

Occult breast cancer presenting as metastatic carcinoma in a right axillary lymph node of a post-menopausal female: A case report and review of literature

Michael E Aghahowa, Kevin N Ezike, Oku S Bassey, Ijeoma A Okwudire-Ejeh, Amba A Amba, Yakubu Shehu

ABSTRACT

Introduction: Occult breast cancer (OBC) is a clinically recognizable metastatic carcinoma from an undetectable primary breast tumor. It is rare and accounts for 0.3–1% of all breast cancers, often presenting with lymph node, bone, or skin metastases. It poses a diagnostic challenge for general surgeons, radiologists, and pathologists.

Case Report: We present the case of occult breast cancer in a 62-year-old, post-menopausal, female, Nigerian, presenting with a solitary, painless, right axillary lymph node enlargement without a clinical or radiological evidence of a breast mass; and also review the literature. The diagnosis of metastatic breast carcinoma was made and confirmed on histology and immunohistochemistry analysis of the axillary lymph node. Histological examination of the subsequent right breast mastectomy specimen revealed the presence of infiltrating ductal carcinoma even though no definite mass lesion was seen on gross examination.

Conclusion: Occult breast cancer can be a diagnostic challenge and should be excluded in any patient presenting with solitary axillary lymphadenopathy. Immunohistochemistry staining patterns can be a mainstay in resolving the differential diagnoses.

Keywords: Abuja, Breast cancer, Lymph node, Occult

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INTRODUCTION

Occult breast cancer (OBC) was first described by Halsted in 1907 as a cancerous axillary gland with non-demonstrable cancer of the mamma [1] and is defined as a clinically recognizable metastatic carcinoma from an undetectable primary breast tumor [2]. This definition of OBC has also evolved to include clinically recognizable metastatic disease with no clinical primary, radiological or pathological, breast carcinoma [2]. This is due to the advancement in the use of modern imaging modalities for breast cancer screening and diagnosis. The yield for the diagnosis of breast cancer has increased significantly with the use of modern imaging modalities like digital mammography, digital breast tomosynthesis (DBT),

ultrasonography, and magnetic resonance imaging (MRI). Occult breast cancer is rare but accounts for only 0.3–1% of all breast cancers, often presenting with lymph node, bone and skin metastases [2]. Occult breast cancer can be a diagnostic and therapeutic challenge to the surgeons and pathologists [2–6].

A woman who presents with an axillary lymph node that is consistent with breast cancer metastasis has a 90% probability of harboring an occult breast cancer [7]. The value of mammography in detecting an occult breast carcinoma is low, with a sensitivity of 29% and specificity of 73% [8]. However, the introduction of modern imaging modalities like DBT and MRI has led to a significant increase in some of what would otherwise have been an OBC, and there is proportional decrease in the incidence of OBC in the real context of the current definition [3]. Furthermore, analysis of immunohistochemistry staining patterns of the presenting mass can be a mainstay in resolving the differential diagnoses [9]. We hereby present the management of a case of OBC in a district hospital in Abuja, Nigeria, and also, a review of literature.

CASE REPORT

The patient is a 62-year old and mother of two children, who presented with a painless right axillary swelling of seven months' duration. There was no associated history of breast swelling or change of skin color, no nipple discharge. There was no other swelling elsewhere. There was no family history of cancer. She previously used hormone replacement therapy (HRT) for three years for unsuccessful in vitro fertilization (IVF) pregnancy. Examination showed a fit looking lady with a 4 cm, hard, regular, mobile, non-tender and smooth surfaced, right anterior axillary lymph node. Both breasts were huge but felt normal on palpation. Ultrasound scan, mammography, and MRI of both breasts were normal. The chest computed tomography (CT) was also normal. Other tests like complete blood counts, serum electrolytes, urea and creatinine, liver function tests, were normal. An excision biopsy of the right anterior axillary lymph node was done and histological examination showed a lymph node tissue with almost complete effacement of architecture due to malignant epithelial proliferation, disposed in sheets, trabeculae, nests, cords, and clusters (Figure 1). Areas of coagulative necrosis were also seen on histological examination. The lymph node capsule was focally invaded but not completely breached by advancing tumor. These features led to a diagnosis of metastatic carcinoma in the lymph node. Immunohistochemistry analysis involving five panels was used for histogenesis: estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) for breast; CDX2 for gastrointestinal; and PAX8 for thyroid, renal cell, and ovarian serous carcinomas, respectively. The immunohistochemistry analysis was positive for

only ER (Figure 2), and hence consistent with infiltrating duct carcinoma of the breast as the primary tumor.

