

CLINICAL REPORT

Eccrine Porocarcinoma with Bowenoid Changes: Epithelial Membrane Antigen is Not a Useful Marker for Malignant Tumours Arising from Eccrine Gland Structures

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A case of eccrine porocarcinoma with Bowenoid changes is reported. We compared the results of immunohistochemical staining for epithelial membrane antigen in the present case with results in Bowen's disease to determine whether the presence of epithelial membrane antigen (EMA) enabled us to differentiate between Bowen's disease and eccrine porocarcinoma with Bowenoid changes. Histologically, the present tumour was characterized by atypical clear cells with Bowenoid changes as well as uniform small cells and intradermal nests with ductal structures. The membrane and cytoplasm of uniform small cells and ductal luminal surfaces were positive for EMA. However, the atypical cells with Bowenoid changes were negative for this. In contrast, tumour cells in Bowen's disease were positive for EMA. Although EMA is known to be a useful marker for some benign tumours derived from eccrine ducts, we found it difficult to distinguish eccrine porocarcinoma with Bowenoid changes from Bowen's disease using immunohistochemical staining for EMA. **Key words:** *Bowen's disease; eccrine porocarcinoma; epithelial membrane antigen.*

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Bowenoid pattern of tumour cells is not an uncommon feature of eccrine poroma and eccrine porocarcinoma (1–3). Here, we present a case of eccrine porocarcinoma with Bowenoid changes. We assessed the usefulness of immunostaining for epithelial membrane antigen (EMA), a tumour marker preferentially expressed in glandular epithelium (4–6), in differentiating between Bowen's disease and eccrine porocarcinoma with Bowenoid changes.

CASE REPORT

A 70-year-old woman had a 2-year history of a slowly growing tumour on her left thigh. Physical examination revealed a slightly elevated 7 × 12-mm reddish nodule (Fig. 1). Initial diagnosis was Bowen's disease.

Histopathological findings showed that the tumour consisted of 4 types of cells. First, variously sized atypical cells with large hyperchromatic nuclei and occasional mitotic figures were present in all epidermis that exhibited hyperkeratosis (Fig. 2a). Although there was no individual cell keratinization, some of these cells had clusters of nuclei, which is a characteristic feature of Bowen's disease. Second, there were tumour cells with atypical nuclei and abundant clear cytoplasm (Fig. 2b). Periodic acid-Schiff (PAS)-positive, diastase-labile deposits of glycogen were found in the cytoplasm of these cells. Third, there was an aggregation of small clear cells with uniform small nuclei (Fig. 2b). None of these 3 types of tumour cells formed duct-like structures. However, the fourth type, atypical cells with faintly eosinophilic cytoplasm, formed nests that were scattered in the upper dermis and formed ductal structures. In addition, the cells in these nests had small cavities in their cytoplasm (Fig. 3a). The ductal structures and small cytoplasmic cavities were positive for carcinoembryonic antigen (CEA) (rabbit anti-human CEA Ab, 1:400, DAKO, Glostrup, Denmark) (Fig. 3b). These features are consistent with malignant tumours derived from acrosyringium, particularly eccrine porocarcinoma. To further confirm that the tumour originated from eccrine gland structures, immunohistochemical staining for EMA (mouse anti-human EMA monoclonal Ab, clone E29, 1:100, DAKO) was performed. The membrane and cytoplasm of small uniform clear cells in the epidermis were positive for EMA, as were the



Fig. 1. Clinical appearance of the tumour on the thigh.

