We report the changes in the findings of imaging examinations (mammography, ultrasonography and contrast-enhanced computed tomography) of three patients with primary breast cancer before and after neoadjuvant chemotherapy, who obtained histologically complete responses after the chemotherapy. The neoadjuvant chemotherapy consisted of four cycles of doxorubicin and docetaxel. All patients were clinically judged as partial responders, because of the remaining tumorous lesions in the imaging examinations. However, these tumorous lesions could be related to the chemotherapy-induced fibrosis and tumor necrosis or the remaining fibrocystic changes. In this study, it was considered very difficult to estimate the extent of residual tumors accurately in patients with primary breast cancer after neoadjuvant chemotherapy by any type of imaging examination.

Key words: breast cancer – histological assessment – neoadjuvant chemotherapy – computed tomography – complete response

INTRODUCTION

There has been considerable interest in the use of neoadjuvant chemotherapy for primary breast carcinoma. The clinical response rates of this type of chemotherapy were reported to be ~60–80% (1–3). However, a histologically complete response, which is defined here as no microscopic evidence of residual cancer cells in the invasive or intraductal component, is extremely rare (1–3). It would be very useful to select patients by imaging examinations who have obtained a histologically complete response and need not undergo surgery after chemotherapy. We report here three histologically complete responders with primary breast carcinoma after neoadjuvant chemotherapy, with regard to the changes in the findings of imaging examinations (mammography, ultrasonography and contrast-enhanced computed tomography).

CASE REPORTS

The neoadjuvant chemotherapy consisted of four cycles of doxorubicin (adriamycin, ADM) and docetaxel (taxotere, TXT). After fully informed consent, the patients received 50 mg/m² of ADM and 60 mg/m² of TXT intravenously on day 1 of each cycle every 3 weeks. They underwent surgery 3–4 weeks after the termination of chemotherapy. Evaluation of efficacy was performed prior to surgery. The details of the three cases are given below.

CASE 1

A 67-year-old postmenopausal woman with a right primary breast carcinoma (T4bN1M0) received the above neoadjuvant chemotherapy. She had no past or family history of malignancies. Physical examination showed an ill-defined mass with skin redness, located in the upper outer quadrant of her right breast. The tumor size was 6.0 × 6.0 cm in diameter at the first consultation. As for the diagnostic procedures, mammography (MMG: Mamnomat 3, Siemens, Germany) revealed an ill-defined tumor shadow with microcalcification in the right breast, the size of which was 5.8 × 5.3 cm in diameter. An irregular hypoechoic–tumorous lesion could be detected in the right breast by ultrasonography (US: EUB-515 with a 7.5 MHz
transducer, Hitachi, Japan), the size of which was 6.3 × 5.0 cm in diameter (Fig. 1A). An irregular tumorous lesion also could be detected in a contrast-enhanced computed tomographic scan (CT: X-Vigor, Toshiba, Japan), the size of which was 4.5 × 3.9 cm in diameter (Fig. 1B). Core needle biopsy revealed an invasive ductal carcinoma, histological grade 3, of the right breast (Fig. 1C). Estrogen receptor (ER) of the right tumor was negative but progesterone receptor (PgR) was positive by
immunohistochemistry. Negative p53 nuclear immunoreaction (RSp53, Nichirei, Tokyo, Japan) and negative c-erbB-2 overexpression (Nichirei) by immunohistochemical staining were observed in this tumor. She received the neoadjuvant chemotherapy to completion and toxicities were tolerable. After the termination of chemotherapy, the tumor size was 2.5 × 2.5 cm by palpation (tumor shrinkage rate: 83%). The imaging examinations (MMG, US and CT) were also re-evaluated prior to surgery. The tumor sizes were 3.7 × 3.3 cm (60%) on MMG and 2.2 × 0.6 cm (92%) on CT (Fig. 1D). The tumor shadow remained but became vague on MMG. The low-density area disappeared on CT. However, on US, the lesion had completely disappeared and only a ductal structure was detected after the chemotherapy (Fig. 1E). In brief, a partial response was obtained clinically. A wide resection of the right breast was carried out 28 days after the termination of neoadjuvant chemotherapy. Histopathological examination revealed that the tumor had completely disappeared with negative lymph node metastasis (0/14). Only foamy changes with lymphocytic infiltration and stromal hyalinization could be observed in the resected specimen (Fig. 1F). The effect of neoadjuvant chemotherapy was therefore evaluated as a histologically complete response. Postoperative adjuvant chemotherapy consisting of two cycles of ADM plus TXT was given to the patient. She is currently disease free 8 months after surgery.

