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Case Report

Clinically node-negative invasive lobular carcinoma of the breast showing multiple lymph node metastases [☆]

Yurie Kitano, Shoji Oura^{*}

Department of Surgery, Kishiwada Tokushukai Hospital 4-27-1, Kamori-cho, Kishiwada-city, Osaka, Japan

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ABSTRACT

A 73-year-old woman was pointed out of her right breast tumor on screening computed tomography (CT). Mammography showed distortion of the mammary gland and skin retraction. Ultrasound (US) showed an irregular tumor with hyperechoic haloes adjacent to the anterior tumor borders. Neither lymphadenopathy nor image findings suggesting lymph node metastasis were detected on US and CT. Core needle biopsy pathologically showed the tumor to be invasive lobular carcinoma. Under the preoperative diagnosis of node-negative breast cancer, the patient underwent mastectomy and sentinel node biopsy. Due to no sentinel node detection, a small but hard lymph node was identified and submitted for frozen section as a sampling node. After confirming the lymph node metastasis on frozen section, axillary lymph node dissection revealed 12 lymph node metastases. Postoperative pathological study showed cancer cell infiltration to the dermis near the nipple-areolar complex. In addition, immunostaining showed the tumor to have low proliferative biology, i.e., Ki-67 labelling index of 10%. Breast surgeons should note that indolent invasive lobular carcinoma with cancer cell infiltration to the skin near the nipple-areolar complex can have multiple lymph node metastases even though showing neither lymphadenopathy nor image findings suggesting lymph node metastasis.

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Introduction

Axillary lymph node metastasis is one of the important prognostic factors in breast cancer. However, all preoperative image modalities unfortunately underestimate lymph node

metastasis in about 10%-20% of breast cancer patients [1–3]. Consequently, in breast cancer surgery, axillary dissection has long been uniformly performed even in clinically node-negative patients.

Axillary lymph node dissection can cause unpleasant lymphedema, often leading to marked deterioration of quality of

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^{*} Corresponding author.

E-mail address: shouji.oura@tokushukai.jp (S. Oura).

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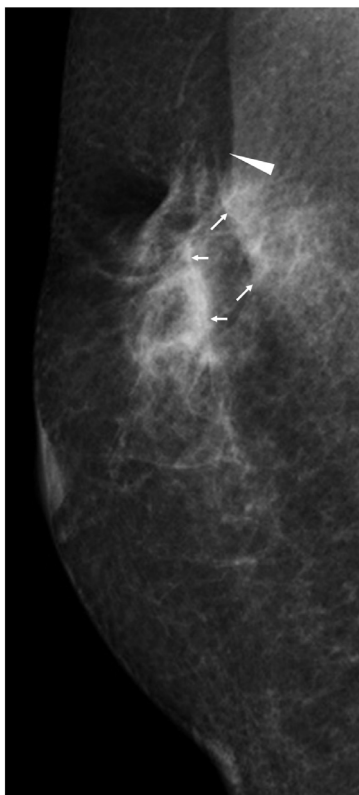


Fig. 1 – Mammography showed distortion of the mammary gland (arrows) and skin retraction (arrowhead).

life (QOL) of breast cancer patients. Therefore, many attempts such as evaluation of axillary nodal status using various images [1–3], 4-node sampling [4], and sentinel node (SN) biopsy [5] have been made to avoid lymphedema. In particular, SN biopsy has rapidly spread all over the world due to its excellent accuracy and has become an essential nodal evaluation modality in breast cancer surgeries.

SN biopsy is generally performed in patients without lymphadenopathy. However, even in the absence of lymphadenopathy, some image findings suggest lymph node metastasis [3]. Conversely, lymph node metastasis except both for micrometastasis and isolated tumor cells is extremely rare when lacking image findings suggesting lymph node metastasis in breast cancer patients with no lymphadenopathy.

We herein report a case of clinically node-negative invasive lobular carcinoma of the breast showing multiple lymph node metastases.

Case report

A 73-year-old woman was pointed out of her right breast tumor on screening computed tomography (CT). The patient had skin retraction just above the tumor in the upper and lateral quadrant of her right breast. No axillary lymph node swelling was palpated. Mammography showed distortion of the mammary gland and skin retraction (Fig. 1). Ultrasonography (US) showed an irregular mass with low internal echoes, attenu-

