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CASE REPORT

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Malignant myoepithelioma of the breast metastasizing to the jaw

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Abstract A breast tumor in a 52-year-old female was interpreted as a malignant myoepithelioma based on morphological and immunohistochemical studies. The tumor consisted of elongated cells with clear cytoplasm and lacked glandular components. The tumor cells were stained positively for keratin, S-100 protein, glial fibrillary acidic protein (GFAP) and muscle-specific actin. Distant metastasis in the right jaw developed 8 years after the initial surgery and the metastatic deposit showed a similar morphology and immunoreactivity. Myoepithelial tumors are generally considered as benign or low-grade lesions and distant metastasis has been rarely documented. The present case presents the possibility of delayed occurrence of distant metastasis in myoepithelial tumor of the breast.

Key words Breast neoplasms · Malignant myoepithelioma · Metastasis · Immunohistochemistry

Introduction

Myoepithelial lesions of the breast have been recognized as a distinct entity only recently, although similar tumors are well known to occur in salivary glands. A comprehensive survey of related histopathological changes revealed that a variety of lesions, including myoepitheliosis, adenomyoepithelioma and malignant myoepithelioma (myoepithelial carcinoma) can in fact develop in the mammary glands [8]. The latter is composed purely of myoepithelial cells. Such tumors are generally considered as benign or low grade, and there have only been four reports of malignant myoepitheliomas accompanied by distant metastasis. Herein, we report one case of a metastasis in the right jaw 8 years after excision of the initial tumor.

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Clinical history

A 52-year-old woman was evaluated in May 1991 for a nodule in her right breast. She had noticed the lesion more than 10 years previously, but only presented at hospital because of recent rapid enlargement. A lumpectomy was performed. The preoperative diagnosis was fibroadenoma, which subsequently changed to fibrous lesion on pathological examination. The postoperative course was unremarkable, and she was discharged 2 weeks after the surgery.

In May 1998, she noted a hard mass in the right jaw. Roentography revealed an osteolytic lesion in the angle. The mass was treated by local excision. A histopathological examination, with a review of the previous breast mass, was performed and a histological diagnosis of malignant myoepithelioma of the breast with metastasis to the jaw was established. Postoperative systemic computed tomography (CT) scans failed to demonstrate any other metastatic lesions.

Materials and methods

All specimens were fixed in 10% formalin. Paraffin-embedded blocks and sections were routinely prepared and stained with hematoxylin and eosin. For immunohistochemistry, the streptoavidin-biotin technique was used with a panel of commercially available antisera: S-100a protein (polyclonal; dilution 1:200), α-smooth muscle actin (monoclonal; dilution 1:100), glial fibrillary acidic protein (GFAP, monoclonal; dilution 1:100), GFAP (polyclonal; dilution 1:500), vimentin (monoclonal; dilution 1:50), keratin (polyclonal; dilution 1:300), high-molecular-weight cytokeratin (34βE12, monoclonal; dilution 1:100), and epithelial membrane antigen (EMA; monoclonal; dilution 1:100) (all antibodies purchased from Dako, Kyoto, Japan).

