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Breast carcinoma with osteoclast-like giant cells: A cytological-pathological correlation with a literature review

Ryuji Ohashi[a,*], Ayako Hayama[a], Miyuki Matsubara[a], Yasuhiko Watarai[a], Takashi Sakatani[a,b], Zenya Naito[a,b], Akira Shimizu[a]

[a] Department of Diagnostic Pathology, Nippon Medical School Hospital, 1-1-5, Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan
[b] Department of Integrated Diagnostic Pathology, Nippon Medical School, 1-1-5, Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan

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ABSTRACT

Breast carcinoma with osteoclast-like giant cells (OGCs) is a rare disease characterized by the infiltration of OGCs in the tumor; however, cytological aspects of this tumor type remain elusive. We examined the cytological features in fine needle aspiration (FNA) biopsy smears obtained from 5 patients who were histologically diagnosed with breast carcinoma with OGCs. We compared FNA and clinicopathological findings with results from the published literature. Histological assessment of the resected samples showed that all tumors exhibited a histological grade 1 phenotype with a predominant cribriform architecture. Four patients were estrogen receptor positive, and 1 patient showed a triple negative phenotype. All patients survived without tumor recurrence. In the FNA smears, tumor cells were arranged in loosely cohesive clusters, characterized by varying degrees of OGCs infiltration and rare formation of solid tumor nests. Occasionally, 2- or 3-dimensional clusters of tumor cells were found, accompanied by OGCs at the peripheral regions. In all patients, tumor cells were small without severe nuclear atypia. None of the patients showed significant background necrosis. In summary, cytological features of breast carcinoma with OGCs are characterized by loose aggregates of low grade tumor cells, the presence of OGCs, and the absence of necrosis, all of which were consistent with features reported previously. This peculiar form of breast tumors should be included in the differential diagnosis, when physicians encounter FNA findings including low grade ductal carcinoma with the admixture of multinucleated giant cells or OGCs.

1. Introduction

Breast carcinoma with osteoclast-like giant cells (OGCs), a rare disease comprising < 2% of all breast cancers, is characterized by the infiltration of OGCs into the tumor [1,2]. Since it was first described by Rosen in 1979, approximately 200 cases of breast carcinoma with OGCs have been described in the literature [3]. In the current world health organization (WHO) classification of breast tumors, carcinoma with OGCs is not listed as a distinct entity, but is briefly described in the chapter of tubular and cribriform carcinoma [4]. In fact, a recent study by Zhou et al. on 42 patients with breast cancer with OGCs revealed that this peculiar tumor predominantly presents with low to moderate histological grade in a cribriform pattern, and has a luminal phenotype [5]. Because of its uniqueness, however, cytological aspects of this unusual tumor remain elusive due to the limited number of studies, most of which are single case reports [6-19]. To confirm the preoperative diagnosis of this tumor, investigation of a series of patients with emphasis on cytomorphology in fine needle aspiration (FNA) smears is necessary. Here, we examined 5 patients with breast carcinoma with OGCs with the aim to correlate the FNA biopsy findings with histological features of the resected tumors. The presence of OGCs was confirmed based on immunostaining of the histiocytic marker CD68. Furthermore, we compared our findings to previously reported cases from the literature to characterize the cytological aspects of this uncommon variant of breast carcinoma.

2. Materials and methods

2.1. Case selection

We identified a total of 8 cases of breast carcinoma with OGCs after searching the archives of the Department of Diagnostic Pathology, Nippon Medical School Hospital (Tokyo, Japan) between January 2005 and August 2016. Of these, we selected 5 patients who had undergone FNA cytology examination before excisional biopsy or operation. FNA cytology was performed by experienced surgeons using a 20-gauge

* Corresponding author.
E-mail address: r-ohashi@nms.ac.jp (R. Ohashi).

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Table 1
Clinicopathological profiles of patients with breast carcinoma with osteoclastic giant cells (OGCs).

Patient	Age	Site	Size (cm)	HG	Growth pattern	ly	v	LN	CD68 + OCG (/10HPF)	ER	PgR	HER2	FU (days)	Status
1	47	RUI	2.3	1	Cribriform-tub	+	–	+	+ + +	+	+	–	4692	Alive
2	50	RUI	2.1	1	Cribriform-tub	+	+	–	+ +	+	+	–	3267	Alive
3	42	LLI	3.0	1	Cribriform-tub	+	–	+	+ +	+	+	–	1294	Alive
4	48	LUO	1.2	1	Cribriform-solid	–	–	–	+	+	+	–	1631	Alive
5	43	LC	2.5	1	Cribriform-tub	+	–	–	+ + +	–	–	–	209	Alive

Abbreviations: RUI, right upper-inner; LLI, left lower-inner; LUO, left upper-outer; LC, left central; HG, histological grade; tub, tubular; ly, lymphatic invasion; v, vascular invasion; LN, lymph nodes status; HPF, high power field; FU, follow-up period.

