

Case Report

Ectopic Breast Cancer Arising within an Axillary Lymph Node

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We report our experience with the diagnosis and treatment of an ectopic breast cancer arising within an axillary lymph node. The patient was a 65-year-old woman diagnosed breast cancer and axillary lymph node metastasis. We performed a partial mastectomy and axillary lymph node dissection. Postoperative pathology revealed no malignant lesions in the breast; however, a nodule in one of axillary lymph nodes had mixed benign and malignant components, leading to a diagnosis of invasive ductal carcinoma derived from ectopic mammary tissue. This case represents a very rare form of breast cancer, and the malignancy was difficult to distinguish from metastasis.

Key words: breast cancer, ectopic breast cancer, axillary lymph node

Ectopic breast tissue results from improper regression of the milk line, an ectodermal thickening extending from the axilla to the groin that is formed during fetal development and then regresses to leave behind anatomic breasts [1]. The reported prevalence of ectopic breast tissue in women ranges from 0.2% to 6%, and the condition is most common in Asian populations [1]. Ectopic breast tissue has the same potential for malignant transformation as eutopic breast tissue [1]. Ectopic mammary tissue is generally found in the subcutaneous tissue and deep dermis of the axilla [1], with infrequent occurrence in the axillary lymph nodes [2]. The reported frequency of ectopic mammary tissue in the sentinel lymph nodes is less than 0.2% [3]. We present a case with a primary breast cancer arising in ectopic mammary tissue within an axillary lymph node.

Case Report

The patient was a 65-year-old woman. She had undergone partial right mastectomy and sentinel lymph node biopsy for right breast cancer 15 years prior to the current presentation. The pathological result was ductal carcinoma *in situ* (DCIS), but there were no metastases in the sentinel nodes harvested. She underwent 5 years of tamoxifen treatment after surgery. During follow-up, she underwent tumor resection twice for intraductal papilloma, but there were no findings suggesting malignancy.

Fifteen years after the tumor resection, a screening Positron Emission Tomography-Computed Tomography (PET-CT) scan performed at her request during a routine breast cancer screening visit revealed abnormal ¹⁸F-fluorodeoxyglucose (FDG) accumulation in the right breast Standard Uptake Value ((SUV) max 2.868) and one right axillary lymph node (SUV max 4.131) but no other abnormalities (Fig. 1). She was thus suspected to have axillary lymph node metastasis of breast cancer.

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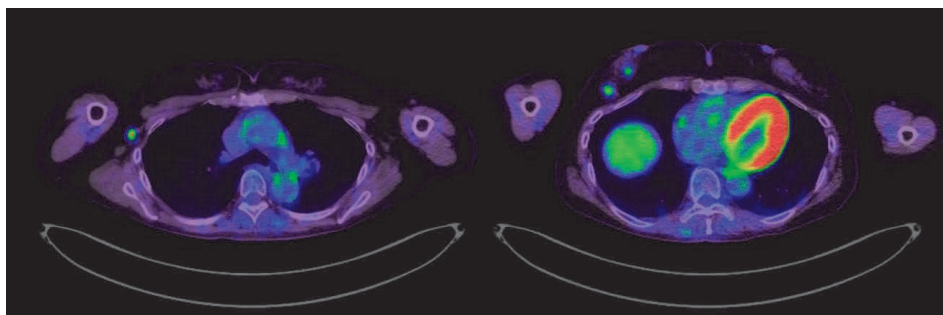


Fig. 1 A screening PET-CT scan showed abnormal FDG accumulation in the right breast (SUV max 2.868) and one right axillary lymph node (SUV max 4.131).

