

Axillary lymph node metastasis as the first manifestation of male occult breast cancer

A Case Report

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Abstract

Rational: Occult breast cancer (OBC) is an extremely rare breast cancer and is defined by the presence of axillary metastasis without a primary tumor in the breasts or any abnormality on radiologic examination.

Patient concerns: This case report presents a 49-year-old man who was diagnosed with male OBC, which first manifested as an axillary lymph node metastasis followed by the emergence of infraclavicular lymph node metastasis. Neither the breast nor other organs had any abnormality.

Diagnosis: The pathological examination revealed metastatic adenocarcinoma. Immunohistochemical (IHC) staining results were positive for estrogen receptor (ER), progesterone receptor (PR), and gross cystic disease fluid protein-15 (GCDFFP-15); and negative for human epidermal receptor-2 (Her-2) 1+, cytokeratin (CK) 7, CK20, and thyroid transcription factor-1 (TTF-1).

Interventions: The patient underwent left axillary lymph node dissection but not a mastectomy. After the operation, the patient subsequently underwent chemotherapy, radiotherapy, and endocrinotherapy.

Outcomes: Currently, he has been followed-up for >4 years without any signs of recurrence.

Lessons: Careful physical and imaging examinations combined with pathological analysis are essential in the diagnosis of male OBC. Early surgery remains the primary treatment.

Abbreviations: ALND = axillary lymph node dissection, CK = cytokeratin, ER = estrogen receptor, FBC = female breast cancer, GCDFFP-15 = gross cystic disease fluid protein-15, Her-2 = human epidermal receptor-2, IHC = immunohistochemical, MBC = male breast cancer, OBC = occult breast cancer, PR = progesterone receptor, TTF-1 = thyroid transcription factor-1.

Keywords: axillary lymph node dissection, male, occult breast cancer

1. Introduction

Male breast cancer (MBC) is a rare disease that accounts for <1% of all breast cancers and <1% of all male cancers.^[1] Male occult breast cancer (OBC) is an extremely rare type of MBC without any symptoms in either breasts. Similar to female OBC, male OBC is normally detected by palpable masses in the axilla. Because of the rarity of male OBC, no randomized controlled trial has been published, and little is known about the accuracy of its diagnosis, clinical characteristics, and standard treatments. Here, we report a case of male OBC that was diagnosed in a

middle-aged man and aimed to explore and discuss the clinical and pathological characteristics and treatment of this rare type of breast cancer.

2. Case report

A 49-year-old man accidentally discovered a painless quail egg-sized mass in his left axilla in November 2013 and visited a local hospital for a medical checkup. A breast ultrasonography (US) examination revealed multiple hypoechoic solid masses in the left axilla, with the largest mass measuring 2.6 × 1.3 cm in diameter. Color Doppler US showed that the mass had internal vascularity. Neither breast had any abnormality. The first-stage diagnosis was multiple hypoechoic solid masses in the left axilla. He was then referred to the breast surgical clinic at our hospital for further examination and treatment.

Physical examination revealed a rigid, mobile, painless mass in his left axilla, measuring approximately 4 × 3 cm in diameter, whereas the other side's axilla and both breasts were normal. On November 27, 2013, the patient underwent left axillary mass resection to make an accurate diagnosis. After 7 days, the pathological examination revealed metastatic adenocarcinoma. Immunohistochemical (IHC) staining results were positive for estrogen receptor (ER), progesterone receptor (PR), and gross cystic disease fluid protein-15 (GCDFFP-15) and negative for human epidermal receptor-2 1+ (Her-2 1+), cytokeratin (CK) 7, CK20, and thyroid transcription factor-1 (TTF-1). The patient

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was subsequently admitted to the department of breast surgery and underwent a positron emission tomography with integrated computed tomography (PET-CT) scan of the entire body. The scan revealed several lesions with increased uptake in the left axilla and infraclavicular regions but no lesions in either breast or other organs. Although we recommended mammography, the patient declined. The patient had been smoking and drinking for >30 years, and he had neither significant medical history nor any family member who was diagnosed with cancer. In particular, he had no history of taking hormonal drugs. After consultation, the diagnosis was considered to be male OBC that first manifested as an axillary lymph node metastasis followed by the emergence of infraclavicular lymph node metastasis.

