

Occult breast cancer in an older woman: A case report

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Abstract. Occult breast cancer (OBC) is a relatively rare clinical condition that can complicate differential diagnosis efforts and delay the administration of specific treatments. The individualized therapy of patients with OBC should be performed based on their clinical symptoms, imaging findings and pathological diagnosis. The present case study describes a 51-year-old woman with a painless left axillary tumor. The axillary lymph nodes of the patient were affected by invasive ductal carcinoma, as determined by histological analysis. However, the primary lesion was missed by numerous testing. The patient underwent surgery and testing for positron emission tomography/computed tomography (PET/CT). The present study comprehensively examined this case and offered a systematic analysis of the relevant scholarly works on the diagnosis, treatment and prognosis of OBC. Ultrasonography revealed the presence of three homogenous hypoechoic masses with irregular margins in the left axilla of the patient. PET/CT scanning identified multiple enlarged left axillary hypermetabolic lymph nodes. After that, the patient underwent a nipple-sparing mastectomy and an axillary lymphadenectomy. With the lymph nodes showing metastatic, infiltrating ductal carcinoma from the breast, ductal carcinoma *in situ* of the breast diagnosis was supported by a histological examination. Immunohistochemical staining revealed that resected lymph nodes were positive for both estrogen and progesterone receptors, consistent with the status of the breast as the primary tumor site. Following surgery, the patient underwent adjuvant chemotherapy treatment. At 12 months post-surgery, the patient remained well without evidence of disease. OBC cases lack the typical clinical and imaging findings associated with breast cancer, and a combination of axillary lymph node examination and immunohistochemistry is essential for accurately diagnosing affected patients. Ensuring the best patient outcomes necessitates accurate and prompt diagnosis, achieved by thorough physical examination, cautious utilization of diagnostic

tools, personalized surgical interventions and histological investigation.

Introduction

Occult breast cancer (OBC) is a rare presentation of breast cancer in which axillary lymph node metastasis is the primary or presenting symptom, and both clinical and imaging examinations cannot identify the primary breast lesion. OBC is estimated to comprise 0.3-1.0% of all breast cancer cases (1-3). The most effective method of treating OBC is still controversial because of these low incidence rates and the absence of randomized controlled research that specifically addresses this cancer subtype. Adenocarcinoma of the lymph nodes that has metastatic spread is the primary clinical symptom of patients with OBC and is supported by pathological investigation of the axillary lymph nodes (4-6). The exact diagnostic methodology for OBC is being continuously improved (7). The initial symptoms in individuals finally diagnosed with OBC are typically metastatic tumors in the axillary lymph nodes or other locations (8,9). Standard imaging diagnostic methods may have difficulty detecting initial breast lesions, which lowers the rate of OBC diagnosis and affects the clinical course of treatment and prognosis for patients (7). These difficulties can frequently result in misdiagnosis such that treatment is delayed and patients face a worse prognosis. Thus, the early diagnosis of OBC must be improved to improve patient survival and other prognostic outcomes.

Preoperative primary breast cancer identification can significantly impact the treatment and prognosis assessment of patients with OBC, allowing doctors to choose the most appropriate biopsy and chemotherapy treatment regimens (10). Various clinical methods are currently used to detect and diagnose breast diseases (11). Mammography is among the most common and effective diagnostic technologies, providing high detection rates for early-stage tumors (11,12). By digitizing images and employing different post-processing technologies, mammography can improve diagnostic sensitivity and specificity for OBC instances (13-15). However, using a single imaging modality is often insufficient owing to the influence of a range of factors on imaging findings (16,17). Accordingly, mammography and positron emission tomography/computed tomography (PET/CT) are often combined to diagnose breast diseases reliably (18). Mammography is beneficial for identifying benign and malignant breast lesions and detecting small breast cancer lesions in the deep breast tissue (19,20). PET/CT can help clarify the clinical staging of patients with

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breast cancer but is insufficient to diagnose breast cancer when used in isolation (21-23). When primary breast lesions cannot be detected through mammography and ultrasonography, magnetic resonance imaging (MRI) can be considered an alternative imaging strategy (24). Enhanced MRI and mammography are routinely used to identify breast cancer, but each has advantages and disadvantages. Thus, increasing evidence indicates that they should be combined for the best diagnostic results (25). Although it might be challenging to identify the primary breast lesions, most patients prefer to have a total mastectomy along with axillary lymph node dissection (26). Several retrospective studies have detected no significant differences in predictive outcomes associated with radiotherapy following breast-preserving surgery or total mastectomy (2,13-15). However, due to a scarcity of large-scale clinical research on OBC, these patients have no clear diagnostic or therapeutic standards. Because initial lesions are not apparent in the breast tissue of individuals with OBC, the most appropriate local treatment techniques are similarly uncertain, and it is unclear whether radiotherapy can provide significant survival benefits to these patients (27-29). The objective of the current investigation was to examine the clinicopathological characteristics, imaging manifestations and therapy alternatives of OBC to establish a basis for developing enhanced personalized treatment approaches for this rare form of breast cancer.