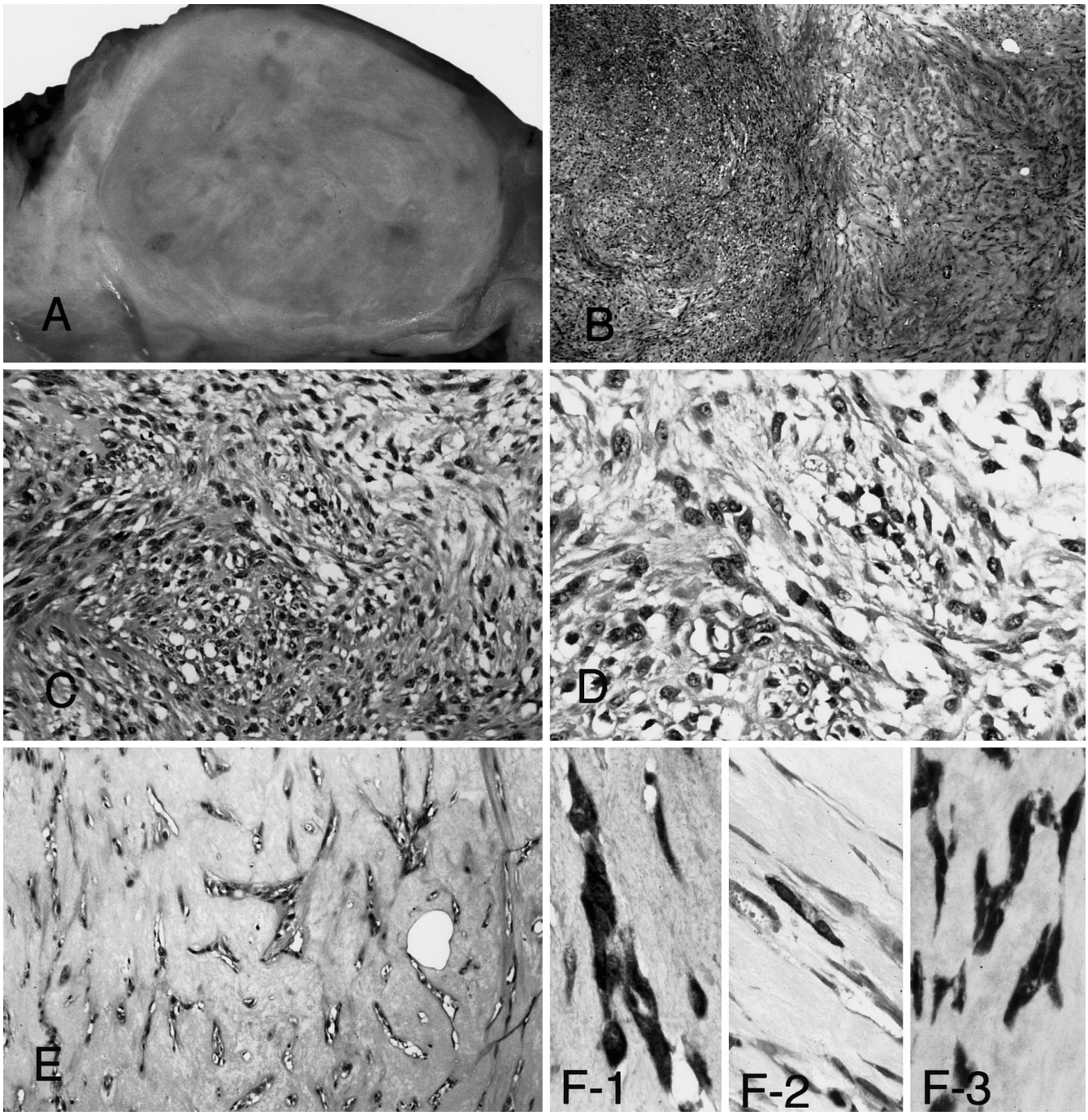

Fig. 1 **A** Cut surface of the lesion revealing a well-circumscribed round mass. **B** Photomicrograph of the primary breast tumor showing proliferation of spindle cells arranged in interlacing bundles (H&E, ×44). **C** Higher magnification of the more crowded left portion (H&E, ×200). **D** Detail of **C**, showing scattered mitoses (H&E, ×400). **E** Higher magnification of the right portion illustrating collagenous stroma and scattered tumor cells (H&E, ×200). **F** Immunohistochemistry of the tumor showing intense cytoplasmic staining for glial fibrillary acidic protein (*GFAP*) (F-1, ×400) and S-100 protein (F-3, ×400), and weak positivity for keratin (F-2, ×400)

Results

Pathological findings

The breast tumor was a well-circumscribed round mass, measuring 65×55×45 mm. The cut surface was homogeneous and pale (Fig. 1A). Microscopic examination revealed a proliferation of spindle cells and dense collagenous bundles, forming interconnecting thin cords with a few layers of elongated cells. The cytoplasm of the tumor cells was clear and their nuclei were oval and vesicular with small nucleoli and slight atypia. Cellularity was low in most areas. However, a focus of crowded

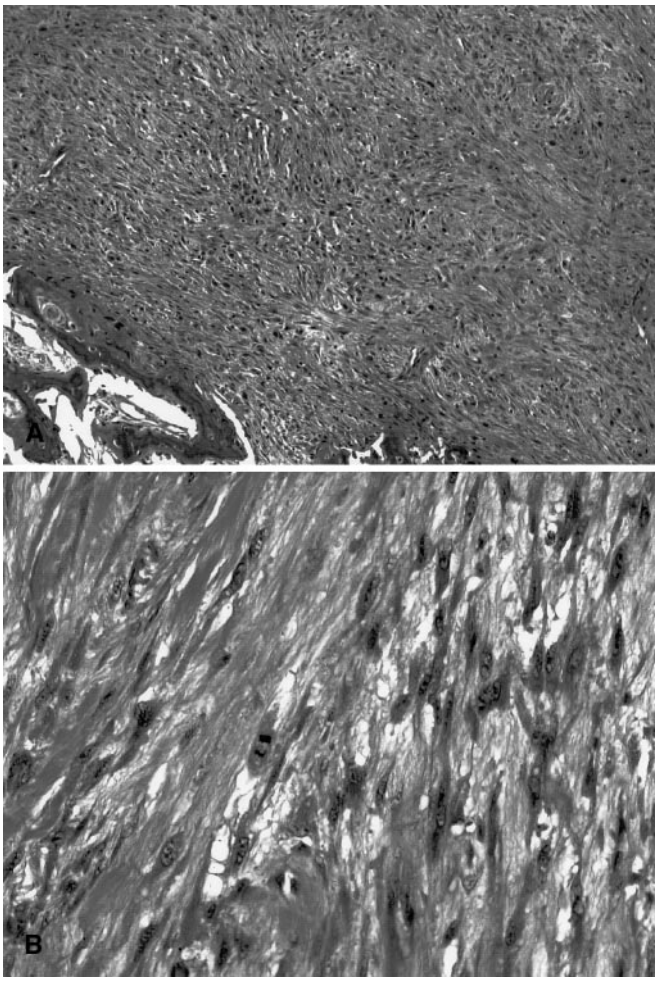

Fig. 2 **A** Photomicrograph of the metastatic tumor invading the bony cortex (H&E, ×100). **B** Higher magnification of **A** (H&E, ×400)

