HMB-45 Negative Clear Cell Perivascular Epithelioid Cell Tumor of the Skin

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SUMMARY
The first case of cutaneous clear cell perivascular epithelioid cell tumor (PEComa) with negative HMB-45 marker is presented. The tumor was a nodule 3x2 cm in size, located on the right foot in a 60-year-old man. The lesion consisted of large irregularly shaped cells with clear cytoplasm, negative for S-100 protein, HMB-45, Melan-A, pancytokeratin, epithelial membrane antigen and CAM5.2. Multifocal positivity for desmin, microphthalmia transcription factor and tyrosinase was found. The diagnosis of cutaneous PEComa of clear cell type was made. Clear cell change is a very unusual finding in PEComa and may pose problems in diagnostic differentiation from other clear cell cutaneous lesions that may be excluded with immunohistochemistry. In our case, the HMB-45 negativity may be explained by extensive clear cell change. Additional studies are necessary to accept the clear cell cutaneous HMB-45 negative PEComa as a new variant of perivascular epithelioid cell tumor.

KEY WORDS: perivascular epithelioid cell tumor, clear cell cutaneous tumor, immunohistochemistry

INTRODUCTION

The perivascular epithelioid cell tumor (PEComa) is a family of related mesenchymal tumors that includes angiomyolipoma of the kidney and liver, lymphangiomatosis, lymphangiomyoma, and a group of uncommon tumors that arise in soft tissue, visceral organs, skin and clear cell ‘sugar’ tumor of the lung (1-3). Similar tumors within the spectrum of PEComa have been reported under several different names including “clear cell myomelanocytic tumour”, “abdominopelvic sarcoma of perivascular epithelioid cells”, and “primary extra-pulmonary sugar tumor” (4,5). Nearly all PEComas display dual expression of melanocytic (HMB-45, Melan A, NKIC3, microphthalmia transcription factor, tyrosinase) and smooth muscle (actin, desmin, caldesmon, calponin) markers. The morphologic spectrum of PEComa ranges from primary spindle cell tumors, purely epithelioid tumors with clear, palely eosinophilic or granular cytoplasm to PEComas with notable pleomorphism or marked stromal sclerosis. Clear cell change is a very unusual finding of PEComa and may pose problems in diagnostic differentiation from other clear cell cutaneous lesions (6). Immunohistochemistry may have a very important role in the exact identification of the tumor, but immunohistochemical results may be variable. We report a case of cutaneous PEComa diffusely composed by HMB-45 negative clear cells and we discuss the immunohistochemical features of the lesion.
CASE REPORT

A 60-year-old man presented a nodule 3x2 cm in size on the right foot that had persisted for 6 months. It was excised and one year later, there was no evidence of recurrence or metastatic disease. Microscopically, the tumor consisted by a small exophytic intradermal lesion composed of large irregularly shaped cells with clear cytoplasm (Fig. 1). There was no evidence of epidermal origin or any junctional component. However, the lesion had a well-formed epidermal collarette. The neoplastic cells were of variable size and had plump but quite uniform vesicular nuclei. The tumor cells were negative for S-100 protein, HMB-45, Melan-A, pancytokeratin, epithelial membrane antigen (EMA) and CAM5.2. There was some unspecific positivity for both CD68 and NKI-C3. Multifocal positivity for desmin (Fig. 2) as well as for microphthalmia transcription factor (MITF) was found (Fig. 3). A deep tumoral rim was composed of epithelioid cells around small vessels. The appearance of the lesion was suggestive for a cutaneous PEComa for clear cell type.

DISCUSSION

PEComas are now recognized at ubiquitous anatomic locations, are most often benign and show a marked female predominance, with a predilection for the retroperitoneum, pelvis, uterus and abdomen (7). The extensive clear cell change of PEComa is typical of clear cell sugar tumor. According to our knowledge, only one cutaneous case of this tumor has been previously reported by de Saint Aubain Somerhausen et al. (8). In the study of ten primary cutaneous PEComas, Liegl et al. (4) defined “clear cell tumor” as a distinctive lesion. These authors describe two cases with purely epithelioid morphology that showed clear to palely eosinophilic cytoplasm. The remaining cases with epithelioid and mixed epithelioid and spindle cell morphology showed variably clear or granular eosinophilic cytoplasm. In our case, the clear cell change was extensive and problems in diagnostic differentiation from other clear cell cutaneous lesions were evident. Among melanocytic markers, HMB-45 is the most sensitive. It was expressed in 100% of primary cutaneous PEComas reported in the literature (4). Melan-A has been reported to be positive in as many as 72% of cases and MITF was strongly expressed in most cases reported. Desmin appears to be the most sensitive muscle cell marker, present in as many as 50% of lesions (4). It is evident that immunohistochemistry has a very important role in the
identification of clear cell PEComas. A combination of melanocytic markers including HMB-45, Melan A, S-100, MITF, smooth muscle markers such as desmin, caldesmon, calponin, and epithelial markers such as cytokeratins and EMA are useful for the differential diagnosis. The possibility that our case might represent a balloon cell melanoma or metastatic carcinoma was essentially excluded by the fact that tumor cells were negative for S-100 protein, HMB-45, Melan-A, pancytokeratin, EMA and CAM5.2. There was some unspecific positivity for both CD68 and NKI-C3. The most important findings were multifocal positivity for desmin as well as nuclear positivity for MITF, indicating that the appearance was diagnostic for a cutaneous PEComa of clear cell type. The negativity of HMB-45 was surprising. Positive staining for this marker is variable. In the study of thirteen PEComas with extensive stromal hyalinization, Hornick and Fletcher (9) report that all tumors were positive for HMB-45 only in scattered cells. In four PEComas examined by Liegl et al. (4), HMB-45 was positive in fewer than 5% of tumor cells. In our case, the HMB-45 negativity could be explained with the extensive change of clear cells that has not been reported in the English literature on cutaneous PEComa.

CONCLUSIONS

In the identification of PEComa, MITF might have a diagnostic value if HMB-45 results negative. However, additional studies are necessary to accept the clear cell cutaneous PEComa with negative HMB-45 marker as a new variant of perivascular epithelioid cell tumor.

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References