Case report

A 51-year-old female patient initially presented with a recently detected left axillary mass (3.1x1.5 cm) when the patient first attended the China-Japan Union Hospital of Jilin University (Changchun, China). No masses were palpable in either breast, and there was no evidence of nipple discharge. No right axillary lymph node enlargement was detected. Ultrasonography revealed three homogenous hypoechoic left axillary masses with irregular margins, the largest measuring ~3.11x1.61 cm. PET/CT scanning indicated an area of increased glucose metabolism co-registered with the left axillary lymph nodes (SUVmax=9.56; Fig. 1). There was no evidence of aberrant glucose metabolism in the basal/myoepithelial layer of the mammary gland. Mammography and ultrasonography were unable to detect any anomalies in either breast. The patient underwent fine-needle aspiration cytology (FNAC) for imaging-detected indeterminate or suspicious lesions. Pathology results for the analyzed left axillary lymph node were consistent with a diagnosis of invasive ductal carcinoma. Immunohistochemistry results were as follows: Ki-67⁺ (70%), estrogen receptor (ER⁺) (90%), progesterone receptor (PR⁺) (80%), HER-2 (score 2+), E-cadherin⁺, androgen Receptor (AR⁺) (90%), CK5/6⁻, p63⁻, calponin⁻, SOX10⁻, GATA-3⁺ and gross cystic disease fluid protein 15 (GCDFFP-15⁺). All analyzed tumor markers were within the normal ranges, including serum AFP, CEA, prostate-specific antigen, carbohydrate antigen (CA) 19-9 and CA 15-3 levels. The individual did not disclose any previous personal or familial instances of malignancies. Based on the findings, the patient was diagnosed with OBC and subsequently underwent a left breast nipple-sparing mastectomy with axillary lymph node dissection.

Post-surgical pathology revealed that the dissected axillary lymph nodes exhibited invasive carcinoma and that the left breast tumor was a predominantly intermediate-grade ductal carcinoma *in situ* (DCIS) (Fig. 2A and D). Immunostaining results confirmed tumor positivity for ER⁺ (60%) (Fig. 2B), Ki-67⁺ (25%) (Fig. 2C), GATA3⁺, ER⁺ (90%) (Fig. 2E), Ki-67⁺ (40%) (Fig. 2F), PR⁺ (80%), HER-2 (score 2+) and E-Cadherin. By contrast, tumor tissue was negative for mammaglobin, WT-1 and PAX-8 (Fig. 2). At 1 year after surgery, the patient was discharged and was recurrence-free. The patient was treated with adjuvant chemotherapy (Table I).

The present investigation was approved by the Ethics Committee of China-Japan Union Hospital (grant no. 2023033009), and the patient provided written informed consent for its publication.

Discussion

OBC was first described in 1907 by Halsted (30). Since then, the diagnostic and therapeutic approach has been the subject of debate, and as more effective diagnostic modalities have been created, its prevalence has decreased (17-20). The current definition of OBC refers to a type of primary breast cancer detected histologically by biopsy of the axillary lymph nodes but without any clinically apparent lesions or radiographic evidence (21-23). The development of OBC still remains poorly understood. For the finding of metastatic carcinoma in axillary nodes with only non-invasive carcinoma in the breast, Terada *et al* hypothesized that the origin of OBC is ectopic breast tissue present in axillary lymph nodes (ALNs) (36,37). Recent developments in radiological imaging demonstrate that a primary breast tumor is absent in patients with OBC (37). According to reports, ectopic breasts found in ALNs can cause proliferative breast lesions (37-41). Immunohistochemistry has identified a variety of cellular subtypes in OBC, including ordinary breast cancer. The progression and metastasis of occult breast cancer may indicate that angiogenesis is activated in the axilla instead of the breast, and that this leads to the primary carcinoma metastasis occurring at a sub-clinical level (42). The determination of more general and personalized treatment options is hampered by the lack of comprehensive clinical research in several retrospective researches (43,44). The absence of an in-breast clinical finding is the original definition of OBC; however, it has since been expanded to include negative mammography and ultrasonography results as well. The immunology field and the distinctions in the microenvironments of lymphoid tissue and breast tissue may be explored further.