ated posterior echoes, ruptured anterior borders of the mammary gland, and hyperechoic haloes adjacent to the anterior tumor borders (Fig. 2A) [6]. Magnetic resonance (MR) imaging of the tumor showed a hypo-intense pattern on T1-weighted images, a slightly hyper-intense pattern on T2-weighted images, and a plateau pattern on time-signal intensity curve, suggesting the presence of considerable amount of collagen fiber in the tumor. Image evaluations using US (Fig. 2B), MR axillography, and CT (Fig. 3) showed neither lymph node swelling nor any image findings suggesting lymph node metastasis. Core needle biopsy of the tumor pathologically showed small atypical cells growing in sporadic and linear fashions with fibrosis, leading to the diagnosis of invasive lobular carcinoma. Under the preoperative diagnosis of node-negative breast cancer, the patient underwent mastectomy and SN biopsy. However, no sentinel nodes were detected on SN biopsy using a fluorescent imaging system. We, therefore, identified a small hard node, 5 mm in size, for frozen section as a sampling node. After confirming the lymph node metastasis on frozen section (Fig. 4A), axillary dissection was performed to the patient and revealed a total of 12 lymph node metastases. Postoperative pathological study showed luminal and indolent, i.e., Ki-67 labelling index of 10%, cancer cells growing in linear, diffuse, and sheet-like fashions with invasion to both the major pectoral muscle and the dermis near the nipple-areolar complex (Figs. 4B–F). After receiving adjuvant dose-dense chemotherapy and postmastectomy radiotherapy, the patient has been well without any recurrences on endocrine therapy for 16 months.

Discussion

Once metastasizing to lymph nodes, cancer cells generally give rise to lymph node swelling and / or metastasis-suggesting nodal image findings such as deletion of a nodal hilum, eccentric cortical hypertrophy, and an increase of depth / width ratio [3]. Based on these clinical and image findings, breast surgeons generally determine the indication of SN biopsy in each case. If doubtful node(s) are detected on images, aspiration biopsy cytology under ultrasound guidance is generally done to the target node(s) to avoid unnecessary SN biopsy.

Invasive lobular carcinomas show more favorable biology than invasive ductal carcinomas and often develop recurrence even after the standard follow-up period of 10 years [7,8]. Indolent biology of invasive lobular carcinoma well explains both the lymph node metastasis without lymphadenopathy and the late recurrence. Although cancer cells were densely present in the small sampling node in this case, pathological examination of the node showed multiple lymphoid follicles without any oppression or deformation (Fig. 4A). Which factor brought about these pathological findings remains uncertain.

In addition to the late recurrence, invasive lobular carcinoma sometimes metastasizes to various sites and organs such as retroperitoneum, uterus, stomach, and colon to which ductal carcinomas hardly metastasize [9,10]. This feature is probably caused by the loss of E-cadherin function in invasive lobular carcinoma. In short, low cell-to-cell adhesion charac-

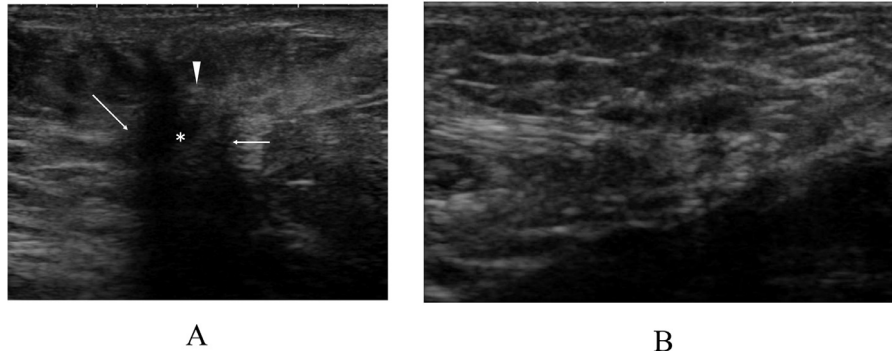


Fig. 2 – Ultrasonography showed (A) an irregular tumor (asterisk) with obscured borders (arrows), attenuated posterior echoes, hyperechoic haloes (arrowhead), and (B) no lymphadenopathy.

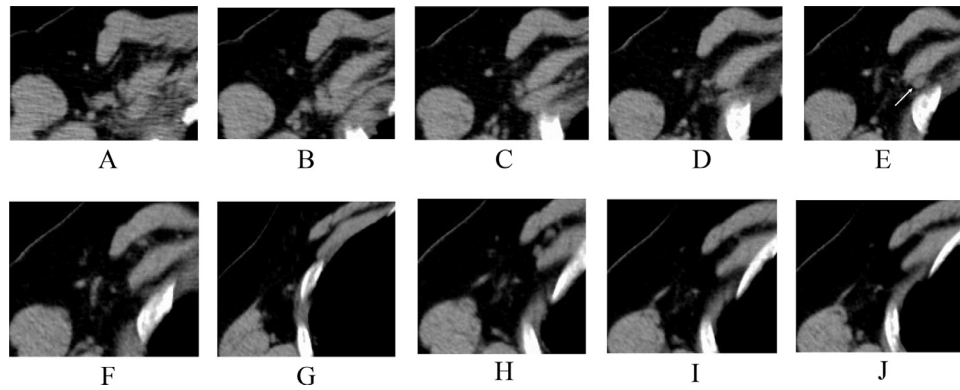


Fig. 3 – Computed tomography (CT). CT (A-J) showed neither lymphadenopathy nor image findings suggesting lymph node metastasis. The largest node detected with CT was oval and 8mm in size (E, arrow).