cells was noted near the center of the tumor, where the mitotic count ranged from 2 to 5 cells per 10 high-power fields. The tumor was composed purely of spindle myoepithelial cell component and lacked any glandular pattern. At the tumor border, the cells were observed to infiltrate and become incorporated into the breast tissue (Fig. 1B–E).

The recurrent tumor was a 50-mm (diameter) mass with an appearance very similar to the original lesion, though mitotic figures were more prominent. At the periphery of the tumor, destruction of the bony trabeculae was apparent (Fig. 2).

Immunohistochemical findings

Spindle cells of the primary tumor exhibited intense positivity for S-100, α-smooth muscle actin, vimentin, GFAP-polyclonal, and GFAP-monoclonal antibodies. Weak immunoreaction for keratin was observed. However, EMA and high-molecular-weight cytokeratin were negative (Fig. 1F). The secondary tumor in the jaw demonstrated similar results.

Discussion

Myoepithelial cells are known to exist between the epithelial cells and the basal membrane in the breast and salivary glands. These cells are characterized by immunoreactivity with smooth muscle actin, cytokeratin, S-100 protein and GFAP antibodies. Myoepithelial differentiation is commonly encountered in neoplasms of salivary glands, with tumor cells expressing vimentin, which is not found in normal myoepithelial cells [2]. Tumors of the breast with differentiation towards myoepithelial cells include adenoid cystic carcinomas, adenomyoepitheliomas, low-grade adenosquamous (syringomatous) carcinomas, malignant myoepitheliomas, and poorly differentiated myoepithelial-rich carcinomas. The malignant myoepithelioma is a tumor composed exclusively of malignant myoepithelial cells, which lacks adenomatous components. Only 13 cases of malignant myoepithelioma of the breast have so far been reported [3, 4]. All occurred in adult patients, most of whom were over 50 years of age. The tumor size varied from 0.9 cm to 21 cm in diameter.

Myoepithelial tumors are generally considered as benign or low grade when malignant. Distant metastasis was documented in only four of the previous cases among malignant myoepithelioma. Lakhani and his colleagues [5] described one patient with a malignant myoepithelioma accompanied by metastatic deposits in the skull, ribs, lumbar spine, and sternum at 6 years after the initial surgery. Scarpellini et al. [6] reported a similar case, in which multiple metastatic lesions were found in the bones, lung and brain about 2 years after the initial treatment. The other two cases demonstrated lung and pleural metastasis after 6 months [7], and regional lymph node metastasis at mastectomy [9]. The sizes of the tumors with early metastases (the latter two cases) were 21 cm and 6×7 cm, respectively, suggesting that metastasis occurs as a late event from large masses. However, it is not conclusive because of the brevity of reported cases and conflicting data [6]. The long history of the primary tumor and the late onset of metastasis are clear evidence of low malignant potential of the present tumor.

For differential diagnosis of a malignant myoepithelioma, for example from sarcomatoid carcinomas, a predominance of cells showing a positive reaction for smooth muscle actin or S-100 protein rather than cytokeratin is important. Differentiation from monophasic variant of sarcomatoid carcinoma should be very difficult. The distinction between a metaplastic spindle-cell carcinoma and a malignant myoepithelioma is not difficult in most cases, as many metaplastic carcinomas have focal areas of epithelial differentiation. Another lesion that could be confused with malignant myoepithelioma is fibromatosis, but the latter is a more irregular and ill-defined lesion in the breast, showing an ex-

aggerated infiltrative pattern. Mitotic figures do not exceed 2–3/10HPF, and their appearance is normal. Differential diagnosis with spindle cell neoplasms of the jaw includes ameloblastic fibrosarcoma, in which benign ameloblastic epithelium coexists with atypical spindle cells.

Recently, GFAP has been found in certain myoepithelial cells in the salivary glands. The antigen has also been detected in salivary-gland tumors with myoepithelial features. Given the close similarities between salivary gland and breast tissue, GFAP might be a myoepithelial marker of breast tumors as well as cytokeratin, S-100 protein, and smooth muscle actin. However, Tavassoli [8] reported a negative reaction for GFAP in myoepithelial lesions, which included one malignant myoepithelioma. Kuwabara and Uda [4] also presented similar results for a clear cell mammary malignant myoepithelioma, although Chen et al. [1] demonstrated GFAP in a myoepithelial carcinoma of the breast with widespread bone metastasis, accompanied by adenomyoepithelioma satellite nodules. Due to the paucity of case numbers, it would thus be premature to conclude any particular significance for GFAP in malignant myoepitheliomas.

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