Occult breast cancer is a medical condition infrequently encountered in clinical practice. The diagnostic process for occult breast cancer is complicated by the challenge of identifying the primary tumor site in affected patients. The diagnosis and treatment of OBC have gained significant research attention since Halsted's initial description of its symptoms, therapy and natural progression (30). Confirming OBC diagnoses requires patients to undergo an axillary mass puncture or mass excision biopsy (31,36). When axillary tumors are pathologically diagnosed as metastatic adenocarcinomas of the lymph nodes, a clinical diagnosis of OBC should be considered (46). Bhatia *et al* revealed that a high proportion of female OBC

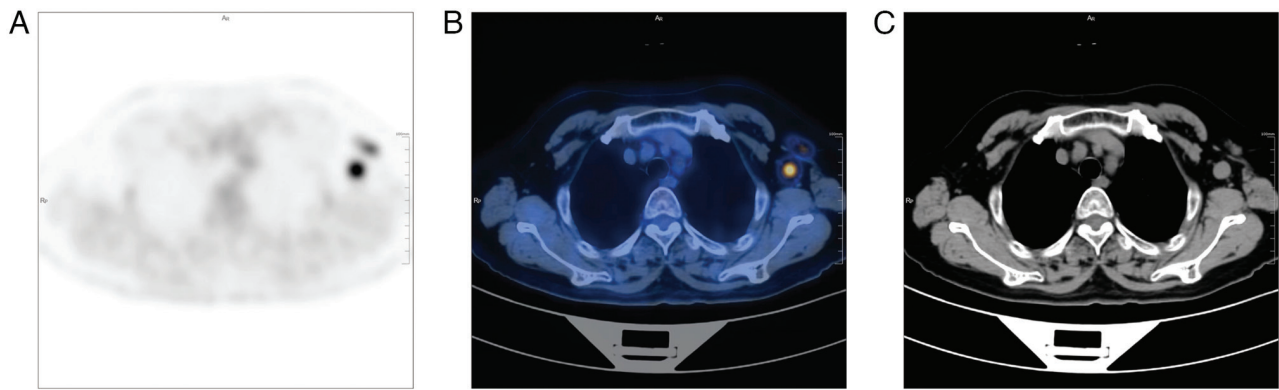


Figure 1. PET/CT images findings. Selected (A) PET, (B) PET/CT and (C) CT images show multiple enlarged hypermetabolic lymph nodes in the left axilla. PET, positron emission tomography; CT, computed tomography.