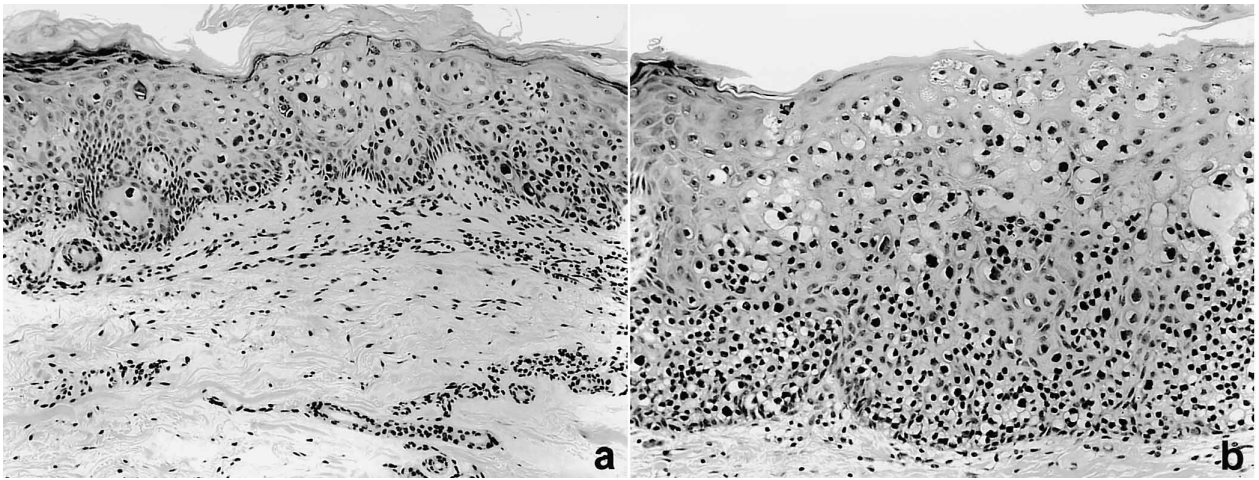


Fig. 2. Histological features of the tumour. (a) Part of the tumour showed Bowenoid changes ($\times 200$). (b) Clear cells in the tumour. In the upper part of the epidermis, there were atypical cells of different sizes with abundant clear cytoplasm. In the lower epidermis, proliferation of small uniform clear cells was observed ($\times 400$).

lining of ductal lumina and the small cavities of tumour nest cells in the dermis (Fig. 4a). However, neither the tumour cells with Bowenoid changes nor the atypical large clear cells were positive for EMA.

DISCUSSION

Eccrine porocarcinoma is a rare tumour that develops primarily in the intraepithelial ductal portion of the eccrine sweat gland (7). Differential diagnosis of eccrine porocarcinoma requires distinguishing from a variety of benign and malignant tumours. The epidermal change must be distinguished from hydroacanthoma simplex, Bowen’s disease, squamous cell carcinoma *in situ* and Paget’s disease. Our case is eccrine porocarcinoma with Bowenoid changes, in which ductal lumina and small

cytoplasmic cystic cavities were only observed in the tumour nests that invaded the dermis. The diagnosis of eccrine porocarcinoma was based on the presence of CEA on the luminal surface of the ducts and in the small cytoplasmic cystic cavities in the dermal tumour nests. To confirm that the present tumour was derived from eccrine gland structures, we used anti-EMA monoclonal antibody to assay for EMA. However, EMA was only expressed in small uniform clear cells in the epidermis and the tumour nests in the dermis (Fig. 4a).

EMA is a 265-kD to 400-kD glycoprotein that was first isolated from human milk fat globule membranes. EMA is present on the luminal membranes of normal glandular epithelia. Adenocarcinomas from various primary sites contain EMA (5). In normal skin, eccrine, apocrine and sebaceous glands are positive for EMA, but squamous

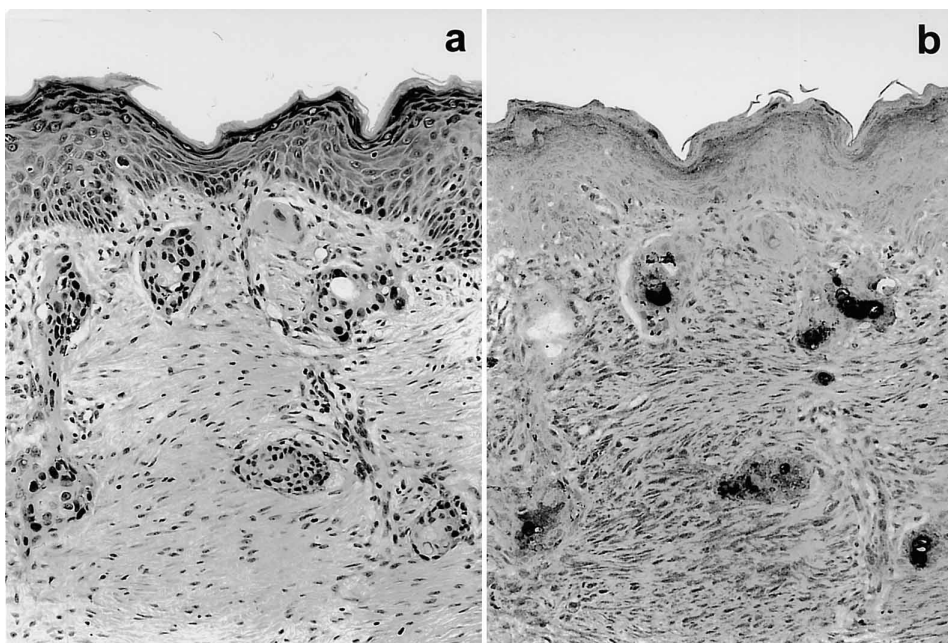


Fig. 3. Invasive tumour nests in the dermis. Atypical tumour cells in the dermis formed ductal structures or contained small cavities in their cytoplasm (a). The small cavities and the luminal surface of the ducts were positive for CEA (b) ($\times 100$) (ABC method).

