

유방의 침윤성 파골양 거대세포 관암종의 세포소견

- 1예 보고 -

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Invasive Ductal Carcinoma with Osteoclast-Like Giant Cell in a Young Woman

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Mammary carcinoma with osteoclast-like giant cells is an unusual neoplasm characterized by giant cells, mononuclear stromal cells, and hemorrhage accompanying a low grade carcinoma. We present the cytological findings in a case of invasive ductal carcinoma with osteoclast-like giant cells that was initially confused with a fibroadenoma, due to its well-demarcated and soft mass and the young age of the patient. A 28-year-old female presented with a 4.5 cm, well demarcated, soft and nontender mass in the right breast. Fine needle aspiration cytology (FNAC) showed a combination of low grade malignant epithelial cell clusters and osteoclast-like giant cells. The atypical epithelial cells were present in cohesive sheets and clusters. Osteoclast-like giant cells and bland-looking mononuclear cells were scattered. An histological examination revealed the presence of an invasive ductal carcinoma with osteoclast-like giant cells. We report here the cytological findings of this rare carcinoma in a very young woman. The minimal atypia of the epithelial cells and its soft consistency may lead to a false negative diagnosis in a young woman. The recognition that osteoclast-like giant cells are rarely present in a low grade carcinoma, but not in benign lesion, can assist the physician in making a correct diagnosis.

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Key words : Osteoclast-like giant cell, Cytology, Aspiration,
Breast, Young woman

INTRODUCTION

Invasive mammary carcinomas containing osteoclast-like giant cells are very rare, constituting 0.5~1.2% of carcinomas in two series.¹ Osteoclast-like giant cells are commonly reported in usual invasive ductal carcinomas, and less commonly in cribriform, tubular, squamous, papillary, apocrine, mucinous, metaplastic,

lobular carcinomas and rarely in ductal carcinoma in situ.^{1,2,3} In the literature, 56 cases describing this tumor have been reported.^{2,3} In Korea, only two cases have been reported.^{4,5} We describe the cytological features of an invasive ductal carcinoma with osteoclast-like giant cells and axillary node metastasis in a young woman; this is the youngest case that has been reported.



Fig. 1. Ultrasonographic examination reveals the 3 cm sized mass with a relatively well-demarcated margin.

CASE

Clinical Presentation

A 28-year-old female patient underwent a fine needle aspiration due to a palpable right breast mass. The patient discovered the right breast mass five months prior. A physical examination revealed a 4.5 cm-sized movable and soft mass in the lower outer quadrant of the right breast. No axillary lymphadenopathy was noted on physical examination. Ultrasonography showed a relatively well-demarcated mass, suggesting a fibroadenoma (Fig. 1). Fine needle aspiration of the mass was performed with a 23-gauge needle and 10 ml syringe. After FNAC, the patient underwent a quadrantectomy with axillary lymph node dissection.

Cytologic Findings

Aspirated material was smeared onto glass slides and allowed to dry or was immediately fixed with 95% ethanol. Air-dried smears were stained with Diff-Quick, and the ethanol-fixed materials were stained with Hematoxylin and Eosin (H&E) and Papanicolaou stain. The smear was cellular and was composed of three-dimensional sheets and clusters of epithelial cells, multinucleated giant cells and scattered mononuclear cells

(Fig. 2). The epithelial cells were predominantly arranged in tightly cohesive three-dimensional branching clusters or in some small clusters with few single dispersed epithelial cells. The cells were intermediate in size with irregular contours and had oval to round nuclei, coarse chromatin, inconspicuous nucleoli, and relatively ill-defined cytoplasm. Multinucleated giant cells were scattered between the epithelial cell clusters. The giant cells had ample and amphophilic cytoplasm, varied in size and number of nuclei, and prominent nucleoli. They often contained 10~15 nuclei. Hemosiderin-laden macrophages were also seen. Mononuclear cells were scattered between the multinucleated giant cells and epithelial cell clusters. These cells had round, eccentric nucleus and abundant cytoplasm. A diagnosis of suspicious low grade carcinoma with multinucleated giant cells was made. Neither necrosis nor granuloma was seen.

