

Case Report

Breast carcinoma with osteoclastic giant cells: case report and review of the literature

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Abstract: Breast carcinoma with osteoclastic giant cells (OGCs) are uncommon. Here, we report a 46-year-old woman with a painless lump in her left breast that has been proved clinically and radiographically. Microscopical examination showed OGCs accompanying invasive ductal carcinoma. Immunohistochemical assay revealed that OGCs derived from macrophages. Despite positive lymph node metastasis, the patient has been well without evidence of recurrence or metastasis one year after the operation. To date, the influence of OGCs on the prognosis of patients is still controversial. Our case may provide insights into further understanding breast carcinoma with OGCs.

Keywords: Breast carcinoma, osteoclastic giant cells, tumor metastasis, prognosis, immunohistochemistry

Introduction

Breast carcinoma with osteoclastic giant cells (OGCs) is rare and described in less than 2% of breast cancer patients [1, 2]. Up to date, a few cases reported in the medical literature. Breast carcinoma with osteoclast-like giant cells was first described by Rosen in 1979 [3]. This tumor is characterized by the presence of OGCs, the nature of which remains controversial. We herein reported a case of breast carcinoma with OGCs accompanied by lymph node metastasis; we discussed its clinical, imaging, light microscopic and immunohistochemical features.

Case presentation

A 46-year-old woman was admitted to our hospital with one-week history of a painless lump in the upper of her left breast. The patient denied any systemic symptoms, weight loss or bone pain. She had no known family history of breast, uterine, or ovarian malignancy. Physical examination revealed that a hard mass was about 4 cm in diameter at 12 o'clock in the left breast and 5 cm away from the nipple. Further, we further touched a well-circumscribed firm mass with good mobility in the left axillary.

Laboratory studies showed 14.52 G/L leukocyte count, 10.40 G/L neutrophils count, 5.57 U/mL CA-199 (gastrointestinal cancer marker) and 13.4 U/mL CA153 (breast cancer marker). All other routine lab parameters were within normal limits. Incisional breast biopsy was performed and frozen pathologic diagnosis was breast carcinoma. Then the patient underwent modified radical mastectomy with axillary clearance, following sentinel lymph node biopsy. Post-operation course were smooth. Adjuvant chemotherapy was administered postoperatively. At the time of writing she has been well without evidence of recurrence or metastasis one year after the operation.

Imaging findings

The woman underwent a radiological examination including breast mammography and ultrasound. Mammography showed an irregular high-density mass shadow in the upper outer quadrant of her left breast (**Figure 1A**). The tumor was 3.0 × 2.6 cm in size, spicule sign edging infiltration and along the duct infiltration in the direction of the nipple. The region around the tumor showed disordered structure, increased local blood supply and wide transparent halo sign. No clear calcification was found