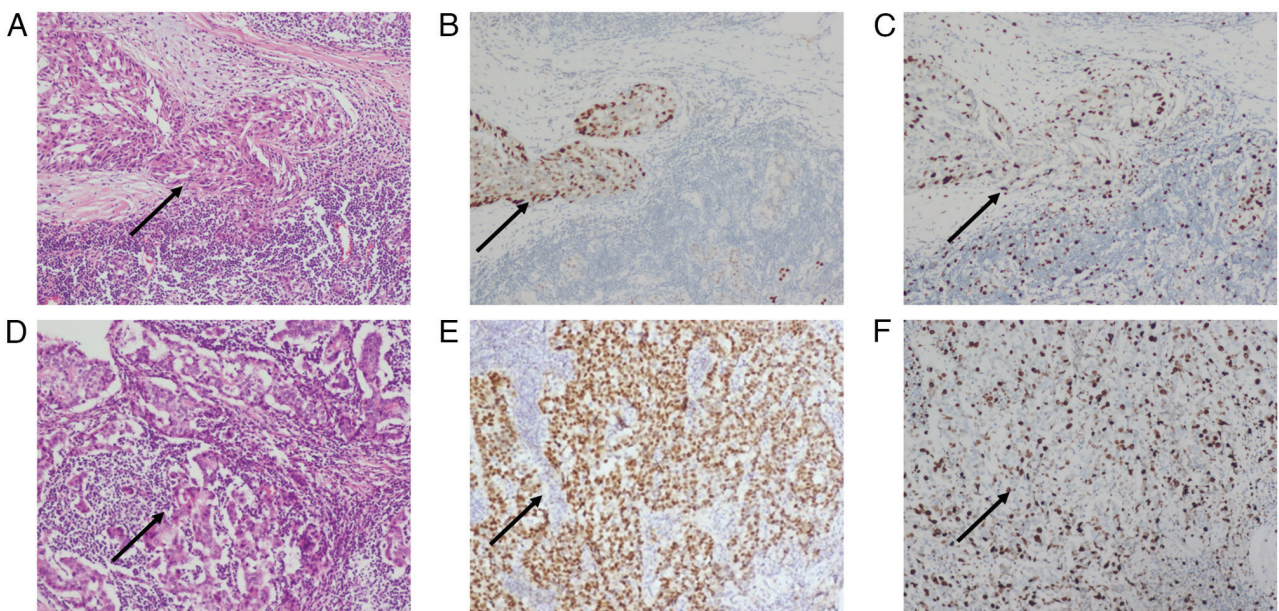


Figure 2. Histopathological analysis and immunohistochemical staining of the primary tumor and lymph nodes metastasis. (A) Breast tumor exhibited a primarily intermediate-grade ductal carcinoma *in situ*. The observed structure exhibited a dense and porous composition, accompanied by nuclear atypia of moderate severity. Hematoxylin and eosin staining shows ductal carcinoma *in situ* (indicated by arrow). (B) Immunohistochemical staining for ER⁺, which identifies ductal carcinoma *in situ* (indicated by arrow). (C) Immunohistochemical staining for Ki-67⁺ (25%), which identifies ductal carcinoma *in situ* (indicated by arrow). (D) Metastatic infiltrating ductal carcinoma (indicated by arrow). Tumor cells are arranged in strip, tubular and pseudopapillary patterns. (E) Immunohistochemical staining for ER⁺, which identifies metastatic infiltrating ductal carcinoma (indicated by arrow). (F) Immunohistochemical staining for Ki-67 (+40%), which identifies metastatic infiltrating ductal carcinoma (indicated by arrow). Magnification, x100. ER, estrogen receptor.

cases are positive for ER and/or PR (47). Immunohistochemical analyses of PR, ER and HER-2 status following the surgical excision of axillary tumors should be considered as a means of aiding patient diagnosis. The patient in the present case study was ER, PR, and HER-2 positive. However, when lesions are negative for ER and PR, it is impossible to rule out the diagnosis of OBC because certain breast cancer cases are hormone receptor-independent (33,48). Future advancements in diagnostic methods and imaging modalities are anticipated to make it easier to detect intramammary lesions, which have historically been challenging to detect. The diagnosis and management of OBC remains debatable due to these factors.

The percentage of cancer cases with cancer of unknown primary (CUP) ranges from 5-10% (49,50), and 10-40% of these patients have metastatic lesions limited to lymph

nodes (51). Only 1% of all cancers have axillary lymph node metastases from an unidentified origin (52). CUP has a higher relative contribution to cancer mortalities because of its high mortality rate (53). The greater success in detecting primary tumors is probably the cause of the declining incidence of CUP (54).

Histologically confirmed metastatic malignant tumors whose primary site cannot be detected after complete clinical and radiological examinations are called CUP (55,56). After completing clinical and pathological diagnostic procedures, the diagnosis of CUP relies on a multidisciplinary consultation to ascertain whether the tumor symptoms align with metastases indicative of CUP or original cancer (57). A subset of CUP, known as OBC, is a metastatic breast cancer confirmed by biopsy that has no recognizable primary breast

Table I. Clinicopathological characteristics.

Characteristic	Value
Age, years	51
Location	Left armpit
Menstrual status	Premenopausal
Axillary staging	N1
Family history	None
Axillary lump size	2.25x0.89-3.11x1.61 cm
Neoadjuvant chemotherapy	No
Molecular classification	Luminal B
Operation method	Nipple-sparing mastectomy with axillary lymph node dissection
Pathological types of primary foci	Ductal carcinoma <i>in situ</i>

tumor (56). Metastasis to the axillary and cervical lymph nodes is frequently observed as an initial sign of ovarian breast cancer (56). Imaging and pathological evaluations to rule out a primary breast tumor can be used to diagnose OBC. The incidence of OBC has been declining due to the development of sophisticated diagnostic techniques (58). Due to the scarcity of data, there is currently insufficient information to formulate comprehensive management standards for OBC. The diagnosis and treatment of OBC pose a significant clinical challenge because of the requirement of conducting a thorough physical examination, utilizing specific radio diagnostic testing, and analyzing pathologic and immunohistochemical findings (32,34). The lack of an intelligent and personalized system to rapidly detect patients with OBC in the early stages is among the existing clinical practice issues.