Histologic Findings

The patient underwent an excisional biopsy. The lump measured 3 × 2 × 1 cm in dimension. On sectioning, it was reddish brown and firm with visible hemorrhage, but not gritty. Microscopically, the tumor cells were arranged in solid nests, with focal tubular formation, composed of ductal epithelial cells admixed with multinucleated giant cells in the background of hemorrhagic stroma (Fig. 3). The ductal epithelial cells had oval to round, small and regular nuclei and inconspicuous nucleoli. There was no feature of associated ductal carcinoma in situ. A large number of multinucleated giant cells abutted against the clusters of malignant ductal epithelial cells. Most of the giant cells were present at the edge of the infiltrating clusters of ductal epithelial cells. The giant cells had multinucleated nuclei, abundant cytoplasm, and prominent nucleoli. After lumpectomy, an additional quadrantectomy was performed. Metastatic carcinoma was found in 10 out of 22 dissected axillary lymph nodes. The metastatic lymph nodes only showed infiltrating ductal carcinoma

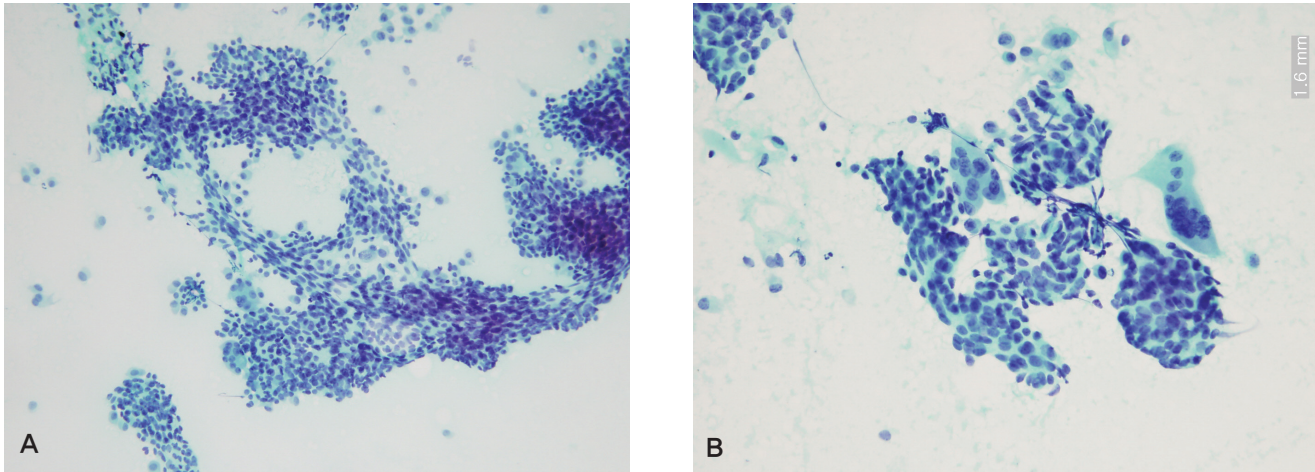


Fig. 2. (A and B) A fine needle aspiration smear shows three-dimensional clusters of low grade ductal carcinoma cells admixed with osteoclast-like multinucleated giant cells and scattered mononuclear cells (Papanicolaou).

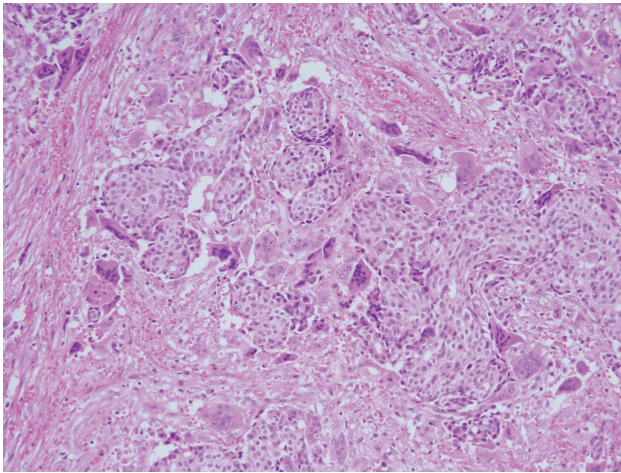


Fig. 3. An excisional biopsy shows an invasive ductal carcinoma with osteoclast-like multinucleated giant cells (H&E).

but not osteoclast-like giant cells.

Immunohistochemical Findings

An immunohistochemical study showed positivity for estrogen receptor (ER, monoclonal 1:50, Neomarker, Fremont, CA, U.S.A.), progesterone receptor (PR, monoclonal 1:50, Neomarker, Fremont, CA, U.S.A.), and E-cadherin (1:100, monoclonal, Zymed, San Francisco, CA U.S.A.), but negativity for p53 (monoclonal 1:50, Zymed, San Francisco, U.S.A.) and Her2/neu (monoclonal 1:50, Neomarker, Fremont, CA, U.S.A.). Osteoclast-like giant cells expressed none of the above

three positive markers. Osteoclast-like giant cells were strongly positive for CD68 (1:100, DAKO, Denmark) and vimentin (1:100, Zymed, San Francisco, U.S.A.) but were negative for cytokeratin (1:100, DAKO, Denmark) and lysozyme (1:50, DAKO, Denmark).