She then received a detailed examination, including mammography, ultrasonography, and contrast-enhanced (CE) magnetic resonance imaging (MRI) (Fig. 2). Mammography showed an enlarged right axillary lymph node and Focal Asymmetric Density (FAD) in the right Middle-Outer region. Breast ultrasonography showed an irregular hypoechoic mass 1.6 cm in size at the 7 o'clock position and enlarged lymph nodes in the right axilla. CE-MRI revealed multiple contrast-enhanced nodules on the lower outer side of the right breast, which raised suspicion of intraductal papilloma or DCIS (American College of Radiology BI-RADS category 4). No abnormalities were detected in the left breast. Blood tests showed tumor markers (CEA and CA15-3) to be within normal ranges. Findings of a needle biopsy of the nodular lesion in the right breast were consistent with a diagnosis of intraductal papilloma and atypical ductal hyperplasia, while aspiration biopsy cytology of the right axillary lymph node showed adenocarcinoma. Therefore, we suspected right breast cancer and right axillary lymph node metastasis and performed a partial right mastectomy and right axillary lymph node dissection. Pathologic diagnosis of the right breast tissue was intraductal papilloma without malignant findings (Fig. 3). One of the 10 removed axillary lymph nodes contained a nodular lesion with benign breast tissue containing p63-positive myoepithelial cells and a malignant component showing proliferation of enlarged atypical cells with nucleolomegaly and loss of p63-positive cells (Fig. 4). A diagnosis of invasive ductal carcinoma (IDC) derived from ectopic mammary tissue was established. Immunohistochemically, tumor cells were estrogen receptor (ER)-positive (positive cell occupancy rate 1-10%) and progesterone receptor (PgR)-negative (no positive cells),

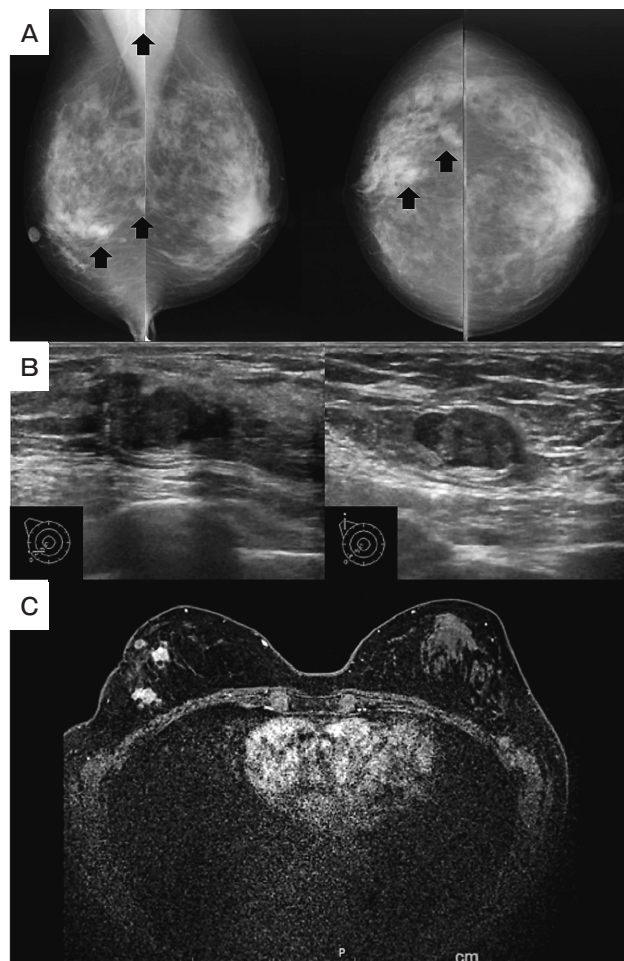


Fig. 2 Additional imaging findings. **A**, Mammography showed an enlarged right axillary lymph node and FAD (black arrows) in the right M-O region; **B**, Breast ultrasonography showed an irregular hypoechoic mass 1.6 cm in size at the 7 o'clock position and enlarged lymph nodes in the right axilla; **C**, CE-MRI revealed multiple contrast-enhanced nodules on the lower outer side of the right breast.

