because non-malignant tumors were found in other organs by PET-CT scan, the oncologist advised a revision of the pathological diagnosis.

Revision was performed in the Department of Pathology in The First Affiliated Hospital of China Medical University. The hematoxylin and eosin-stained sections showed that the atypical tumor cells were large size, with abundant clear cytoplasm, cell nuclear was enlarged and round, hyperchromatic nuclei, and prominent smaller eosinophilic nucleoli. The revision confirmed that the specimen was positive for cytokeratin and EMA with a cytoplasm positive staining, the infiltrated cells had a strong positive reaction to HMB45 and MelanA. P63 was negative. Based on the morphologic and immunophenotypic findings, we concluded that this was a PEComa of sacral ligament.

Discussion

Recent studies showed that the expression of cytokeratin had also been seen in some tumors of non-epithelial origin such as epithelioid sarcoma, epithelioid angiosarcoma [1], mesothelioma, synovial sarcoma [2], osteosarcoma [3], interstitial reticulum cell sarcoma [4] and chordoma [5]. Here, we reported a case of CK (pan)-positive PEComa in sacral ligament. While both PEComa and carcinoma express cytokeratin (pan), therefore, cytokeratin and EMA immunohistochemical studies could not be utilized as markers to distinguish PEComa from carcinoma.

Morphologically, the epithelioid appearance is another deceptive feature of PEComa, while this is also a typical appearance of carcinoma or melanoma. If the neoplastic cells are epithelioid or spindle cells arranged around vascular channels, and with moderate clear cytoplasm and vesicular nuclei, it suggests the possibility of PEComa. In this case, we need to detect HMB45 and MelanA to confirm the diagnosis of PEComa.

According to Folpe AL [6], the majority of PEComa have a relatively better clinical course. However, if the tumor shows tumor size >5.0 cm, infiltration, high nuclear grade, increased cellularity, mitotic activity (>1 mitosis per 50 HPF) and tumor necrosis, it may have a more aggressive course. In our case, because of the extensive presence of atypical epithelioid cells and tumor size >5.0 cm and relative high ki67 index, we diagnosed it as an “uncertain malignant potential” PEComa. Our patient is on periodic follow-up for the last 18 months and remains asymptomatic.

In addition, the differential diagnosis also includes some other tumors which can possess epithelioid or spindle cells, such as: clear cell sarcoma, clear cell carcinoma, conventional melanoma, epithelioid smooth muscle neoplasm, endometrial stromal sarcoma, gastrointestinal stromal tumor and paraganglioma. Based on the classic histologic structure and immunostaining, the correct diagnosis can be made. Tumor cells are positive for melanocytic markers, namely HMB45, MelanA and smooth muscle actin (SMA). Our case demonstrated the characteristic histological features along with HMB45 and MelanA positivity confirming the diagnosis of PEComa. But actin (SMA) is not positive in our case. According to Sundram U [7], smooth muscle marker negative do not exclude the diagnosis of PEComas. It is essential for using a panel of antibodies to make the correct diagnosis.

In summary, this case was misdiagnosed with carcinoma because of the positive immunoreaction toward epithelial cells markers. However, the presence of HMB45 and MelanA, p63 negative confirms the diagnosis of PEComa. This case emphasizes that epithelial markers (CK and EMA) expression can be a potential pitfall for confusing PEComa with carcinoma.

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Disclosure of conflict of interest

None.

Authors' contribution

WLJ and ZQF participated in the histopathological evaluation, performed the literature review,
acquired photomicrographs and drafted the manuscript. JAL carried out the immunohistochemical stains evaluation. QXS conceived and designed the study. SLM gave the final histopathological diagnosis and revised the manuscript. All the authors read and approved the final manuscript.

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References


[7] Sundram U, Harvell JD, Rouse RV, Natkunam Y. Expression of the B-cell proliferation marker MUM1 by melanocytic lesions and comparison with S100, gp100 (HMB45), and MelanA. Mod Pathol 2003; 16: 802-10.