Breast carcinoma with osteoclastic giant cells

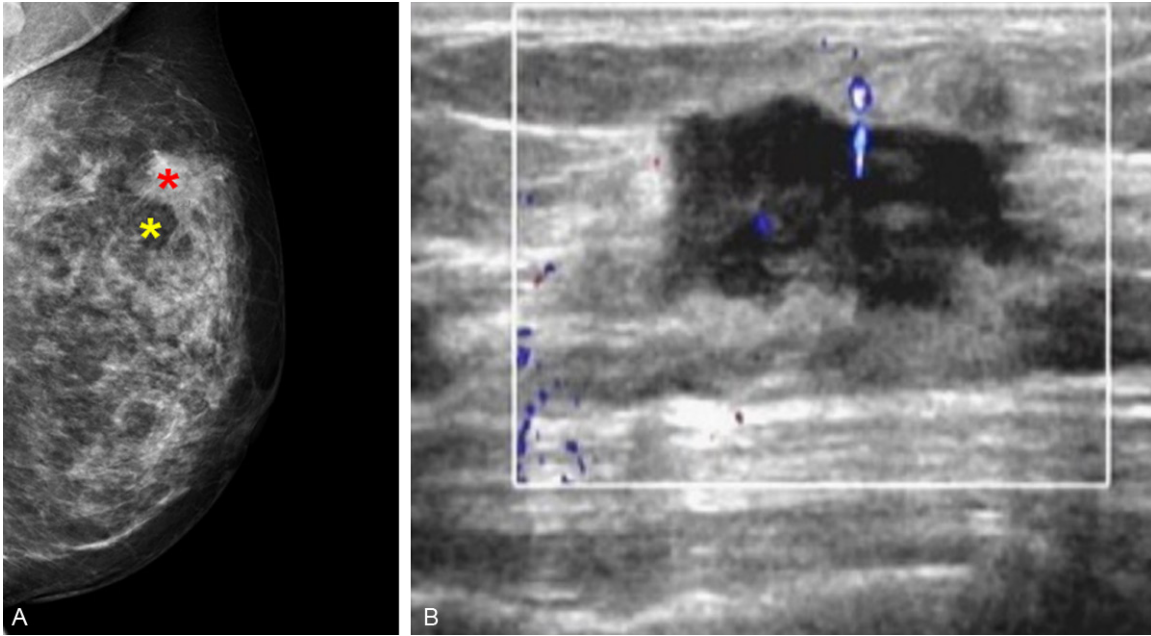


Figure 1. Imaging features. A. Mammography showed an irregular high-density mass shadow in the upper outer quadrant of her left breast. The tumor was 3.0 × 2.6 cm in size (Red star). The region around the tumor showed wide transparent halo sign (Yellow star). B. Ultrasound revealed an irregularly shaped hypoechoic mass without posterior echo enhancement.

within and around the lesion (Breast Imaging Reporting and Data System (BI-RADS) category 4). Ultrasound revealed an irregularly shaped hypoechoic mass without posterior echo enhancement (**Figure 1B**). Invasive breast carcinoma accompany axillary lymph node metastasis was suspected on ultrasonography.

Pathological findings

Grossly, the tumor was a well-defined, red-brown mass with bleeding. Microscopically, sections showed neoplastic cells arranged in cords, sheets, and glandular pattern with low degree of pleomorphism and infrequent mitosis (**Figure 2**). The stroma was collagenized and fresh hemorrhages as well as abundant hemosiderin-laden macrophages were also noted. Besides these, many OGCs and a few mononuclear histiocytes were seen in the vascular stroma, more so at the periphery. The giant cells had abundant eosinophilic cytoplasm and contained numerous small uniform nuclei. The nuclei were uniform and round to oval with some convolution in shape. The size and nuclear number of OGCs often vary from 80 per 10 high power fields with a number of nuclei up to 12 in one cell. No granulomas, necrosis or inflammatory infiltrate were observed. Three sentinel lymph nodes were inspected for intra-

operative rapid histology, and only one positive node was observed. Similar histological signs could be found between primary and metastatic lesions, such as the organization of carcinoma cells, osteoclastic-like giant cells, scattered hemorrhage and focal flake hemosiderin deposition. The 12/12 axillary lymph nodes resected from the axillary tail were free of tumor.

Immunohistochemically, the OGCs were positive for CD68, a histiocytic marker and negative for E-cadherin and cytokeratin (CK), epithelial markers. In contrast, cancer cells were negative for CD68, but positive for E-cadherin and CK, suggesting that those cells resulted from dedifferentiation of ductal carcinoma and retained the nature of carcinoma. The cancer cells were also positive for estrogen receptor (ER; weak, 95%), progesterone receptor (PR; strong, 95%) and negative for p53 and human epidermal growth factor receptor type 2 (Her-2; 0+), while the OGCs were negative for ER, PR and Her-2. Following the WHO classification, the diagnosis was breast carcinoma with OGCs.

Discussion

Carcinoma with osteoclastic giant cells (OGCs) has been described in several organs such as gallbladder [4], liver [5] and thyroid [6], other