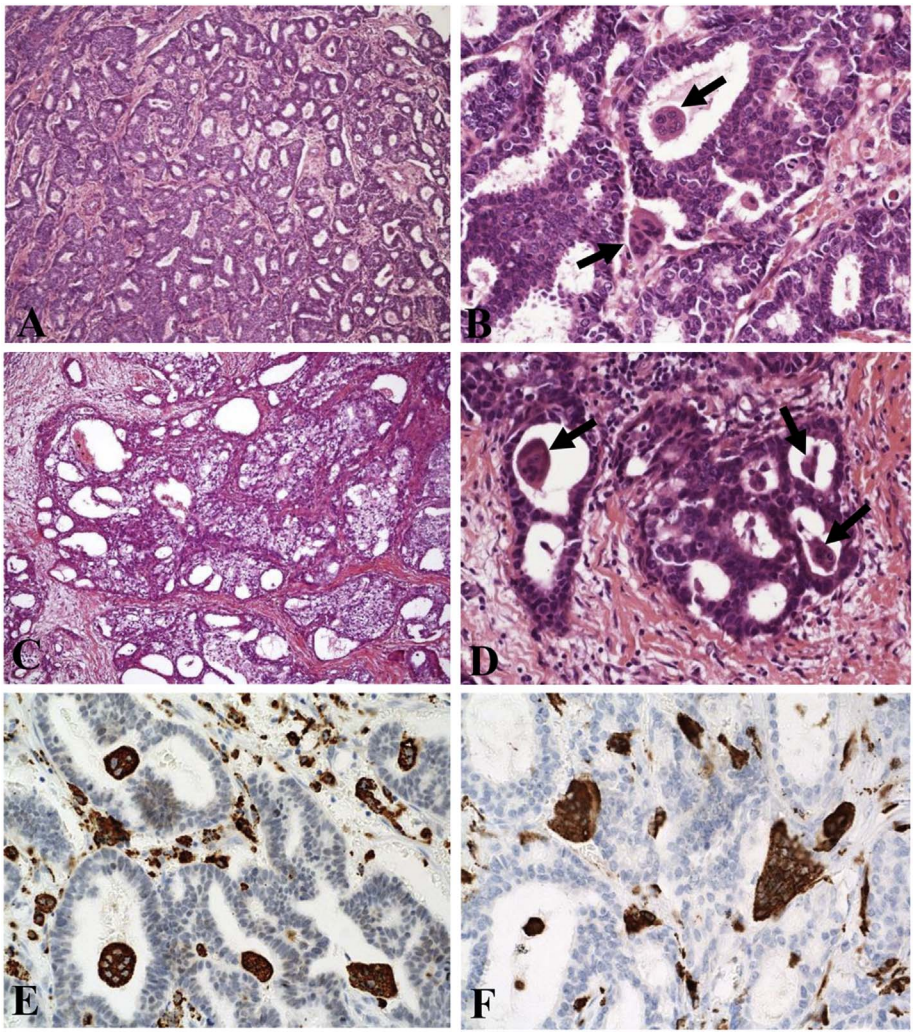

Fig. 1. Representative histological findings of breast carcinoma with OGCs (A–D) and immunohistochemical expression of CD68 (E, F) from patient 1 (A, B, E) and patient 4 (C, D, F). Histology of the tumor was mainly represented by cribriform configuration (A, C) with a focal solid pattern (C). Most OGCs were identified within the tubular lumina formed by carcinoma cells (B, D, arrows). OGCs were identified with positive CD68 staining (E, F). Hematoxylin & eosin staining (A–D). Original magnification × 100 (A, C) and × 400 (B, D, E, and F).

needle attached to a 20 ml syringe. Specimens were smeared on glass slides and immediately fixed with solution containing 95% ethanol. Then the cytological slides were stained according to the routine protocol. Patients with breast carcinomas metastasized from other organs were excluded. No patients received neoadjuvant chemotherapy prior to surgery. None of the patients showed evidence of distant metastasis at the time of surgery. Patients' consent and approval of the Ethics Committee of Nippon Medical School Hospital were obtained for the use of clinical samples for research purposes.

2.2. Immunohistochemical stainings

In the first phase of the study, we reviewed all the hematoxylin and eosin sections to assess the morphological characteristics of the tumors. Histological grade was established using a modified Scarff-Bloom-Richardson histological grading system [20]. We prepared paraffin blocks of all the patients, and performed immunohistochemical staining with primary antibodies using the standard avidin-biotin-peroxidase complex technique. For the identification of OGCs, we used monoclonal mouse anti-human CD68 (PG-M1, dilution 1:100; Agilent, Santa Clara, USA) [21]. Other primary antibodies included monoclonal rabbit anti-human estrogen receptor (ER) (SP1, dilution 1:1; Ventana Medical Systems, Tucson, AZ), monoclonal rabbit anti-human progesterone receptor (PgR) (1E2, dilution 1:1; Ventana Medical Systems), monoclonal rabbit anti-human HER2/neu (4B5, dilution 1:1; Ventana Medical Systems), and monoclonal mouse anti-human Ki67 (M7240, dilution 1:100; Agilent, Santa Clara). After deparaffinization, endogenous peroxidase activity was blocked by incubating sections in 0.3% hydrogen peroxide in methanol for 30 min. Antigen retrieval treatment was performed for some cases with Immunosaver (Nisshin EM, Co., Ltd.,