On December 17, 2013, the patient underwent left axillary lymph node dissection (ALND) and infraclavicular lymph node dissection but not a mastectomy. The pathological examination after the surgery revealed fibrous tissue hyperplasia without a malignant lesion in the left axilla (Fig. 1). The skin and surgical margin were free of malignant involvement. In total, 40/41 dissected axillary lymph nodes (level I and II), 7/7 dissected axillary lymph nodes (level III), and 1/1 dissected infraclavicular lymph nodes showed signs of metastasis (Fig. 2). According to the 8th American Joint Committee on Cancer staging system of breast cancer, the tumor-node-metastasis classification was T0N3aM0 Stage IIIC. IHC staining (Figs. 3–6) showed positivity for ER (90%), PR (50%), and GCDFP-15 (+); and negativity for Her-2 (1+), CK7, CK20, and TTF-1. The postoperative pathological examination also showed malignancy in the left axillary and infraclavicular lymph nodes that had metastasized from the breast. The patient recovered well with no occurrence of complications. Seven days after the surgery, the patient underwent adjuvant chemotherapy (TEC scheme: paclitaxel 330 mg, pharmorubicin 120 mg, and cyclophosphamide 1.0 g, every 3 weeks for 6 cycles). The patient had good tolerance and completed his chemotherapy on April 14, 2014. He subsequently underwent adjuvant radiotherapy, which was completed in May 2014. The patient was then discharged and subsequently administered tamoxifen (20 mg/day). The patient has currently being followed up for >4 years with no signs of recurrence.

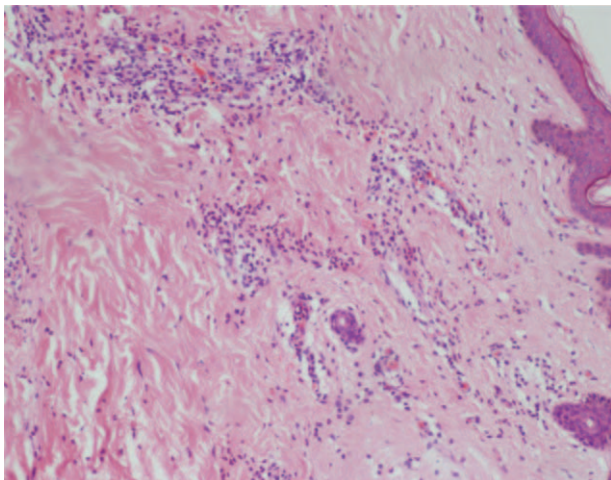


Figure 1. Postoperative HE staining of fibrous tissue hyperplasia without a malignant lesion. HE=hematoxylin and eosin.

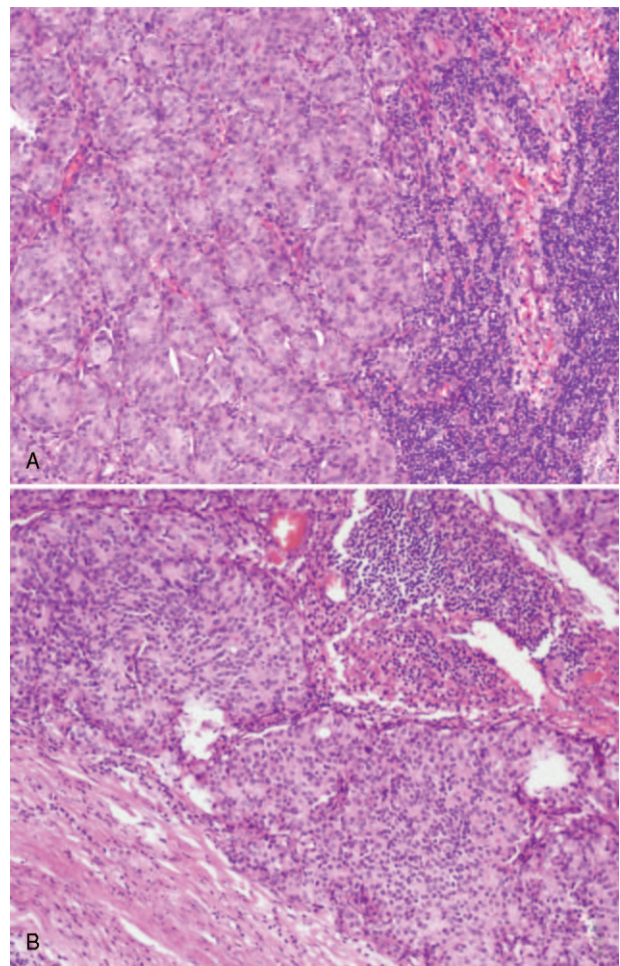


Figure 2. Postoperative HE staining. Adenocarcinoma metastasized to the axillary lymph nodes (A) and infraclavicular lymph node; (B) the images show the lymph node tissue invaded by tumor cells. HE stain, $\times 100$. HE=hematoxylin and eosin.

