Int Surg 2024;**107–108:**35–38
DOI: 10.9738/INTSURG-D-22-00005.1

Consideration of the Process of Lymph Node Metastasis in Invasive Breast Cancer With Squamous Cell Differentiation

Mayu Aoki[1,2], Takaaki Fujii[1,2], Chikako Honda[1,2], Yuko Nakazawa[1,2], Misato Ogino[1,2], Sayaka Obayashi[1,2], Ken Shirabe[2]

[1]*Division of Breast and Endocrine Surgery*

[2]*Department of General Surgical Science, Graduate School of Medicine, Gunma University, Gunma, Japan*

Background: Breast cancer with squamous differentiation is a relatively rare condition. Clinically, lymph node metastasis is uncommon in metaplastic carcinoma We treated a patient with lymph node metastasis of the ductal carcinoma component of invasive ductal carcinoma with squamous cell differentiation.

Case Report: An 84-year-old postmenopausal Japanese woman had a left-breast mass with an enlarged lymph node in the left axilla. A biopsy revealed an invasive ductal carcinoma with squamous cell differentiation. A left mastectomy with axillary lymph node dissection was performed. The histologic evaluation revealed invasive ductal carcinoma with squamous cell differentiation. One lymph node was positive for metastasis consisting of ductal carcinoma without squamous cell differentiation.

Conclusion: This case suggests that lymph node metastasis in ductal carcinoma with squamous differentiation may first involve the ductal carcinoma component, and then differentiation may occur in the involved lymph nodes. This is an interesting case highlighting the process of the progression of lymph node metastasis in cases with breast cancer with squamous cell differentiation.

Key words: Breast cancer – Squamous cell differentiation – Lymph node metastasis

Breast cancer with squamous differentiation is a relatively rare condition. Squamous cell carcinoma of the breast is classified as a special type of invasive carcinoma and is a very rare condition, accounting for only 0.1% of all breast cancers.[1,2] Some types of metaplastic carcinoma are completely

Corresponding author: Takaaki Fujii, MD, PhD, FACS, Division of Breast and Endocrine Surgery, Department of General Surgical Science, Graduate School of Medicine, Gunma University, 3-39-22 Showa-machi, Maebashi, Gunma 371-8511, Japan.
Tel: +81 0272208224; Fax: +81 0272208230; E-mail: ftakaaki@gunma-u.ac.jp

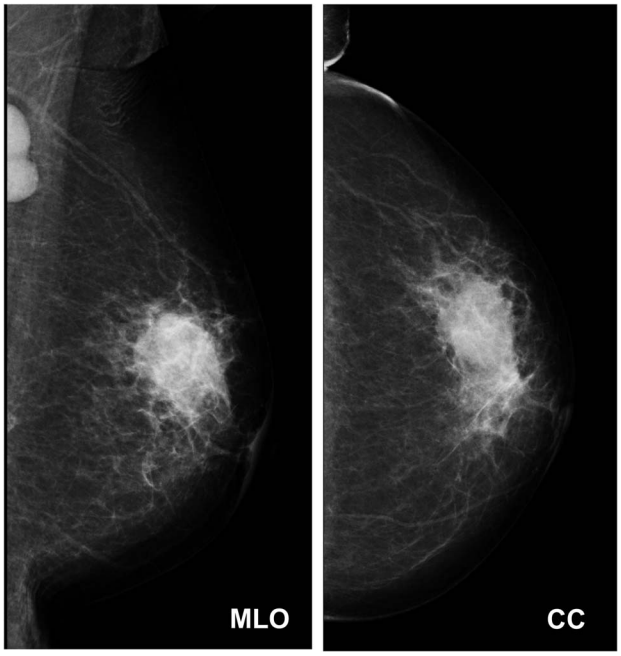

Fig. 1 Mammography revealed a large, dense mass in the left breast. CC, craniocaudal; MLO, mediolateral oblique.

composed of a metaplastic component, whereas others are a mixture of invasive ductal carcinoma and a metaplastic component. Breast cancer with a squamous component has been reported to have a poor prognosis.[2–6] We encountered a case of lymph node metastasis of a ductal carcinoma component in a patient with invasive ductal carcinoma with squamous cell differentiation. From this case, we discuss the progression process of lymph node metastasis in a case of squamous differentiated breast cancer.