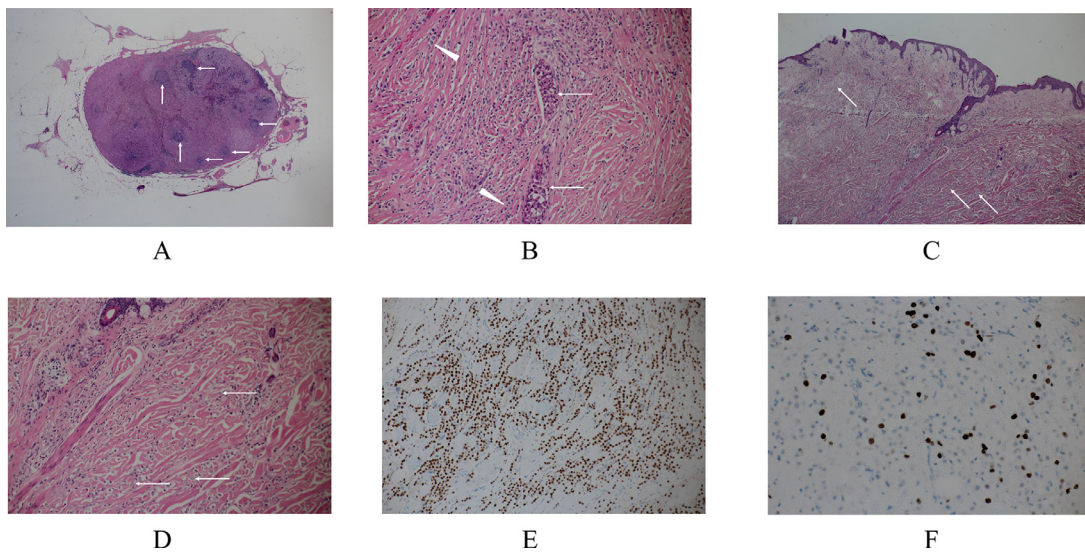


Fig. 4 – Pathological findings. (A) The small sampling node, 5 mm in size, had multiple lymph follicles without any oppression or deformation (arrows). (B) Magnified view showed an indian file pattern (arrowheads) in the collagenous stroma and lymphovascular invasion (arrows). (C) Low magnified view showed small atypical cells infiltrating toward the dermis. (D) Magnified view showed small atypical cells lining in lines near the dermis. (E) Immunostaining showed the tumor cells to be rich in estrogen receptor, i.e., Allred score of 8. (F) Ki-67 labelling index was low as 10%.

teristic of invasive lobular carcinoma facilitates exfoliation of cancer cells from the primary tumor and contributes to the metastasis of them to the uncommon sites.

Lymphatic flow in the breast is known to be most intense in and around the nipple-areolar complex. The sub-areolar area, therefore, is most frequently chosen for the tracer injection site in SN biopsy [11]. This fact means that breast cancer located near the nipple-areolar complex more easily metastasizes to lymph nodes than that located far from the nipple-areolar complex, even if they have exactly the same size and biology. In addition to the decreased cell-to-cell adhesion characteristic mentioned above, the location of invasive lobular carcinoma should have further promoted lymph node metastasis in this case. Therefore, if cancer cells in the lymph nodes have indolent biology, many metastatic lymph nodes can remain unswollen with no metastasis-suggesting image findings for a relatively long term.

It is very important to predict the possibility of multiple lymph node metastases based on clinical and / or image findings before surgery. On ultrasound, hyperechoic haloes adjacent to the anterior tumor borders are formed by massive back scattering of ultrasounds due to the difference of acoustic impedance between fat cells and cancer cells infiltrating into the fat tissue. Therefore, the presence of hyperechoic haloes adjacent to the anterior tumor borders observed in this case suggested the presence of a lot of cancer cells near the skin. In addition, skin retraction implies the presence of fibrosis caused by cancer cells near the skin. These findings naturally do not directly imply lymph node metastasis. Physicians, however, should pay much attention to these image and clinical findings to properly cope with multiple lymph node metastases in clinically node-negative patients with indolent invasive lobular breast carcinoma.

Conclusion

Breast oncologists should note that indolent invasive lobular carcinomas with cancer cell infiltration to the skin near the nipple-areolar complex can have multiple lymph node metastases even if showing a clinical node-negative phenotype.

Patient consent

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Author contribution

YK designed the concept of this study. SO drafted the manuscript.

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