Case Report

Two Case of Breast Cancer with Cartilaginous and Osseous Metaplasia

Jun Ninomiya*,†, Tetsunari Oyama‡, Jun Horiguchi*,†, Yukio Koibuchi*,†, Takashi Yoshida*,†, Kotoro Iijima*,†, Miho Yoshida*,†, Daisuke Takata*,†, Yuichi Iino*,†, and Yasuo Morishita*†

Second Department of Surgery*†, and Second Department of Pathology‡, Department of Emergency and Critical Care Medicine‡, Gunma University Faculty of Medicine Maebashi, Japan.

Invasive breast cancer (IBC) with cartilaginous or osseous metaplasia is rare. Here we report two cases of this unusual variation. Case 1: The patient was a 33-year-old woman with a right breast tumor, 2.2 cm in size. Mammograms (MMG) presented no specific findings, but ultrasound (US) showed a cystic-like lesion. Excisional biopsy confirmed IBC with cartilaginous and osseous metaplasia. Biopsy was followed with a modified radical mastectomy. One lymph node was positive, and both estrogen receptor (ER) and progesterone receptor (PgR) were negative. Case 2: The patient was a 43-year-old woman with a left breast tumor, 4.2 cm in size. MMGs presented no findings but US showed an irregular shaped, low-echoic area, suggesting malignancy. Core needle biopsy confirmed IBC with cartilaginous metaplasia. A total adenectomy and lymph node dissection with breast reconstruction using a latissimus dorsi muscle flap were performed. Two of 18 lymph nodes were positive for metastasis and both ER and PgR were negative. IBC with cartilaginous or osseous metaplasia seem to be divided into two types pathologically, with or without intervening spindle cells, which is related to the prognosis. Matrix producing carcinoma (MPC) has no intervening spindle cells and a better prognosis than other types, however, MPC has been reported to have the same prognosis as ordinary breast cancer after for adjusting its stage. Our two cases were MPC’s and no recurrence has been detected 5 and 3 years from the initial therapy, respectively.


Key words: Breast cancer, Cartilaginous, Osseous, Metaplasia

According to the categories of breast cancer classification, IBC accompanied with heterologous elements is classified as a special type, and generally called metaplastic breast cancer. Although the most commonly encountered heterologous elements in the mammary gland are bone and cartilage, IBC with cartilaginous or osseous metaplasia is rare with a reported frequency of 0.03-0.2% of all breast cancer. We report here two cases of breast cancer with cartilaginous osseous metaplasia and refer to the literature.

Case 1

A 33-year-old woman noticed a right breast tumor and consulted a doctor. The tumor was diagnosed as a fibroadenoma and monitored with the patient visiting our department as the tumor gradually increased. The tumor, located in the inner area of the right breast was 2.2 x 2.2 cm in size, regular shaped, elastically firm, with an even surface, and a relatively well-defined border. Mobility was good and no dimpling was visible. Mammograms (MMG) showed neither tumor shadow nor microcalcification. An ultrasonogram (US) demonstrated a cystic lesion accompanied by an internal echo (Fig 1). To confirm the histological diagnosis an excisional biopsy was performed. The specimen was a circumscribed brown tumor, 2.6 x 2.2 cm in size, including the necrotic tissue. The tumor was diagnosed as IBC with cartilaginous and osseous metaplasia (Fig 2; A). Invasive ductal cancer showed gradual transition to metaplasia without intervening spindle cells, indicating a matrix producing carcinoma (MPC). A modified radical mastectomy was performed. Only one of 27

Reprint requests to Jun Ninomiya, Second Department of Surgery, Gunma University Faculty of Medicine, 3-39-15, Showa-machi, Maebashi Gunma 371-8511, Japan.
E-mail: j.ninomiya@nifty.ne.jp

Received January 8, 2003; accepted August 21, 2004
The patient was treated with chemotherapy using tegafur-uracil (UFT) 300 mg/day orally for two years. No recurrence has been recognized for 5 years after surgery.

**Case 2**

A 43-year-old woman noticed a left breast tumor and visited a doctor. As the tumor was suspected to be malignant, the patient was referred to our department. The tumor was located in the upper area of the left breast. It was $4.2 \times 3.0$ cm in size, irregular shaped, elastically firm with an uneven surface. The border of the tumor was indistinct. The tumor was accompanied by a slight dimple, however, no fixation to the muscle or the skin was recognized. MMGs showed neither a tumor shadow nor microcalcification. US presented an irregular hypoechoic lesion with boundary echo enhancement, internal echo, and attenuation of posterior echo, suggesting malignancy (Fig 3). Core needle biopsy of the tumor confirmed it to be invasive ductal carcinoma with cartilaginous metaplasia. A total glandectomy and lymph node dissection with breast reconstruction using a latissimus dorsi muscle flap were performed. The specimen was a gray solid tumor $2.5 \times 1.7$ cm in size and had an indistinct border (Fig 4). The pathological diagnosis was the same as that of the core needle biopsy (Fig 2; B). Invasive cancer cells transformed gradually to the metaplastic lesion without intervening spindle cells, indicating MPC. Two of 18 dissected lymph nodes were positive for metastasis but included no metaplastic lesion. The metastatic lymph node included no metaplastic lesion. ER and PgR were both negative.
areas. ER and PgR were both negative. Immunohistochemically, the tumor exhibited successive positive staining for cytokeratin 19, cytokeratin 5/14, and vimentin from the ductal part to the metaplastic part, demonstrating an alteration of characteristics according to histological differentiation. Gradual staining changes were seen to be a sign of transformation to sarcoma (Fig 5).