Breast carcinoma with osteoclastic giant cells

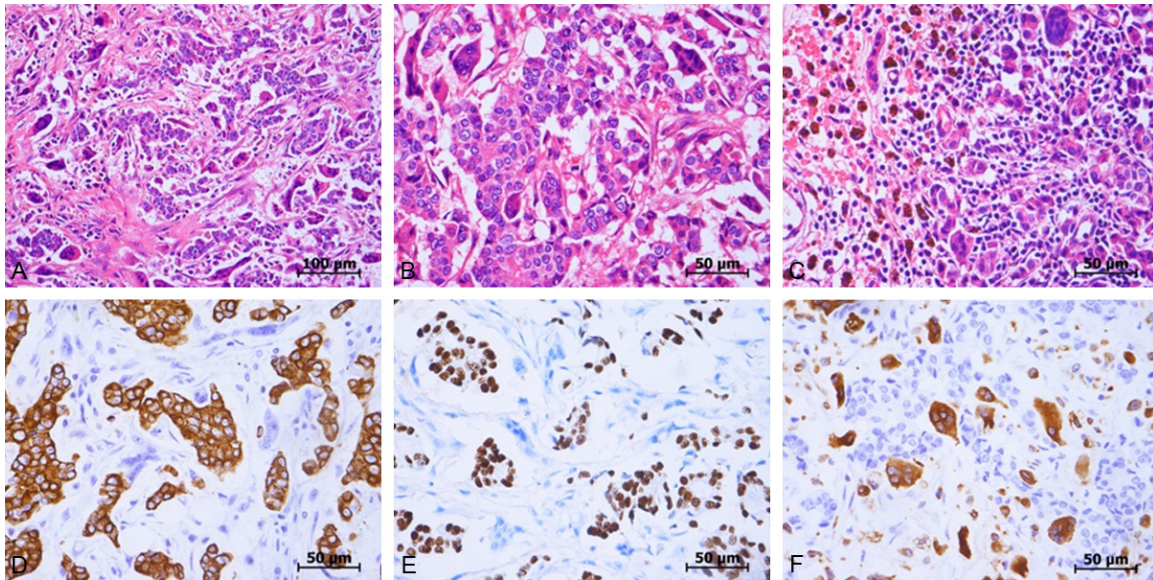


Figure 2. Histological features. A. Low power view of the primary tumor. B. High power view of the primary tumor. C. High power view of lymph node metastases. D. Immunohistochemical positive reaction of carcinoma cells for CK. E. Immunohistochemical positive reaction of carcinoma for PR. F. Immunohistochemical positive reaction of OGCs for CD68.

than pancreas [7] and urinary tract [8]. To date approximately 200 cases of carcinoma with osteoclastic giant cells have been reported. Carcinoma with osteoclastic (or osteoclast-like) giant cells of the breast constitutes only 0.5-1.2% of breast carcinoma [1, 2]. OGCs can occur in invasive ductal, lobular, papillary, or squamous types of breast carcinoma [2, 9, 10]. In approximately one third of cancers with osteoclast-like giant cells there is axillary node metastasis, leading to a worse prognosis for patients with this form of carcinoma [11]. Here, we reported a case of breast carcinoma with OGCs accompany lymph node metastasis.

Initial diagnosis of mammary carcinoma is often based on fine needle aspiration or core needle biopsy. Cytologic finding of osteoclast-like giant cells include large cells with abundant cytoplasm and centrally located nuclei ranging in size and number [12]. There are also prominent, associated nucleoli. Diagnosis of osteoclast-like giant cells can be extremely difficult on cytologic examination as these cells can be bland in appearance and have a similar appearance to foreign-body giant cells associated with fat necrosis. As a result, malignant cells may be missed, leading to a false negative diagnosis [2]. Sometimes, the OGCs may be missed, causing a cytological mimicker of benign tumors such as fibroadenoma [13].

Breast carcinoma with OGCs is characterized by the presence of OGCs admixed with malignant epithelial cells. They often showed hyperchromatic nuclei that are atypical with occasional small nucleoli and fine chromatin structure. Mitotic figures are typically rare [14]. OGCs also presented in many other lesions and diseases, such as tuberculosis, sarcoidosis and granulomatous mastitis. However, in contrast, breast carcinoma has no histological features consistent with granulomatous disease [2].

The mechanism for formation of osteoclast-like giant cells is still unknown. A recent study showed that secretion of specific cytokines, such as VEGF and MMP12, led to a characteristic inflammatory and hypervascular stroma, which is commonly observed in breast carcinoma with OGCs, regardless of histology of tumoral cells. Therefore, appearance of OGCs may not be antitumoral immunological reactions, but rather pro-tumoral differentiation of macrophage responding to hypervascular microenvironments induced by breast cancer [15].

To our best knowledge, no formal studies have been performed to investigate the role of OGCs in overall survival. The OGCs are of a different origin than the carcinoma and are possibly a reactive infiltrate [16, 17]. Patients with benign

giant cells adjacent to bone that expressed a CD68 pattern were found to have good prognosis. The presence of OGCs suggests a less aggressive tumor with a good outcome [13]. Several related analysis in other types of breast cancer, however, suggested a less favorable prognosis for patients with carcinoma with OGCs [11, 17]. In the present case, the patient was alive with no evidence of recurrence 1 year after the operation despite positive lymph node metastasis.

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Disclosure of conflict of interest

None.

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