



Original contribution

Metaplastic carcinoma of the breast[☆]

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Summary The purposes of this study were to investigate whether the biological characteristics or outcomes of patients with metaplastic carcinoma, invasive ductal carcinoma, or invasive lobular carcinoma of the breast differ; to determine whether the metaplastic carcinoma subtypes have similar malignant potentials; and to identify accurate predictors of outcome in patients with metaplastic carcinoma. The subject comprised 6137 invasive ductal carcinoma patients, 301 invasive lobular carcinoma patients, and 46 metaplastic carcinoma patients of the breast. The metaplastic carcinomas were classified according to the World Health Organization classification. Multivariate analyses clearly demonstrated that the metaplastic carcinoma patients had a significantly poorer outcome than the invasive ductal carcinoma patients or the invasive lobular carcinoma patients independent of the nodal status or age not exceeding 39 years, whereas patients with triple-negative metaplastic carcinomas or triple-negative invasive lobular carcinomas had a poorer outcome than those with triple-negative invasive ductal carcinomas. Although no significant differences in clinical outcome were observed among the metaplastic carcinoma subtypes in multivariate analyses, an age not exceeding 39 years, the presence of skin invasion, and the presence of a squamous cell carcinoma component in nodal tumors were significant outcome predictors for metaplastic carcinoma patients. In conclusion, the results of this study clearly demonstrated that metaplastic carcinoma is more aggressive than invasive ductal carcinoma or invasive lobular carcinoma. Although the metaplastic carcinoma subtypes had no prognostic significance, an age not exceeding 39 years, the presence of skin invasion, and the presence

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of a squamous cell carcinoma component in nodal tumors were significant predictors of outcome among metaplastic carcinoma patients.

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1. Introduction

The World Health Organization (WHO) classifies metaplastic carcinoma (MPC) into (1) epithelial type and (2) mixed type [1]. Epithelial-type MPC is in turn classified into (1) squamous cell carcinoma, (2) adenocarcinoma with spindle cell differentiation, and (3) adenosquamous carcinoma, whereas mixed type of MPC is classified into (1) carcinoma with chondroid metaplasia, (2) carcinoma with osseous metaplasia, and (3) carcinosarcoma [1]. Several studies have investigated whether the biological characteristics of these MPC subtypes differ [2-19] and whether outcome predictors exist for patients with these MPC subtypes [2-7,9,10,13-15,18]. However, almost all these studies involved survival analyses performed for a small number of MPC cases or that only used univariate analyses [2-7,9,10,13-15,18]. Thus, whether the presently used subtype classification reflects the malignant potential of these lesions remains uncertain; and which factors are the most important predictors of outcome in patients with MPC remains controversial.

Furthermore, although patients with MPC are thought to exhibit a poorer outcome than patients with invasive ductal carcinoma (IDC) or invasive breast carcinoma [15,18], the survival periods of patients with MPC, IDC, or invasive lobular carcinoma (ILC) have not been compared using consecutive cases treated during the same period. Thus, no direct evidence indicating that MPC is more aggressive than IDC or ILC presently exists.

The purposes of this study were (1) to investigate whether the biological characteristics or outcomes of patients with MPC, IDC, or ILC of the breast differ; (2) to determine whether the MPC subtypes have similar malignant potentials; and (3) to identify accurate predictors of outcome in patients with MPC. The results of this study clearly demonstrated that patients with MPC have a significantly poorer outcome than patients with IDC or ILC; that the MPC subtype has no prognostic significance; and that an age not exceeding 39 years, the presence of skin invasion, and the presence of a squamous cell carcinoma component in nodal tumors were significant predictors of outcome among patients with MPC.

2. Materials and methods

2.1. Cases

The subject comprised 6137 consecutive cases of IDC, 301 consecutive cases of ILC, and 46 consecutive cases of MPC of the breast; all the subjects had undergone surgery at the

National Cancer Center Hospital between January 1982 and March 2007. For the MPC cases, all the breast carcinomas diagnosed as squamous cell carcinoma, epidermoid carcinoma, MPC, carcinosarcoma, carcinoma with spindle cell metaplasia, carcinoma with chondroid metaplasia, or carcinoma with osteoid metaplasia at the National Cancer Center Hospital between January 1982 and March 2007 were reviewed; 46 cases of MPC were subsequently identified.

Clinical information was obtained from the patients' medical records. All the patients were Japanese women, ranging in age from 20 to 98 years (median, 53 years). Overall, 2094 patients were premenopausal and 3056 were postmenopausal. A partial mastectomy had been performed in 1208 patients, a modified radical mastectomy had been performed in 3340, and a standard radical mastectomy had been performed in 1139. A level I and II axillary lymph node dissection had been performed in all the patients, and some of the patients had been received a level III axillary lymph node dissection.

The protocol (20-112) for this study was approved by the Institutional Review Board of the National Cancer Center.

2.2. Neoadjuvant therapy and adjuvant therapy

Because standardized neoadjuvant therapy and adjuvant therapy for patients with breast cancer were started in the 1990s at the National Cancer Center Hospital, the effect of neoadjuvant therapy or adjuvant therapy was examined in patients with IDCs, ILCs, or MPCs that had been surgically treated since January 1990. Neoadjuvant therapy was performed in 467 out of 2039 patients with IDC, 28 out of 111 patients with ILC, and 4 out of 46 patients with MPC, whereas adjuvant therapy was performed in 1756 out of 2303 patients with IDC, 101 out of 122 patients with ILC, and 18 out of 46 patients with MPC. Among these patients, 378 received chemotherapy, 749 received endocrine therapy, and 693 received combined chemoendocrine therapy. In the 1980s, the main chemotherapy regimens in use were anthracycline based; but nonanthracycline-based regimens were used in some patient populations. In the 1990s, the chemotherapy regimens in use were anthracycline based and were combined with or without taxane. In the 1980s, the endocrine therapy regimens in use were tamoxifen combined with or without a gonadotropin-releasing hormone agonist, whereas an aromatase inhibitor was additionally used in the 1990s.

2.3. Histologic examination of IDCs and ILCs

The following IDC and ILC characteristics were obtained from the pathologic diagnostic records, which

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