Because lymphatic invasion was severe (Fig 6), the patient underwent 12 courses of biweekly CTF therapy; cyclophosphamide (CPA) 100 mg/m², THP-adriamycin 30 mg/m² and 5-FU 500 mg/m² followed by sequential oral administration of UFT 300 mg/day and CPA 100 mg/day every two weeks for two years. No recurrence has been recognized 3 years after surgery.

**Discussion**

Although the most commonly encountered
heterologous elements in mammary gland are bone and cartilage, these are unusual features in breast cancer. The frequency of breast cancer with cartilaginous or osseous metaplasia is reported to be 0.03-0.2% of all breast cancers. The clinicopathological features of breast cancer with cartilaginous metaplasia have been reported to be: 1) comparatively large tumor size, with occasional lesion exhibiting rapid enlargement, 2) lack of no specific findings on radiographic examinations, 3) occasional cystic pattern on echography, 4) grossly, the tumor tends to be well circumscribed, and includes necrotic or hemorrhagic tissue, 5) overt invasive ductal breast cancer shows transition to a cartilaginous or osseous matrix both with and without intervening spindle cells, 6) the frequency of metastasis to the lymph nodes is low, and 7) ER and PgR status are often negative. In our cases, except for the US examination in case 2, tumor size, gross appearance of the specimens, pathological characteristics, lymph node metastasis, and ER status were the same as the features described above. Regarding etiology, the term carcinomasarcoma has been adopted, suggesting that carcinoma and sarcoma have developed separately but simultaneously. Immunohistochemical studies using cytokeratin, vimentin, and epithelial membrane antigen have demonstrated that metastatic elements have the biphasic character of both epithelium and mesenchyme. Although only case 2 was able to undergo immunostaining, the tumor exhibited successive positive staining of cytokeratin 19, cytokeratin 5/14, and vimentin from the ductal to metaplastic area. It was interesting that immunostaining altered gradually according to histological differentiation: the tubular part of the ductal carcinoma was mainly positive for cytokeratin 19 (luminal cell marker) and partially positive for cytokeratin 5/14 (basal cell marker), the solid and trabecular area were mainly positive for cytokeratin 5/14 and partially positive for cytokeratin 19, and metaplastic area stained positively for vimentin. Since even in the same ductal carcinoma, the staining pattern changed according to differentiation as the tissue approached metaplasia. The tumor originally might have begun as metaplasia.

The overall 5-year survival rates has been reported to be 68% and 60% in the literature. In the study by Wargotz, et al., metaplastic breast cancer without intervening spindle cells was designated as a matrix producing carcinoma (MPC). The overall 5-year survival rate was 68%, which is the same as that of ordinary invasive ductal breast cancer. Chhieng, et al. conducted an analysis, in which 32 patients with metaplastic breast cancer were compared to 112 matched patients with ordinary invasive ductal breast cancer. The overall 5-year survival rate of metaplastic breast cancer patients was 60% and the duration of time to recurrence and survival were longer than those in the control group, but there was no statistically significant difference. In Japan, there are some reports which have analyzed metaplastic breast cancer clinicopathologically. However, due to the lower frequency, there are few reports that include a large sample from one facility. Nakamura, et al. investigated five cases of IBC with cartilaginous metaplasia, and four of five were classified as the MPC type and their prognosis was the same as ordinary invasive ductal carcinoma. One of the cases with intervening spindle cells died only 19 months after the first treatment.

Metaplastic breast cancer with intervening spindle cells, especially with a high predominance of spindle cells, high cellularity, high mitotic activity and high nuclear pleomorphism similar to sarcoma, has been reported to have a poor prognosis. A poor prognosis was seen in the case reported by Nakamura et al. and in 26 of 29 cases of IBC with cartilaginous metaplasia reported by Kaufman et al. and Oberman, in which most of the cases were thought to have intervening spindle cells. To evaluate the outcome of metaplastic breast cancer, the presence of intervening spindle cells, the proportion of the metaplastic elements and the malignant potential seem to be important. Our two cases had no intervening spindle cells. In the MPC type, prognosis is dependent on the tumor size and staging, and not on lymph node metastasis, which is an important prognostic factor in ordinary invasive ductal breast cancer.

As for the treatment of the metaplastic breast cancer, the efficacy of adjuvant chemotherapy has not been established and monoclonal therapy with Trastuzumab was also not too promising due to the low positivity rate of the HER2/neu receptor. Because of the absence of a large series of randomized or observational data, confirmed treatment for metaplastic breast cancer is not available yet. However, Bellino et al. recommended that surgical and adjuvant treatment should be followed according to the guidelines for most other common breast cancers. The two
patients we reported underwent surgical and adjuvant treatments based on breast cancer guidelines and have been free from recurrence 5 and 3 years from the initial therapy respectively. Although the observation time has been limited, in concordance with the literature; they are anticipated to have the same prognosis as patients with ordinary invasive ductal carcinoma according to their tumor size.

About 40 of these cases have been reported in Japan; however, they are generally reported from various facilities and include a mixture of the MPC type and the sarcomatous type. To better define the clinicopathological features and prognosis, IBC with cartilaginous or osseous metaplasia should be classified as either the MPC type or the sarcomatous type.

References