CASE 2

A 61-year-old postmenopausal woman with a left primary breast carcinoma (T3N0M0) received the above neoadjuvant chemotherapy. She had no past or family history of malignancies. Physical examination showed an ill-defined, stony-hard mass located in the upper inner quadrant of her left breast. The tumor size was 5.5 × 3.3 cm at the first consultation. MMG revealed an ill-defined tumor shadow without microcalcification in the left breast, the size of which was 3.3 × 2.8 cm in diameter. An irregular hypoechoic-tumorous lesion could be detected by US, the size of which was 3.1 × 3.0 cm in diameter. A lobulated tumorous lesion also could be detected on CT, the size of which was 3.0 × 2.5 cm in diameter. Core needle biopsy revealed an invasive ductal carcinoma of the left breast, histological grade 3. ER and PgR were both negative. Positive p53 nuclear immunoreaction but negative c-erbB-2 overexpression were observed in this tumor. She received the neoadjuvant chemotherapy to completion and toxicities were tolerable. After the termination of chemotherapy, the tumor size was 3.0 × 2.5 cm (60%). Therefore, a partial response was obtained clinically. A modified radical mastectomy (Auchincloss mode) was carried out 27 days after the termination of neoadjuvant chemotherapy. Histopathological examination revealed that the tumor had completely disappeared but without lymph node metastasis (0/13). With regard to the initial site of the tumor, only inflammatory changes with foamy macrophages and hemosiderin deposits could be observed in the resected specimen. The effect of neoadjuvant chemotherapy was therefore evaluated as a histologically complete response. Postoperative adjuvant chemotherapy consisting of two cycles of ADM plus TXT was given to the patient. She is currently disease free 6 months after surgery.

CASE 3

A 67-year-old postmenopausal woman with a right primary breast carcinoma (T3N0M0) received the above neoadjuvant chemotherapy. She had no past or family history of malignancies. Physical examination showed an ill-defined, stony-hard mass incompletely fixed to the skin, located in the upper outer quadrant of her right breast. The tumor size was 5.2 × 5.2 cm in diameter at the first consultation. MMG revealed an ill-defined spiculated tumor shadow with microcalcification in the right breast, the size of which was 3.0 × 3.0 cm in diameter (Fig. 2A). An irregular hypoechoic–tumorous lesion could be detected by US, the size of which was 4.0 × 4.0 cm in diameter. An irregular tumorous lesion also could be detected on CT, the size of which was 3.0 × 2.5 cm in diameter. Core needle biopsy revealed an invasive ductal carcinoma of the right breast, histological grade 3. ER and PgR were both negative. Positive p53 nuclear immunoreaction and positive c-erbB-2 overexpression were observed in this tumor. She received the neoadjuvant chemotherapy to completion and toxicities were tolerable. After the termination of chemotherapy, the tumor size was 2.5 × 2.5 cm (77%). The imaging examinations (MMG, US and CT) were also re-evaluated prior to surgery. On MMG, the lesion became smaller (2.0 × 1.5 cm: 67%) and the tumor specification became vague but microcalcification was unchanged (Fig. 2B). US illustrated a definite reduction in tumor size after the chemotherapy (1.5 × 0.9 cm: 92%). It could not be differentiated from fibrocystic changes, e.g. adenosin. With regard to CT, the irregular tumorous lesion became smaller but still remained after the chemotherapy (2.0 × 1.5 cm: 60%). Therefore, partial response was obtained clinically. A wide excision was carried out 27 days after the termination of neoadjuvant chemotherapy. Histopathological examination revealed that the right breast tumor had completely disappeared without lymph node metastasis (0/13). With regard to the initial site of the tumor, only fibrocystic changes with an aggregate of foamy and hemosiderin-laden macrophages and an inflammatory cell infiltrate could be observed in the resected specimen. The effect of neoadjuvant chemotherapy was therefore evaluated as a histologically complete response. Postoperative adjuvant
Neoadjuvant chemotherapy for breast cancer

Chemotherapy consisting of two cycles of ADM plus TXT was given to the patient. She is currently disease free 10 months after surgery.

**DISCUSSION**

In these three cases with primary breast carcinoma after neoadjuvant chemotherapy, the resected specimen showed no microscopic evidence of residual cancer cells including an intraductal component in the primary lesions. There was histological evidence of tumor regression in each specimen. All patients were judged clinically as partial responders, because of the remaining tumorous lesions in the imaging examinations. However, these tumorous lesions could be related to the chemotherapy-induced fibrosis and tumor necrosis or the remaining fibrocystic changes.

Helvie et al. (4) documented that MMG was more sensitive than clinical examination in the prediction of residual carcinoma after chemotherapy. However, it was very difficult to evaluate the clinical meaning of the remaining microcalcifications after chemotherapy as in case 3. We previously reported that CT scanning was useful for evaluating histological tumor extension of breast carcinomas (5). Several authors have documented that contrast-enhanced magnetic resonance imaging could identify the residual disease in patients with breast cancer after neoadjuvant chemotherapy (6,7). Recently, the RECIST Working Group reported that US should not be used for the evaluation of cancer treatment (8). In this study, it was considered very difficult to estimate the extent of residual tumors accurately in patients with primary breast cancer after neoadjuvant chemotherapy by any type of imaging examination. In all specimens, chemotherapy-induced diffuse fibrosis and tumor necrosis were evident. The remaining tumorous lesion or microcalcification on the imaging examinations prior to surgery was not related to the cancerous changes but mainly to fibrosis or granulomatous changes due to tumor necrosis. These were the main reasons why imaging examinations tended to overestimate the residual tumor cells after chemotherapy.

The evaluation of the residual mass on the imaging examinations requires further studies. This will allow the selection of patients who may not need additional surgery.
References