Based on available findings, MRI has demonstrated the capability to generate three-dimensional images, hence aiding oncologists in detecting a primary breast lesion when conventional breast imaging modalities have proven ineffective in identifying the origin of the lesion. This has been observed in ~75% of the cases (59). For the treatment of OBC, mastectomy and breast preservation have been suggested (35), with or without lymphadenectomy, for diagnosis and locoregional control (26,60). Most patients diagnosed with OBC initially seek medical input regarding a mass in the armpit without any palpable breast mass (61,62). Several factors can contribute to the unusual presentation of OBC (62,63). The growth of primary intramammary lesions may have been hindered due to immune-mediated inhibition, leading to relatively modest lesions. Furthermore, fibrous mastitis is responsible for the thickness of the breast tissue, which in turn hampers the identification of minor breast lesions (64). In the current case, the lymph nodes of the patient displayed indications of invasive cancer. A number of metastatic cancer cells exhibited diffuse infiltration at the microscopic scale, destroying the typical lymph node architecture. Consequently, only limited quantities of lymphocytes were observable amidst clusters of cancer cells. Tumor tissue morphology within lymph nodes is typically similar to that in primary lesions, with strip-like, papillary, acinar and clumpy presentations (65-68). In OBC cases where an axillary mass is the first symptom, lymph nodes are generally nodular and diffusely infiltrated by tumor

cells, as in the present case, destroying the integrity of normal lymphoid structures. The appearance of tumor nuclei is determined mainly by the degree of differentiation. High-grade nuclei are commonly found in poorly differentiated areas, including large nuclei, vesicular nuclei, uneven chromatin and even tumor giant cells. On the other hand, well-differentiated epithelial papillary areas are predominantly composed of low-grade nuclei equal in size to the nuclei of normal breast cells, with mitotic figures being infrequent (45-49).

There is currently a lack of specific examination procedures for OBC. Nevertheless, it is anticipated that future developments in the field of medical imaging will contribute to the identification of small breast lesions, thereby significantly enhancing the probability of early detection (70,71). Among various techniques, imaging techniques have emerged as practical tools for detecting and monitoring responses to therapy in patients with breast cancer (Table II). Mammography and ultrasonography are the traditional breast cancer screening approaches, but these fail to detect occult lesions in some patients (72,73). Compared to more conventional methods, full-field digital mammography has shown significant gains in image quality and contrast while exposing individuals to less radiation (74). Breast tumors and other high-density lesions can be seen anatomically in the breast tissue using mammography, which measures their size, density, borders and development (19,75,76).

Combining digital breast tomosynthesis with grid positioning technology can accurately diagnose microcalcifications in patients with OBC with negative palpation, further improving tumor detection rates (77-82). MRI can detect undetectable lesions via color Doppler ultrasonography or mammography while allowing for the observation of internal blood flow, thereby providing a high level of detection sensitivity (54-56). As a result, it offers an efficient method of evaluating soft tissue that is especially useful for identifying deep breast lesions. It also enables the evaluation of the quantity, size and extent of these lesions (57-59). Prior MRI results have revealed OBC lesions that present as lump-like regions of irregular circular enhancement or non-lump-like areas of uneven enhancement (84,85). Clinicians can successfully identify breast lesions in numerous cases by using MRI, PET/CT and other systemic diagnostic techniques while ruling

Table II. Imaging techniques employed in identifying patients with breast cancer.

Author, year	Techniques	Functions	(Refs.)
Mariscotti <i>et al</i> , 2014; Kim <i>et al</i> , 2016; An <i>et al</i> , 2014	MRI	MRI can be used on women who have just been diagnosed with BC to determine the extent of the tumor and other lesions with excellent sensitivity, in addition to the first identification of BC. An MRI is routinely utilized before surgery	(91-93)
Van <i>et al</i> , 2006	MR mammography	MR mammography is a valuable addition to traditional imaging in preoperative local breast cancer staging	(147)
Zeeshan <i>et al</i> , 2018; Li <i>et al</i> , 2019	DM	DM is a medical imaging technique that provides superior image quality while minimizing radiation exposure. It can detect breast cancer at its early stages, offering patients a favorable prognosis and potentially increasing their life expectancy	(148,149)
Seeram <i>et al</i> , 2019	FFDM	To enhance the perceptibility of fine details and differences in brightness within a picture, hence improving the ability to identify abnormalities in breast tissue, FFDM is employed. This technique involves the use of a digital detector that is coupled to a computer system for the acquisition and processing of radiographic images of the breast	(150)
Jadvar <i>et al</i> , 2014; Koolen <i>et al</i> , 2014	PET/CT	The use of PET/CT is crucial in breast oncology. It frequently serves as a primary staging and therapy monitoring tool rather than identifying primary BC. The most widely used radiopharmaceutical for imaging BC with PET/CT is ¹⁸ F-FDG	(151,152)
Singh <i>et al</i> , 2016; Ruiz-Ortega <i>et al</i> , 2016; Kozegar <i>et al</i> , 2017; Mohammed <i>et al</i> , 2018; Moon <i>et al</i> , 2018; Kim <i>et al</i> , 2015	US	US is a widely accepted and commonly employed diagnostic modality for evaluating breast complaints. US is the recommended modality for performing breast biopsies	(100-105, 153-158)
Cai <i>et al</i> , 2015; Nakashima <i>et al</i> , 2017; Mercier <i>et al</i> , 2015; Roganovic <i>et al</i> , 2015	DBT	DBT utilizes three-dimensional imaging to provide a range of physical perspectives for breast examination. The addition of DBT to conventional digital mammography has the potential to enhance sensitivity	(159-162)
Das <i>et al</i> , 2006	X-ray mammography	X-ray mammography is the primary technique for identifying breast cancer in its early stages. But due to the lack of specificity in X-ray mammography, numerous unnecessary biopsies are performed	(163)
Brem <i>et al</i> , 2008; Yoon <i>et al</i> , 2015; Tan <i>et al</i> , 2016; Yu <i>et al</i> , 2016; Cho <i>et al</i> , 2016	BSGI	Compared with scintimammography, BSGI is more sensitive and can identify breast tumors <1 cm in size. BSGI is especially useful for imaging BC in dense breasts and multifocal and multicentric diseases	
Simanek <i>et al</i> , 2016; Berrington <i>et al</i> , 2009	SPECT/CT	SPECT/CT, which combines a gamma camera and non-diagnostic CT, is crucial for detecting BC metastasis. SPECT/CT provides more precise anatomical information compared with planar sentinel lymph node scintigraphy when imaging sentinel lymph nodes	(164-170)