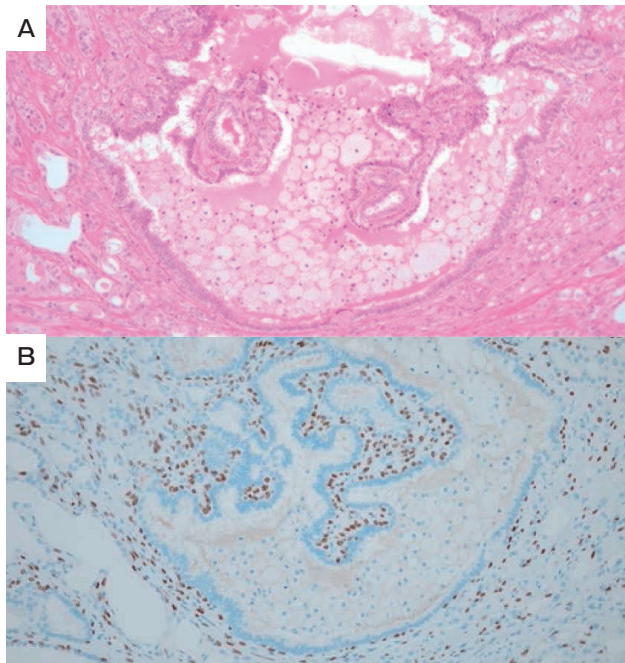


Fig. 3 Pathological image of intraductal papilloma in the right breast. **A**, The image shows papillary proliferation of epithelial cells without atypia in the ducts (hematoxylin and eosin). The bilayer of glandular epithelial cells and myoepithelial cells maintained its p63 expression (**B**).

with a human epidermal growth factor receptor-2 (HER2) score of 3 by the Immunohistochemistry (IHC) method, and a Ki-67-positive rate of 17.4%. The patient is currently receiving postoperative adjuvant treatment with radiotherapy and anti-HER2 agent administration.

Discussion

The incidence of ectopic breast tissue ranges from 0.2% to 6%, and this condition is most common in Asian populations [1]. Although it is known that malignant lesions may arise from these tissues, the incidence of primary ectopic breast carcinoma and the rate of malignant transformation of ectopic breast tissue remain unknown [1]. According to previous reports, 58% to 91% of primary ectopic breast cancers occur in the axilla [4,5]. Occurrences have also been reported in the parabasal sternum, sub-mammary region, and vulvar region [6,7]. Thus several reports have described malignant lesions arising from ectopic mammary tissue in the axilla, but there are very few reports of such lesions arising within axillary lymph nodes as in our

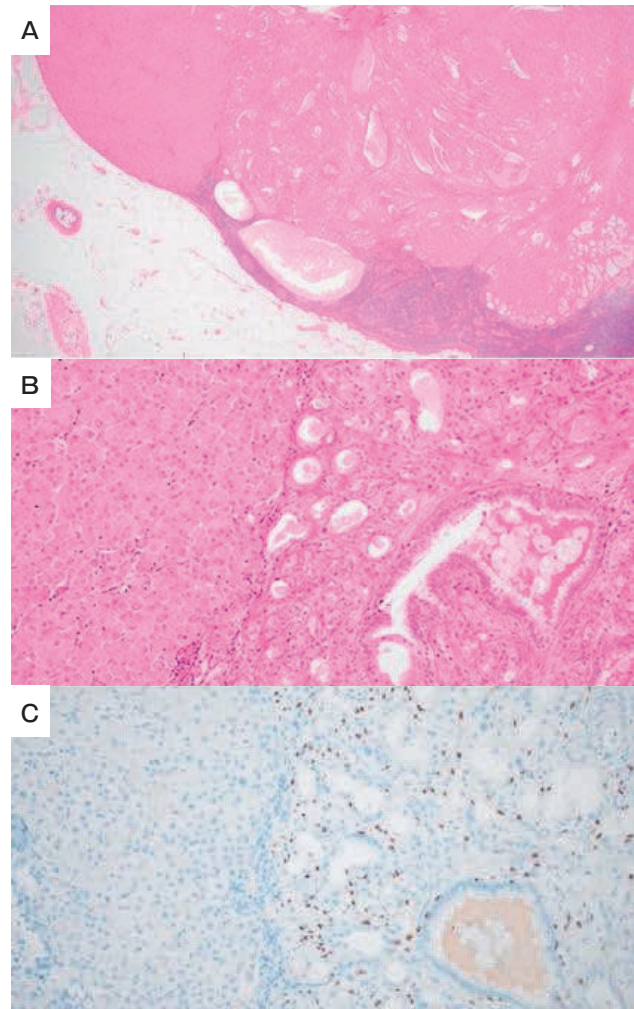


Fig. 4 Pathological image of the axillary lymph node. **A**, The image shows coexistence of benign and malignant sites within existing lymph node structures (hematoxylin and eosin). In **B**, (hematoxylin and eosin, and **C**, (p63), the benign site is on the right and the malignant site is on the left. In areas of malignancy, the nuclear bilayers disappear, and nuclear atypia and nucleoli become prominent.

present case.