DISCUSSION

A mammary carcinoma with osteoclast-like giant cells is a rare type of breast carcinoma, ranging from 0.5 ~ 1.2% of all breast carcinomas. Microscopically, the majority of infiltrating carcinomas are invasive ductal carcinomas and other types include lobular, cribriform, tubular, adenoid cystic, squamous, papillary, mucinous and metaplastic carcinoma.³

In cases of mammary carcinoma with osteoclast-like giant cells, patients ranged in age from 28 to 88 years; the average age at diagnosis was about 53 years. Mammographically and ultrasonographically, the well-circumscribed margin of most tumors suggested a benign lesion such as a fibroadenoma, cyst or medullary carcinoma. Reported diameters have ranged from 0.5 to 10 cm, with the majority measuring less than 3cm.² The fine-needle aspiration cytology of these tumors showed high cellularity, with a mixture of epithelial components and osteoclast-like giant cells.

The epithelial components showed those of the usual invasive mammary carcinoma. The osteoclast-like giant cells were present at the edges of the tumor nests and in the glandular lumens. Mononuclear cells were scattered in the hemorrhagic background.² In the case presented here, the same cytological features were present.

While the mechanisms by which the osteoclast-like giant cells are produced are not completely understood, these cells seem to form by a fusion of stromal histiocytes. Ultrastructurally, the cytoplasm of the multinucleated giant cells contains either abundant mitochondria or vesicles and lysosomes, in contrast to the sparsity of organelles in the cytoplasm of the carcinoma cells. Multinucleated giant cells lack desmosomes and other types of intercellular junctions, which are present in epithelial cells. In multinucleated giant cells, the microvillous tufts are present and are similar to those encountered in histiocytes. Their presence is not an indication of epithelial differentiation. Immunohistochemically, multinucleated giant cells did not stain for cytokeratin and carcinoembryonic antigen, but were positive for vimentin. Among the histiocytic markers, the cells were negative for lysozyme, acid phosphatase, alpha 1-antitrypsin, but were immunoreactive for CD68.^{2,6} In our case, multinucleated giant cells were positive for CD68 and vimentin, but were negative for cytokeratin and lysozyme.

Osteoclast-like giant cells have been observed in breast lesions ranging from benign to malignant. Vicandi and colleagues⁷ described at least four types of multinucleated giant cells that can be seen in association with breast lesions. The first type of multinucleated giant cells is related to granulomatous inflammatory conditions such as tuberculosis and foreign body reaction. The second type is multinucleated giant cells of stromal type that is associated with benign breast lesions and phyllodes tumors. These cells show no expression of histiocytic markers and are positive for CD34. The third type is the malignant, anaplastic giant cell that occurs in pleomorphic carcinomas and sarcomas. The final type is the osteoclast-like giant cell that is

accompanied by a breast carcinoma. Among these four types, the important differential diagnosis of carcinoma with osteoclast-like giant cells is a benign breast lesion with multinucleated giant cells. A benign breast lesion contains cohesive epithelial components and few single cells. It also contains myoepithelial cells; hemosiderin-laden macrophages are uncommon in a benign lesion. However, a malignant tumor with osteoclast-like giant cells does not include myoepithelial cells and can contain hemosiderin-laden macrophages. The present case showed similar cytological features of an invasive mammary carcinoma with osteoclast-like giant cells that has been described in the literature. However, despite the high cellularity, a diagnosis of malignancy was not straightforward, as cellular smears showed a lack of discohesion, and a scarcity of single cells. In the present case, some hemosiderin-laden macrophages were present around the tumor component, and myoepithelial cells were absent. Furthermore, the multinucleated giant cells were immunoreactive for CD68.

After the fine needle aspiration diagnosis, the histologic findings from the lumpectomy and subsequent quadrantectomy showed the presence of an invasive ductal carcinoma with osteoclast-like giant cells. The metastatic tumor was identical to the primary carcinoma in 10 out of 22 dissected lymph nodes, which did not contain osteoclast-like giant cells. While our case did not include osteoclast-like giant cells in the metastatic tumors in the lymph nodes, the presence of a metastatic tumor with osteoclast-like giant cells was reported in seven cases.^{1,2,7,8}

In conclusion, this report describes a case of invasive ductal carcinoma with osteoclast-like giant cells in the youngest woman so far among all of the reported cases. An admixture of cohesive clusters of mammary carcinoma and abutting bland-looking multinucleated giant cells, and occasional hemosiderin-laden macrophages, are helpful in the understanding of the diagnostic findings.

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