FFDM, full-field digital mammography; US, Ultrasonography; SPECT, single-photon emission computed tomography; PET, positron emission tomography; DM, digital mammography; 3D, three-dimensional; MRI, magnetic resonance imaging; BSGI, breast-specific gamma imaging; DBT, digital breast tomosynthesis; DM, digital mammography.

out the possibility of other malignant tumor sources in the body and spotting any metastases existing within other tissues or organ compartments (86,87). The sensitivity and specificity of PET-CT for axillary lymph node metastasis are 95 and

65%, respectively, and it is commonly used to evaluate patients with OBC with negative mammography results. PET/CT is of particular value for the differential diagnosis of OBC, given its ability to recognize axillary lymph node metastasis and

primary lesions of non-breast origin (88). In the present case, the patient received PET/CT imaging, which revealed several enlarged hypermetabolic left axillary lymph nodes. Pathology revealed that these lymph nodes exhibited metastases, and the left breast tumor was primarily intermediate-grade DCIS. When routine examination results are inconclusive or difficult to interpret, PET/CT can provide practical diagnostic assistance, particularly in individuals with locally advanced or metastatic disease. Although a number of investigations have suggested the potential efficacy of PET/CT in detecting OBC, its utility in this specific patient cohort is constrained due to the small size of lesions (89).

Breast-specific γ imaging (BSGI) is a high-resolution imaging approach that can detect occult breast lesions at sub-centimeter resolution with improved sensitivity and specificity compared with MRI. BSGI enables the detection of small tumor foci even in dense breast tissue (90,91). The technique known as radioisotope occult lesion localization involves administering a solution of water-soluble non-ionic iodine contrast agent and radionuclide-labeled albumin gel close to the suspected lesion location, followed by a localization biopsy under the supervision of a γ -ray detector. Implementing this radionuclide localization method reduces the possibility of requiring additional surgical procedures while also considering the post-surgical aesthetic outcomes and their impact on patient appearance (92,93). However, radionuclides are limited by their short duration of activity, such that they can only be injected within one day of the operation (94-96). If primary lesions in the breast tissue are successfully detected in patients with OBC, they can receive a definitive diagnosis.

Nevertheless, there are cases where identifying these initial abnormalities remains elusive, even after undergoing numerous supplementary investigations (13,97). In the case of these individuals, it is imperative to distinguish between OBC and alternative types of malignancies, including auxiliary breast cancer, thyroid carcinoma, lung cancer and melanoma (33,98). The detection of accessory breast cancer relies primarily on pertinent exams and a thorough clinical history. The absence of accessory breast tissue identified during ALND can be considered sufficient evidence to dismiss it as a potential etiological factor for the disease (99). Tumor tissue in these cases with exhibit morphological characteristics similar to those of the primary tumor, and a primary focus may also be found via chest CT, abdominal CT or other examinations (100). The tumor may be poorly differentiated and difficult to detect based on its histological morphology when it is organoid, acinar or lamellar, although further immunohistochemistry analyses can aid in diagnosis (3,69-71). When encountering inexplicable growth of axillary lymph nodes, it is essential to evaluate the possibility of OBC as a potential diagnosis. When breast and accessory breast examinations yield negative results, and the clinical primary tumor site remains uncertain, it is advisable to pursue pathological evaluation. Small amounts of invasive ductal carcinoma tissue and tumor thrombus are observed within the intravascular lymphatic vessels, suggesting a potential case of OBC.