A simple right mastectomy and complete level 2 axillary node clearance was done. On gross examination, the breast did not reveal any definite mass lesion. However, grayish white trabeculations covering an area which measured 11 cm in widest diameter were seen across the upper quadrants. A similar area but smaller, measuring 5 cm was also seen in the inner lower quadrant. Twelve palpably enlarged lymph nodes, ranging in sizes from 0.3 to 1 cm in widest diameter were harvested from the axillary fat. On histological examination, the smaller, lower quadrant trabeculations showed a malignant epithelial proliferation disposed in trabeculae, sheets, nests, cords, clusters, and single atypical cells (Figure 3); and the constituent cells had moderate grade, pleomorphic, vesicular nuclei, prominent nucleoli, and variable cytoplasm, leading to a diagnosis of infiltrating duct carcinoma (NOS), Nottingham grade II, with tumor free margins.

None of the excised 12 right axillary nodes contained tumor deposits but they showed features of reactive lymphoid hyperplasia. The patient has remained symptom free on routine postoperative follow-up for 12 months.

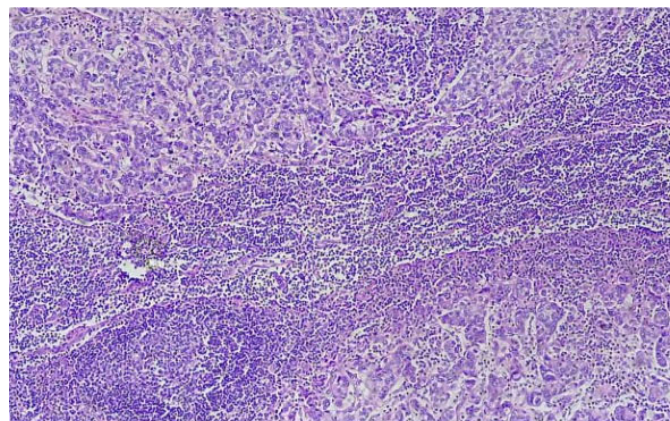


Figure 1: Axillary lymph node with architecture effaced by a malignant epithelial proliferation disposed in sheets, trabeculae, nests, cords, and clusters; H&E $\times 10$.

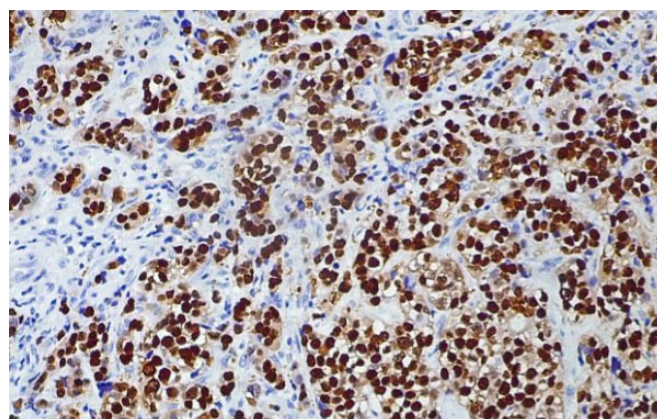


Figure 2: Axillary lymph node with malignant epithelial cells showing strong and diffuse nuclear staining for estrogen receptor (ER); Immunohistochemistry $\times 20$.

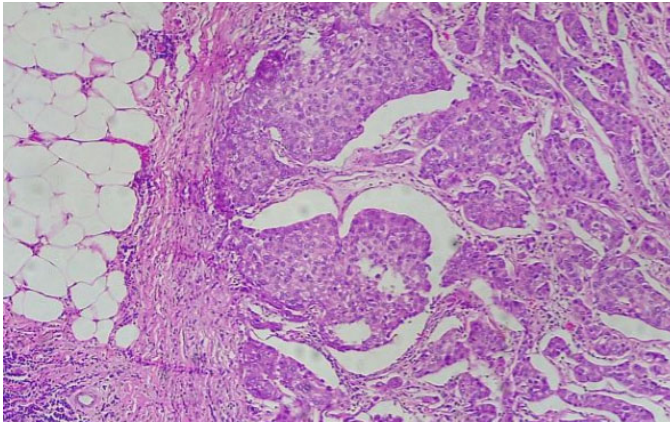


Figure 3: Right breast showing malignant epithelial proliferation disposed in sheets, trabeculae, and clusters; H&E $\times 10$.

DISCUSSION

Occult breast (OBC) is described as an axillary metastatic carcinoma without detection of a primary breast lesion and is uncommon, accounting for less than 1% of all breast cancers [2–4]. Axillary lymphadenopathy is the initial presenting sign in only 1% of breast cancer patients [7]. Occult breast cancer though said to be rare, mostly presents with enlarged axillary or cervical lymph node or metastasis to bone or skin. Our patient presented with a hard, mobile, right anterior axillary lymph node without a clinically detectable swelling in the breasts. The bilateral whole breast ultrasound scans and mammography done were negative for breast cancer. This presentation is similar to the cases reported by Scoggins et al. and Frattaroli et al. respectively, where ultrasound scan and mammography could not detect any primary lesion in the breast [8, 10].