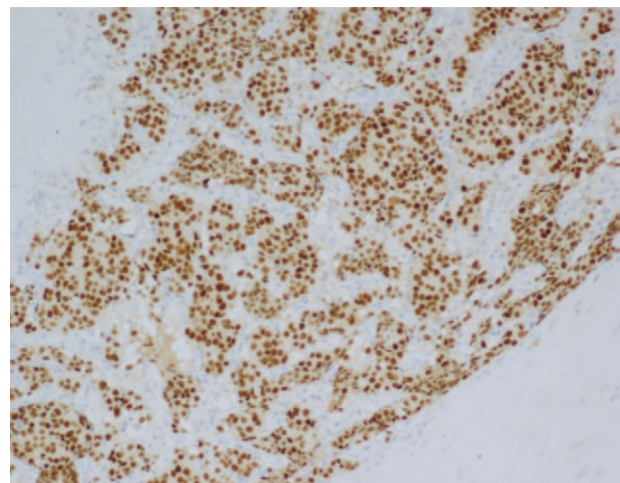


Figure 3. IHC staining showing positive expression of ER in carcinoma cell nuclei. The ER positivity index was 90%, and the image is at 100 \times magnification. ER=estrogen receptor, IHC = Immunohistochemical.

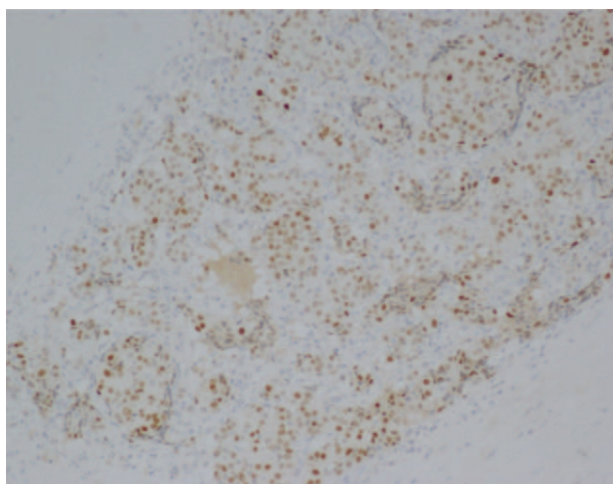


Figure 4. IHC staining showing positive expression of PR in carcinoma nuclei. The PR positivity index was 50%, and the image is shown at 100× magnification. IHC = Immunohistochemical, PR=progesterone receptor.

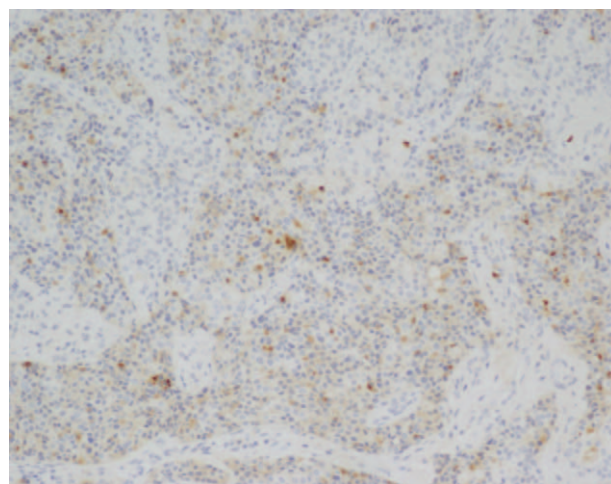


Figure 6. IHC staining showing positive expression of GCDFFP-15. The image is shown at 100× magnification. GCDFFP-15=gross cystic disease fluid protein-15, IHC = Immunohistochemical.

3. Method

This case was approved by the Institutional Review Board of Jilin University Second Hospital, Changchun, Jilin, China. The patient signed the informed consent form and agreed to the publication of his information.

4. Discussion

OBC is a rare type of breast cancer defined by the presence of axillary metastasis with no primary tumor in the breasts or any abnormality on radiologic examinations such as mammography. Approximately 0.2% to 0.9% of female breast cancer (FBC) cases are OBC.^[2] Male OBC is an extremely rare type of MBC and OBC. It has no symptoms in either breasts and is usually detected by a palpable mass in the axilla.^[3–5] Unlike FBC, which has a bimodal age distribution, MBC has a unimodal distribution with a peak incidence at 71 years, which is approximately 10

years later than that in FBC.^[6] Cases usually occur from ages 40 to 78 years,^[7] and our case was in this range.