A consensus on the optimal technique for treating OBC has not yet been reached (16), and there is an ongoing debate on the choice between radical mastectomy and breast-conserving surgery for patients. Surgical interventions available for

individuals with OBC include mastectomy, breast-conserving surgery or a combination of radiation and ALND. The relative benefits of these three interventional strategies appear similar, with a high local recurrence rate for patients that undergo ALND alone and with patients with OBC facing an overall survival (OS) rate that is relatively poor (72-74). Some small-scale studies have supported the benefits of breast-conserving therapy for patients with OBC (75-77). By contrast, some researchers have cast doubt on the benefits of ALND combined with radiotherapy as an alternative treatment for these patients. When comparing a breast-conserving surgery group to a radical surgery group in a retrospective analysis of clinical data from 750 patients with OBC, Walker *et al* (7) found no significant differences in 10 year OS, with the outcomes in both groups being improved compared with those in the untreated and ALND groups.

He *et al* (28) reported similar levels of therapeutic efficacy in patients with OBC that underwent either mastectomy or a combination of ALND and subsequent radiotherapy. Some authors have posited that treatment can be temporarily discontinued in patients where primary breast lesions cannot be located, following axillary tumor removal and close observation (109). Considering the low rates of OBC incidence and the lack of extensive retrospective investigations of this patient population, breast-conserving surgery or mastectomy should be carried out as necessary when lesions are subsequently discovered (13,69). However, additional research is required to elucidate the comparative advantages of these various therapy alternatives. According to Olson *et al* (44), breast-conserving surgery may be advantageous for patients who do not have a successfully circumscribed primary lesion following MRI scanning. By contrast, De Bresser *et al* (59) suggested that while MRI offers a high degree of specificity to detect primary tumor foci in patients with OBC, its specificity is limited. Additionally, this study recommended that in cases where MRI detects breast lesions, a biopsy should be conducted using ultrasound or MRI guidance. Subsequently, if deemed suitable based on the biopsy results, breast-conserving surgery should be carried out. Kemeny (110) proposed mastectomy as the most appropriate treatment option for female patients exhibiting axillary lymph node metastases without any identified primary breast lesion and negative mammography results. By contrast, Copeland and McBride (111) suggest that radical mastectomy cannot be performed in cases where the primary breast lesion cannot be located.

Merson *et al* (26) compared surgical approaches for treating patients with OBC with axillary lymph node metastasis. This study observed no significant differences in 5- or 10-year survival rate when comparing the breast-conserving surgery and radical mastectomy groups. Because the effects of total mastectomy are comparable to those of ALND and radiotherapy, it indicates that patients with negative mammography results do not necessarily need to undergo mastectomy. The therapeutic results for patients with OBC undergoing ALND are the same as those undergoing ALND in conjunction with mastectomy or breast conservation surgery (2).

Studies of local treatment options suggest that patients with OBC that do not undergo mastectomy can benefit from radiotherapy (105,112). According to some reports, systemic treatment is considered the most suitable approach

for patients with OBC who do not have a detectable primary breast lesion (107,113,114). This approach involves treating the problem as a systemic disease and enabling breast preservation. This can have the benefit of alleviating the psychological distress often associated with breast surgery. The prognosis results of patients are not improved by local treatment, even in cases where breast abnormalities are discovered (115). In the subset of patients with OBC in whom digestive tract metastases are the first symptom, the disease should be treated as a form of advanced breast cancer and treated through appropriate combinations of chemotherapy, endocrine therapy, targeted therapy and other systemic treatments (116-118). If patients exhibit gastrointestinal bleeding, perforation, obstruction or other difficult-to-treat complications, palliative surgery can be performed to prolong the median survival duration of this patient population (119).

Due to the systemic nature of breast cancer, surgical intervention represents but a single component of the comprehensive therapy approach. Adjuvant therapy options for patients with OBC encompass a range of interventions, such as endocrine therapy, chemotherapy, targeted therapy, targeted regional radiation, and immunotherapy regimens. The selection of these treatment modalities is guided by established treatment guidelines for non-OBC patients and the specific clinical characteristics and needs of the particular patient under consideration. Neoadjuvant chemotherapy (NAC) for OBC can help target axillary lymph nodes and facilitate their surgical removal in these patients while preventing the development of drug-resistant tumor cells, eliminating small metastatic foci, reducing tumor cell activity and restricting metastatic spread (120-123). Some reports have suggested that NAC treatment for patients with OBC can be administered based on the immunohistochemical staining of axillary lymph node biopsy samples, patient age, ultrasound and ¹⁸F-FDG PET/CT imaging findings (123-127). In general, managing individuals with OBC should encompass a comprehensive treatment approach comprising surgical intervention, chemotherapy, radiotherapy, endocrine therapy, targeted therapy and other suitable interventions. When determining the appropriate course of action, it is crucial to thoroughly consider patient-specific factors, pathological classification, and staging outcomes.