One out of the seven cases reported by Yu et al. in China was suspected to have OBC on ultrasound scan and mammography [11]. Zhong et al. also in China reported that 8 out of the 17 patients they studied had positive findings of OBC on ultrasound scan and 3 out of 9 cases had positive findings on mammography [12]. However, an MRI of the breasts done for our patient, though said to be sensitive in about 75% of cases, was also not able to detect the primary lesion which is similar to the report by Barbieri et al. [2]. Although positron emission tomogram (PET) scan was not available, it would have been useful in detecting any tumor metastasis in this patient.

The mainstay of diagnosis in our patient was the histological examination and immunohistochemistry of the excised right axillary lymph node. These not only gave the histological diagnosis of a metastatic disease but also pointed to its ER positivity status of breast origin. This is similar to the findings of other researchers [2, 4–6, 8, 10, 11, 13]. The immunohistochemistry pattern of OBC is variable. However, immunohistochemistry becomes the mainstay of diagnosis especially when the primary site is not detected after intervention, particularly those

of estrogen and progesterone receptors and those of other second line panels like GATA-3, E-Cadherin, and mammoglobin [14, 15]. Altan and Altundag have stated that the immunohistochemistry patterns especially for ER and PR in the lymph node are invaluable as seen in our case where the ER positivity in the lymph node gave insight to the primary site [9], as seen in Figure 2. These immunohistochemistry staining patterns also play a role in the therapeutic modality and prognostic outcome of the patient [14].

Our patient had right simple mastectomy and axillary node clearance. Even though the histological examination of the mastectomy specimen of our patient confirmed infiltrating duct carcinoma (NOS) with tumor free margins, as seen in Figure 3, this is not always the case; for instance, Wang et al. found primary tumor in the mastectomy specimens in only 28 out of 38 cases reported [4]. It has also been reported by other authors that some of such excised breasts did not contain the primary lesion [4, 9, 10]. It is sometimes assumed that the lesion was so small that it escaped detection by histology [4]. Altan and Altundag state that the outcome of OBC is similar to primary breast cancer and that the number of lymph node involvement is a strong prognostic factor [9]. The histological type of the cancer, grade of axillary node invasion, and the presence of metastases determine the surgical management of breast cancer [16]. The fact that none of the 12 lymph nodes isolated from our patient's axilla contained tumor deposits may portend overtreatment rather than a favorable prognosis [16].

The non-detection of the primary lesion in a mastectomy specimen may pose a medico-legal challenge for the surgeon especially in a situation where none of the preoperative investigations like ultrasound, mammography, and MRI suggested a lesion in the breast. Therefore, where the immunohistochemistry analysis and test for other markers are negative for breast cancer, it is necessary to diligently search for a primary cancer elsewhere in organs like the thyroid and the abdomen, pelvis, including the rectum. Once the diagnosis of OBC is clear, specific treatment like axillary node clearance and mastectomy or breast conserving surgery combined with irradiation or chemotherapy should be offered to the patient.

CONCLUSION

The diagnosis of OBC can be a challenge to the surgeon when it presents with a sole axillary lymphadenopathy. It may be missed or under reported in our environment where the capacity for extensive investigation including immunohistochemistry and tumor markers is not readily available. Both breasts ultrasound scans, mammography, MRI, biopsy of lymph node as well as immunohistochemistry analysis, and test for other tumor markers are very useful in the diagnosis of OBC. The specific treatment should be rationalized to

include mastectomy and axillary node clearance or breast conserving surgery and radiotherapy. The surgeon must avoid a medico-legal scenario by properly counseling and obtaining informed consent from the patient, that there is a slight chance of missing the tumor in an excised breast.

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Author Contributions

Michael E Aghahowa – Conception of the work, Design of the work, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Kevin N Ezike – Design of the work, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Oku S Basse – Design of the work, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Ijeoma A Okwudire-Ejeh – Design of the work, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Guarantor of Submission

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Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

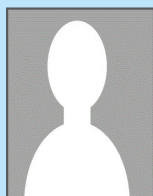
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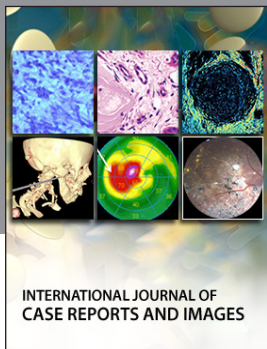
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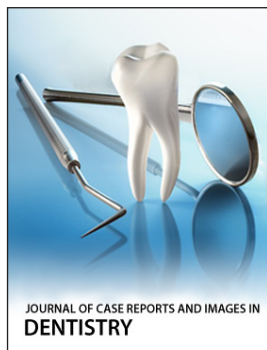
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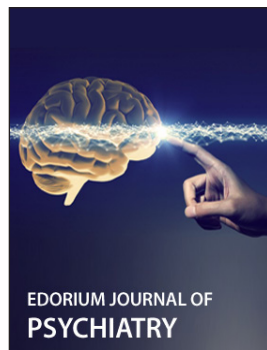
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