Process of Lymph Node Metastasis in Invasive Breast Cancer with Squamous Cell Differentiation: A Case Report

MAYU AOKI  
Gunma University Graduate School of Medicine School of Medicine: Gunma Daigaku Daigakuin Igakukei Kenkyuka Igakubu

Takaaki Fujii  
Gunma Daigaku  https://orcid.org/0000-0001-8357-391X

CHIKAKO HONDA  
Gunma University Graduate School of Medicine School of Medicine: Gunma Daigaku Daigakuin Igakukei Kenkyuka Igakubu

YUKO NAKAZAWA  
Gunma University Graduate School of Medicine School of Medicine: Gunma Daigaku Daigakuin Igakukei Kenkyuka Igakubu

MISATO OGINO  
Gunma University Graduate School of Medicine School of Medicine: Gunma Daigaku Daigakuin Igakukei Kenkyuka Igakubu

SAYAKA OBAYASHI  
Gunma University Graduate School of Medicine School of Medicine: Gunma Daigaku Daigakuin Igakukei Kenkyuka Igakubu

REINA YAJIMA  
Gunma University Graduate School of Medicine School of Medicine: Gunma Daigaku Daigakuin Igakukei Kenkyuka Igakubu

KEN SHIRABE  
Gunma University Graduate School of Medicine School of Medicine: Gunma Daigaku Daigakuin Igakukei Kenkyuka Igakubu

Research Article

Keywords: Breast cancer, squamous cell differentiation, lymph node metastasis.

DOI: https://doi.org/10.21203/rs.3.rs-633897/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

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 histological 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.

Background

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 very rare condition, accounting for only 0.1% of all breast cancers (1, 2). Some types of metaplastic carcinoma are completely 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.

Case Presentation

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 20x20x14 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 was diagnosed as left breast cancer cT2N1M0 cStage IIb, and a left mastectomy with axillary lymph node dissection was performed. The resected specimen showed a relatively well-defined mass.
The histological 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 sheet-like pattern, indicating invasive ductal carcinoma of the breast. However, approx. 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 sheet-like 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 histological development of squamous cell differentiation, including ectopic squamous cell origin and squamous cell differentiation of adenocarcinoma or breast tissue. Since 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, 8). Our patient’s case was diagnosed as invasive ductal carcinoma with dominant area of squamous differentiation.

Metaplastic carcinoma of the breast exhibits clinicopathological features that are distinct from those of ductal carcinoma (2–6, 9, 10). Clinically, metaplastic breast carcinoma is an aggressive disease, but lymph node metastasis is uncommon (2–6, 9, 10). In our patient’s case, 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, 11). 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.

**Declarations**

**Ethics approval and consent to participate**

Written consent was obtained from patient for the use of their records and imaging in future studies.

**Consent for publication**

Not applicable

**Availability of data and material**

The datasets used in the current study are available from the corresponding author on reasonable request.

**Competing interests**

The authors declare that they have no competing interests

**Funding**

None.

**Authors’ contributions**

MA and TF collected data and wrote the initial draft of the manuscript. CH., YN, MO, SO and RY collected data. TF and KS interpreted the results and were involved in drafting the work and revising it critically for important intellectual content. TF approved the final version to be published. All authors have read and approved the final manuscript.

**Acknowledgements**

The authors would like to thank Ms. Fumie Takada and Ms. Harumi Kanai for their secretarial assistance. FT and HK belong to Department of General Surgical Science, Gunma University Graduate School of Medicine. Maebashi, Gunma, 371-8511 Japan.

**References**

1. Oberman HA. Metaplastic carcinoma of the breast. A clinicopathologic study of 29 patients. Am J Surg Pathol. 1987;12:918–29.
2. Okada N, Hasebe T, Iwasaki M, Tamura N, Akashi-Tanaka S, Hojo T, Shibata T, Sasajima Y, Kanai Y, Kinoshita T. Metaplastic carcinoma of the breast. Hum Pathol. 2010;41:960–70.

3. Beatty JD, Atwood M, Tickman R, Reiner M. Metaplastic breast cancer: clinical significance. Am J Surg. 2006;191:657–64.

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;14:166–73.

5. Luini A, Aguilar M, Gatti G, Fasani R, Botteri E, Brito JA, Maisonneuve P, Vento AR, Viale G. 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;101:349–53.

6. Pai T, Shet T, Desai S, Patil A, Nair N, Parmar V, Gupta S, Budrukkar A, Sarin R, Badwe R. Impact of squamous differentiation in breast carcinoma. Int J Surg Pathol. 2016;24:483–9.

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;204:131–9.

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;29:1324–8.

9. Rayson D, Adjei AA, Suman VJ, Wold JE, Ingle JN. Metaplastic breast cancer: Prognosis and response to systemic therapy. Ann Oncol. 1999;10:413–9.

10. Kaufman MW, Marti JR, Gallager HS, Hoehn JL. Carcinoma of the breast with pseudosarcomatous metaplasia. Cancer. 1984;52:1908–17.

11. Nassar A, Sookhan N, Santisteban M, Bryant SC, Boughey JC, Giorgadze T, Degnim A. Diagnostic utility of snail in metaplastic breast carcinoma. Diagn Pathol. 2010;5:76.

Figures
Figure 1

Mammography revealed a large dense mass in the left breast. MLO: medio-lateral oblique, CC: cranio-caudal.

Figure 2

Sonography revealed an irregular hypoechoic mass of 20 x 20 x 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).

**Figure 3**

The histological evaluation revealed that invasive ductal carcinoma with squamous cell differentiation (HE, x25) (a). About 40% of the tumor showed differentiation into squamous epithelium with broad polygonal cytoplasm and individual cell keratinization (HE, x100) (b).

![Histological evaluation of invasive ductal carcinoma](image)

**Figure 4**

One lymph node was positive for metastasis consisting of ductal carcinoma without squamous cell differentiation (HE, x100).