Ectopic mammary tissue is infrequent within axillary lymph nodes. Furthermore, even if such tissue is identified within an axillary lymph node, it usually has the structure of a normal mammary gland, and proliferative lesions are very rare [8]. Only four cases of ectopic mammary proliferative disease arising within an axillary lymph node have been reported: one was diagnosed as cystic carcinoma [9] and the other three as intraductal papilloma [10,11,12].

The prevailing hypothesis is that ectopic mammary tissue within an axillary lymph node arises during the embryonic period [13]. However, it has been noted that previous surgical or needle manipulations may have resulted in mammary inclusion bodies in the lymph nodes [14, 15]. Among the above-cited four cases with ectopic mammary proliferative disease arising within an axillary lymph node, the cystic carcinoma case had no history of breast disease or surgery, but the three intraductal papilloma cases had undergone previous resection of an intraductal papilloma of the breast [9-12]. Ichihara in particular discusses the association between intraductal papilloma arising within sentinel lymph nodes and previous surgical biopsies but reaches no conclusion about the relevance of this association [12]. The present patient also had a history of previous surgery involving the axillary lymph nodes, and this might have been the reason for the development of ectopic mammary tissue.

Primary ectopic breast carcinoma histology is notable for benign breast lobules interspersed with cutaneous adnexal structures and malignant glands, which show positive staining for hormone receptors such as ER and PgR [1, 5]. It is noteworthy that HER2neu, a carcinoembryonic antigen, and various cytokeratins may also be expressed [1]. The absence of malignancy in eutopic breast tissue also supports the diagnosis of a primary ectopic breast carcinoma [1].

Our present patient had a mix of benign and malignant lesions within the same nodule in an axillary lymph node. In the benign area, a bilayer of glandular epithelial cells and myoepithelial cells was well preserved and nuclear atypia was absent. Papillary growths into the ducts were present throughout the lesion, suggestive of an intraductal papilloma, but there were no obvious malignant findings. On the other hand, in areas corresponding to malignancy, the bilayer structure of glandular and myoepithelial epithelium disappeared, and obvious nuclear atypia with distinct nucleoli were observed (Fig.4). There were no areas corresponding to non-invasive carcinoma in this lesion. Whereas the benign component had no expressions, cells in the malignant component were more than 1% positive for ER with a HER2 score of 3+ by immunohistochemistry. The simultaneous presence of these two regions within a single nodule led us to the diagnosis of primary breast cancer arising from ectopic mammary tissue. Such findings are not usually seen in lymph

node metastases of breast cancer. Furthermore, there was no evidence of malignant lesion in the breast. The lesion in the breast was an intraductal papilloma that grew in a papillary fashion within the ducts, with the bilayer of nuclei maintained (Fig.3). There were no findings raising suspicions of malignancy. The lesion and the intraductal papilloma component present in the nodule within the axillary lymph node were very similar, but the relevance of this similarity is unknown.

For the reasons detailed above, we diagnosed the malignant axillary lesion as a primary breast cancer rather than axillary lymph node metastasis.

Currently, no guidelines exist for the management of such a malignancy, and the role of prophylactic ectopic breast tissue excision has not been determined [2]. Primary ectopic breast cancer in the axilla is prone to metastasize to lymph nodes from the early stage and is generally considered to carry a poor prognosis [6]. This poor prognosis may be related to the 40.5-month average diagnostic delay [1] due to the difficulties in accurately assessing lesions associated with ectopic breast cancer, which is rare [2]. In previous reports, it was advocated that patients with stages I, II, and IIIA-B disease receive radical excision of the malignancy and axillary lymphadenectomy with adjuvant radiotherapy, and if indicated, hormonal treatment and/or chemotherapy [1]. In our present case, when we applied the criteria for eutopic breast cancer, the cancer was diagnosed as stage I (pT1cN0). The prognosis of ectopic breast cancer arising within the axillary lymph nodes, as in our case, is unknown because of the small number of cases, but as with other ectopic breast cancers, a decision was made to administer adjuvant radiotherapy and drug therapy. These treatments are ongoing.

Conclusion

We have presented a case with invasive ductal carcinoma, presumably arising from ectopic mammary tissue in an axillary lymph node. The patient had a history of breast cancer, making it difficult to distinguish this lesion from axillary lymph node metastasis, but the coexistence of a benign mammary lesion within the lymph node (intraductal papilloma) was the decisive factor in establishing the diagnosis.

Ectopic mammary tissue in the axillary lymph node is rare, but it is possible for breast cancer to develop at this site as well as in the breast.

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