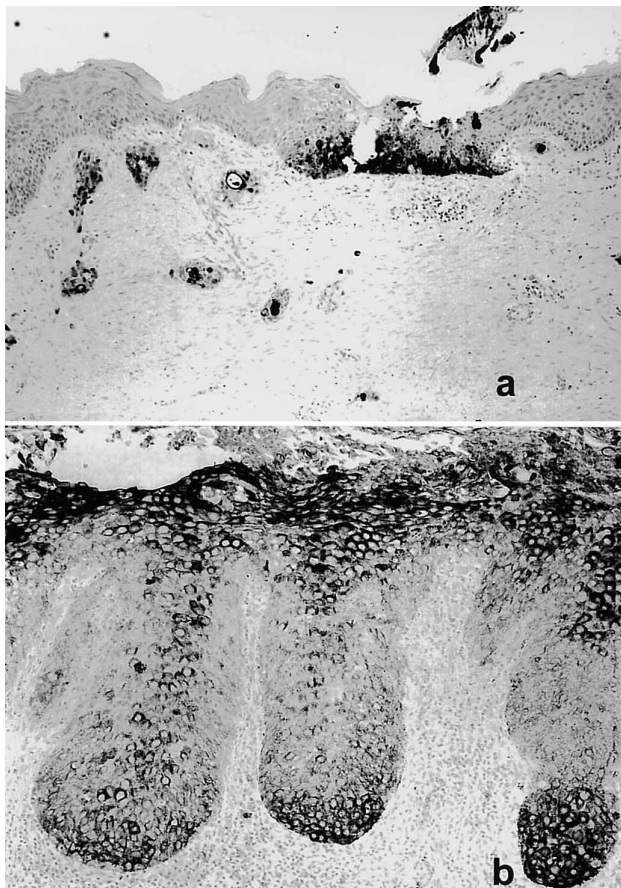


Fig. 4. Immunolocalization of EMA (ABC method). (a) EMA reactivity was observed on the membrane and in the cytoplasm of small uniform cells, but not in atypical clear cells or cells with Bowenoid changes. The luminal surface of dermal tumour nests was also positive for EMA ($\times 100$). (b) Representative result of EMA staining for 5 cases of Bowen's disease. Strong EMA staining on the membrane and weak staining in the cytoplasm was observed ($\times 200$).

epithelium is negative (6, 8). The outer cells of both the intraepidermal and upper portion of intradermal eccrine ducts contain EMA, as do the luminal surfaces and intercellular canaliculi of eccrine glands (9). These findings are consistent with reports that benign tumours derived from eccrine gland structures are positive for EMA (8, 9). Studies have found that eccrine poroma is positive for EMA not only on the luminal surface of ductal structures but also in the cytoplasm and on the plasma membrane of tumour cells (8, 9).

To determine whether EMA staining enables differentiation between Bowen's disease and eccrine porocarcinoma with Bowenoid changes, we compared results of immunohistochemical staining in the present case with results for 5 cases of Bowen's disease. Three of the 5 cases of Bowen's disease were positive for EMA, which was consistent with the previous report (10). There was a strong positive reaction in the lower epidermis in 2 cases, and in the entire epidermis in one case (Fig. 4b). These data suggest that transformed keratinocytes are capable of expressing EMA. This is further supported by evidence

that superficial layers of squamous cell carcinoma express EMA (4). In contrast, it appears that EMA expression in the cytoplasm and on the plasma membrane but not luminal surfaces of ductal structures is lost during malignant transformation of eccrine gland structures, as indicated by comparison of EMA staining between eccrine poroma (8), and the present eccrine porocarcinoma. This is in striking contrast to the finding that almost all adenocarcinomas including metastatic lesions from breast, stomach, pancreas and colon are positive for EMA (5).

In eccrine porocarcinomas, the rates of recurrence and lymph node metastasis are 11.7% and 9.6%, respectively (11). Thus, it is important to make a correct diagnosis and differentiate between Bowen's disease, Bowen's carcinoma and eccrine porocarcinoma with Bowenoid changes. Although EMA is a useful marker of some benign tumours from eccrine gland structures (8), eccrine porocarcinoma with Bowenoid changes cannot be differentiated from Bowen's disease by immunohistochemical staining for EMA.

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