Case Report

An 84-year-old postmenopausal Japanese woman was referred to our division for the examination of a large mass in her left breast. The physical examination revealed a 3.0-cm palpable mass that was elastically firm in the upper external quadrant of the left breast; a 2.5-cm enlarged lymph node was palpable in the left axilla. Mammography revealed a large, dense mass in the left breast (Fig. 1). Sonography revealed an irregular hypoechoic mass of 20 × 20 × 14 mm with partially indistinct borders, internal heterogeneity, and posterior echo enhancement in the upper external quadrant of the left breast and an enlarged lymph node in the left axilla (Fig. 2). There was no finding of distant metastasis.

A core needle biopsy revealed an invasive ductal carcinoma with squamous cell differentiation. The patient received a diagnosis of left breast cancer cT2N1M0 Stage IIB, and a left mastectomy with axillary lymph node dissection was performed. The resected specimen showed a relatively well-defined mass. The histologic evaluation revealed that tumor cells with enlarged nuclei with well-defined nucleoli and eosinophilic cytoplasm proliferated while forming large-to-medium-sized foci in a plump or sheetlike pattern, indicating invasive ductal carcinoma of the breast. However, approximately 40% of the tumor showed differentiation into squamous epithelium with broad polygonal cytoplasm and individual cell keratinization (Fig. 3). These findings are compatible with invasive ductal carcinoma with squamous cell differentiation.

Immunohistochemical staining was negative for estrogen and progesterone receptor, and the HER2 score was 0. One of 22 dissected lymph nodes was positive for lymph node metastasis. Histologically, tumor cells with enlarged nuclei with well-defined nucleoli and eosinophilic cytoplasm, similar to the ductal carcinoma component of the primary tumor, were proliferating in full and sheetlike foci in the metastatic lymph node (Fig. 4). However, there was no evidence of squamous cell differentiation in the lymph node. The patient has not received adjuvant therapy or radiotherapy because of her advanced age and low performance status. The patient has remained alive for 48 months without locoregional or systemic recurrence of the tumor.

Discussion

Metaplastic carcinoma is a heterogeneous group of neoplasms characterized by squamous, spindle cell, or mesenchymal differentiation with or without adenocarcinoma component.[1–3] Metaplastic carcinoma of the breast is a relatively rare tumor, and the reported data are limited. There are several hypotheses regarding the histologic development of squamous cell differentiation, including ectopic squamous cell origin and squamous cell differentiation of adenocarcinoma or breast tissue. Because ductal carcinoma and squamous cell carcinoma coexist in many cases, it is generally thought that squamous cell differentiation develops from conventional ductal carcinoma.[2,7–9] Our patient's case was diagnosed as invasive ductal carcinoma with dominant area of squamous differentiation.

Metaplastic carcinoma of the breast exhibits clinicopathologic features that are distinct from those of ductal carcinoma.[2–6,10–12] Clinically, metaplastic breast carcinoma is an aggressive disease, but lymph node metastasis is uncommon.[2–6,10–12] In our patient's case,