Clinically, when a swollen axillary lymph node without a primary lesion occurs, the most important goal is to clarify whether it is benign or malignant and then to confirm the original organ.^[7] A review of many studies revealed that swollen axillary lymph nodes were most commonly metastasized from breast cancer,^[8] followed by lung cancer, prostate cancer, melanoma, and digestive cancers (such as stomach cancer and colon cancer). Performing comprehensive and systematic physical and imaging examinations is necessary to identify the primary origin.

We can also obtain information from histological examination and IHC of the metastatic lymph nodes. The assessment of hormonal receptors and Her-2 is useful for the differential diagnosis of breast cancer. In this case, we performed left axillary mass resection, and the IHC staining results were ER (+), PR (+), Her-2 (1+), and GCDFFP-15 (+). Thus, we diagnosed the axillary lesion as a primary breast cancer with axillary lymph node involvement. Several studies have consistently revealed a higher percentage of hormonal receptor positivity in MBC. ER and PR were more likely to be positive in MBC than in FBC (90% vs. 75% and 80% vs. 65.9%, respectively.^[9] The positivity for ER and PR in our case also belonged to this type. Both ER and PR play crucial roles in judging whether the primary disease underlying the axillary metastatic lymph nodes is breast cancer. However, if ER and PR staining are negative, breast cancer should not be excluded. The cases reported by Gu et al^[4] and Zhang et al^[10] both showed negativity for ER and PR. The final diagnosis must be confirmed after detailed consultations and imaging examinations. All examinations should reveal no evidence of a primary lesion, excluding a small tumor in the breast or other organs. In our case, we used PET-CT to scan the entire body and found nothing except increased uptake lesions observed in the left axilla and infraclavicular regions. Imaging examinations will help us make an accurate diagnosis and assist in subsequent clinical treatments.

Owing to the rarity of male OBC, no randomized controlled trial has been published, and little is known about its standard treatments. Most treatments are based on clinical trials in female OBC. Sohn et al^[11] compared 142 OBC patients who underwent

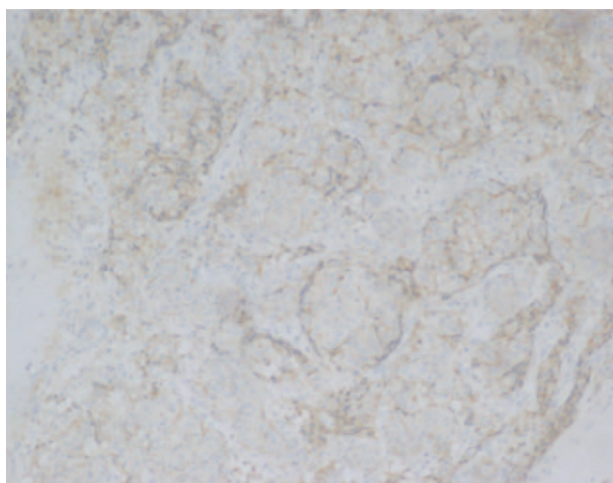


Figure 5. IHC staining showing negative expression of Her-2. The Her-2 negativity index was 1+, and the image is shown at 100× magnification. IHC = Immunohistochemical.

different treatments. The results showed no statistically significant differences in overall survival (OS) between patients who underwent only ALND, breast-conserving surgery plus ALND, and mastectomy plus ALND, with a *P*-value of 0.061. They suggested that mastectomy is not necessary, which was also demonstrated in another study.^[12] Furthermore, they inferred that postoperative radiation is crucial for OBC patients with axillary metastasis. The National Comprehensive Cancer Network guidelines recommend either mastectomy with ALND or ALND with whole-breast irradiation for T0, N1, and M0 stage disease and systemic chemotherapy and endocrine therapy, combined with surgery, for Stage II and III disease.^[13] Systematic treatment guidelines recommend the same default treatment for MBC as postmenopausal FBC.^[14] The patient in our case underwent chemotherapy, radiotherapy, and endocrinotherapy after surgery.

Male OBC is a rare entity whose pathology and biology remain unclear. Because of the unknown clinical manifestations, OBC is usually detected later than other types of breast cancers. The diagnosis is often made at later stages, and the tumor size is usually bigger.^[15] Age has been accepted as a risk factor that guides unfavorable prognosis. Another unfavorable prognostic factor for OBC is bad axillary lymph node status. Walker et al^[12] stated that patients with <10 positive lymph nodes had a 10-year OS rate of 72.2% compared with 52.1% for patients with >10 positive lymph nodes, with a *P*-value of 0.003. Male OBC may have its own characteristics, and little is known about it owing to its low incidence rate. We believe that this report provides additional information on male OBC and its management. Large-scale multicenter clinical trials are necessary to determine more accurate treatments that can improve outcomes.

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