The identification of pertinent prognostic variables in patients with OBC is ongoing. The prognosis of patients becomes poorer as the number of metastatic axillary lymph nodes increases in breast cancer (83-85). There is also evidence that hormone receptor status, tumor marker expression, primary tumor pathological type, number of axillary lymph nodes, the timing of axillary lymph node diagnosis and the presence or absence of distant supraclavicular metastasis are all related to patient outcomes (86-88). In individuals diagnosed with OBC, nodal status may offer value as an independent predictor of poor outcomes (2,10,26), and those patients harboring distant metastases exhibit a very poor prognosis and a short survival interval. Vlastos *et al* (35) also discovered a connection between outcomes of patients with OBC and the quantity of positive axillary lymph nodes. However, deciding between primary surgery and simple lymph node dissection does not significantly affect patient survival rates.

The 10 year survival rate of patients with atypical axillary metastases is 50-71%, with this rate being slightly improved compared with that associated with stage II disease (35,69,128). Significant prognostic factors include hormone receptor status and the number of involved axillary lymph nodes (35,128). Generally, the 5 year overall survival of patients with 1-3 involved lymph nodes tends to be improved compared with that of patients with 4+ involved nodes (35).

When comparing patients with early breast cancer and OBC, Montagna *et al* (129) found no substantial improvements in 5-year disease-free or overall survival. However, the disease advances more rapidly when patients are determined to have triple-negative breast cancer (TNBC), and patients were at a higher risk of death or recurrence. ER is associated with a poor prognosis in TNBC cases (4,15), and systemic endocrine therapy is an essential element that can influence the survival of individuals diagnosed with hormone receptor-positive breast cancer (130).

The presenting symptom in patients with OBC is typically painless axillary lymph node enlargement, which may coincide with distant tumor metastasis and paraneoplastic neurological syndromes in some cases (131). Patients should undergo prompt breast examination, ultrasonography and mammography when isolated enlarged axillary lymph nodes are detected (132,133). Breast-conserving surgery, mastectomy and ALND should be considered if primary breast lesions are detected through these assessments (134-136). If no primary breast lesion is detected, it is recommended that patients undergo FNAC, core needle biopsy or other forms of puncture biopsy (137-139). If the patient is ultimately diagnosed with metastatic cancer, immunohistochemical staining for ER, PR, HER-2, Ki-67 and GCDP-15 should be performed together with other tests, including thyroid ultrasound scans and CT scans of the chest, abdomen and pelvis to detect or distinguish between OBC and other forms of metastatic cancer (100,140,141). Each OBC patient's specific conditions should be considered, and neoadjuvant chemotherapy, adjuvant chemotherapy, radiotherapy and targeted therapy should be explored as potential approaches to improving patient survival and prognosis (142). OBC cases are sporadic, and large-scale studies of populations of patients with OBC are thus lacking, with most research instead consisting of analyses of small patient cohorts (143). Accordingly, the basis for diagnosing and treating this cancer type is relatively limited, and additional evidence is needed to establish the most appropriate clinical management of affected patients (142). The further investigation centered on the pathogenesis and attributes of OBC to discern the immunological elements that contribute to the expansion of primary lesions in affected individuals holds promise for enhancing targeted therapeutic interventions, finally improving prognostic outcomes (29,143,144). The present comprehensive discussion of current issues facing the diagnosis of OBC, the importance of sentinel lymph nodes and internal mammary lymph nodes in treating OBC and the standardized treatment of OBC will benefit from rapid advances in artificial intelligence, sequencing and big data technologies in clinical practice (145,146). Formulating robust diagnostic and treatment guidelines will help patients with OBC receive a timely and accurate diagnosis to begin

treatment as quickly as possible. An improved prognosis for patients with OBC will also result from the continued use of targeted medications, immunotherapies and other cutting-edge pharmacological drugs.

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All data generated and/or analyzed during this study are included in this published article.

Authors' contributions

CL and HX conceived the review and acquired data. CL and HX participated in the process of writing and reviewing the manuscript. CL and HX confirm the authenticity of all the raw data. All authors contributed to the conception and revision of the manuscript and approved its submission. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The China-Japan Union Hospital Medical Ethics Committee approved the present study (approval no. 2023033009). Written informed consent was obtained during the initial data collection for participation.

Patient consent for publication

The patient and control subject consented to the publication of this case report and accompanying images.

Competing interests

The authors declare that they have no competing interests.

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