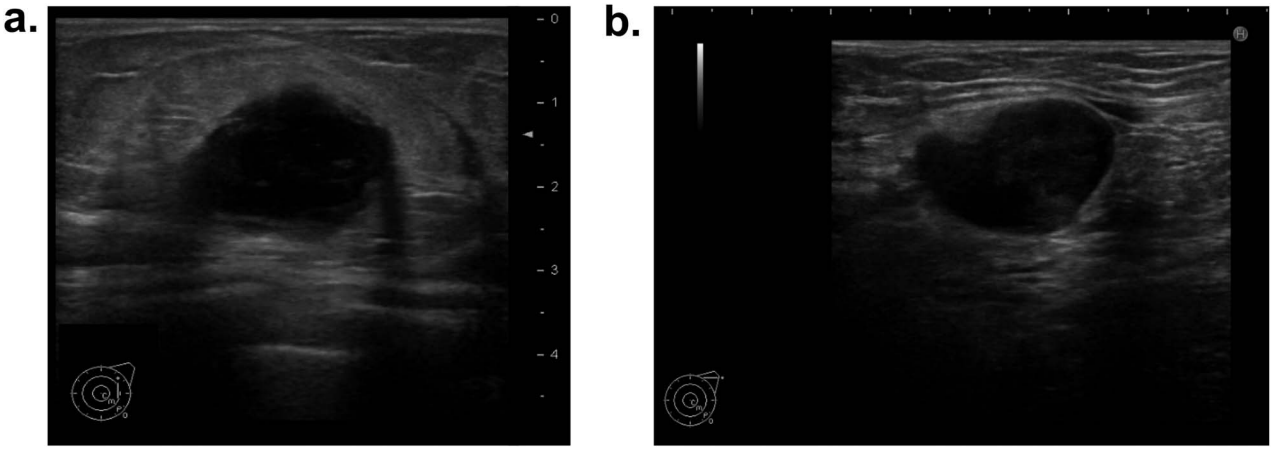

Fig. 2 Sonography revealed an irregular hypoechoic mass of 20 × 20 × 14 mm with partially indistinct borders, internal heterogeneity, and posterior echo enhancement in the upper external quadrant of the left breast (a), and an enlarged lymph node in the left axilla (b).

the lymph node metastasis consisted only of a ductal carcinoma component, and there was no squamous cell component in the involved node, suggesting that the ductal carcinoma component, not the squamous component, metastasized to the lymph node. There are several case reports of invasive ductal carcinoma with squamous cell carcinoma and positive axillary lymph nodes.[2,13] A study of breast carcinoma with squamous cell differentiation revealed that all of the lymph node metastases had a ductal carcinoma component (the same as the primary tumor), and ductal-squamous differentiation was observed in the several involved lymph nodes.[2] These results and our patient's case suggest that lymph node metastases may first be metastasized by ductal carcinoma components, and then differentiation occurs as the cancer cells proliferate.

Conclusion

Our patient's case suggests that lymph node metastasis in invasive ductal carcinoma with squamous cell differentiation may first involve the ductal carcinoma component, and then differentiation may occur in the involved lymph nodes. This is an interesting case illustrating the process of the progression of lymph node metastasis in cases with breast cancer with squamous cell differentiation.

Acknowledgments

The authors would like to thank Ms Fumie Takada and Ms Harumi Kanai for their secretarial assistance; both women are with the Department of General

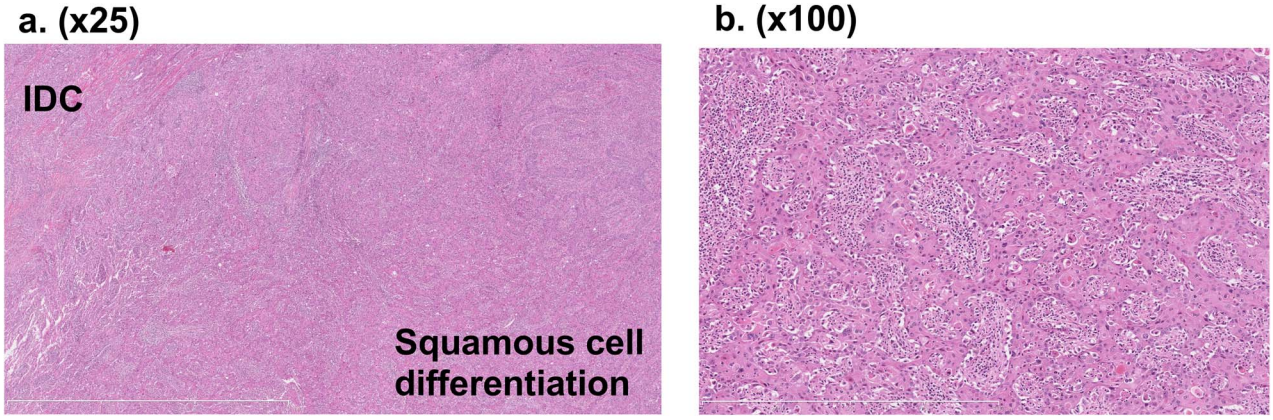

Fig. 3 (a) The histologic evaluation revealed invasive ductal carcinoma (IDC) with squamous cell differentiation (hematoxylin-eosin, original magnification ×25). (b) About 40% of the tumor showed differentiation into squamous epithelium with broad polygonal cytoplasm and individual cell keratinization (hematoxylin-eosin, original magnification ×100).

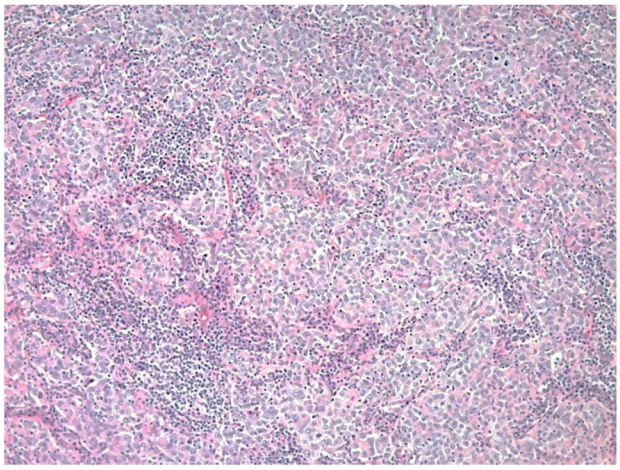

Fig. 4 One lymph node was positive for metastasis consisting of ductal carcinoma without squamous cell differentiation (hematoxylin-eosin, original magnification ×100).

Surgical Science, Gunma University Graduate School of Medicine. Maebashi, Gunma, Japan.

References

1. Oberman HA. Metaplastic carcinoma of the breast: a clinicopathologic study of 29 patients. *Am J Surg Pathol* 1987;**11**(12):918–929
2. Okada N, Hasebe T, Iwasaki M, Tamura N, Akashi-Tanaka S, Hojo T *et al*. Metaplastic carcinoma of the breast. *Hum Pathol* 2010;**41**(7):960–970
3. Beatty JD, Atwood M, Tickman R, Reiner M. Metaplastic breast cancer: clinical significance. *Am J Surg* 2006;**191**(5):657–664
4. Pezzi CM, Patel-Parekh L, Cole K, Franko J, Klimberg VS, Bland K. Characteristics and treatment of metaplastic breast cancer: analysis of 892 cases from the National Cancer Data Base. *Ann Surg Oncol* 2007;**14**(1)166–173
5. Luini A, Aguilar M, Gatti G, Fasani R, Botteri E, Brito JA *et al*. Metaplastic breast cancer, an unusual disease with worse prognosis: the experience of the European Institute of Oncology and review of the literature. *Breast Cancer Res Treat* 2007;**101**(3):349–353
6. Pai T, Shet T, Desai S, Patil A, Nair N, Parmar V *et al*. Impact of squamous differentiation in breast carcinoma. *Int J Surg Pathol* 2016;**24**(6):483–489
7. Lien HC, Lin CW, Mao TL, Kuo SH, Hsiao CH, Huang CS. p53 overexpression and mutation in metaplastic carcinoma of the breast: genetic evidence for a monoclonal origin of both the carcinomatous and the heterogeneous sarcomatous components. *J Pathol* 2004;**204**(2):131–139
8. Wada H, Enomoto T, Tsujimoto M, Nomura T, Murata Y, Shroyer KR. Carcinosarcoma of the breast: molecular-biological study for analysis of histogenesis. *Hum Pathol* 1998;**29**(11):1324–1328
9. Lien HC, Hsu CL, Lu YS, Chen TWW, Chen IC, Li YC *et al*. Transcriptomic alterations underlying metaplasia into specific metaplastic components in metaplastic breast carcinoma. *Breast Cancer Res* 2023;**25**(1):11
10. Rayson D, Adjei AA, Suman VJ, Wold JE, Ingle JN. Metaplastic breast cancer: prognosis and response to systemic therapy. *Ann Oncol* 1999;**10**(4):413–419
11. Yang X, Tang T, Zhou T. Prognosis and clinicopathological characteristics of metaplastic breast cancer: a meta-analysis. *Medicine (Baltimore)* 2022;**101**(49):e32226
12. Kaufman MW, Marti JR, Gallager HS, Hoehn JL. Carcinoma of the breast with pseudosarcomatous metaplasia. *Cancer* 1984;**53**(9):1908–1917
13. Nassar A, Sookhan N, Santisteban M, Bryant SC, Boughey JC, Giorgadze T *et al*. Diagnostic utility of snail in metaplastic breast carcinoma. *Diagn Pathol* 2010;**5**:76