

Case Report

Unusual Metastatic Lymph Node to Retro-Scapular Area in Occult Breast Cancer: A Case Report

Lina Wahbeh^a Abdulla Alzibdeh^a Shatha Abutaha^a Issa Mohamad^a
Ramiz Abuhijli^a Hussam Haddad^b Hikmat Abdel-Razeq^{c, d}
Fawzi Abuhijla^a

^aDepartment of Radiation Oncology, King Hussein Cancer Center, Amman, Jordan;

^bDepartment of Pathology, King Hussein Cancer Center, Amman, Jordan; ^cDepartment of Internal Medicine, King Hussein Cancer Center, Amman, Jordan; ^dSchool of Medicine, The University of Jordan, Amman, Jordan

Keywords

Breast cancer · Lymph nodes · Subscapular region · Occult breast cancer · Case report

Abstract

Introduction: Breast cancer typically metastasizes to axillary, internal mammary and supraclavicular lymph node chains. In contrast, occult breast cancer (OBC), a rare form of breast cancer, usually presents as axillary lymphadenopathy and rarely metastasizes regionally or distally. **Case Presentation:** In this case report, we present a 45-year-old female patient with unusual presentation of breast cancer initially as axillary lymphadenopathy without breast mass. She was diagnosed by magnetic resonance imaging as OBC and later presented with a rare pathological spread to the ipsilateral subscapular region. The retro-scapular nodal disease was first detected via follow-up computed tomography scan and confirmed by positron emission tomography after 18 months of her initial diagnoses. This occurred following completion of OBC management, which included neoadjuvant chemotherapy, axillary lymph node dissection, without mastectomy, followed by adjuvant radiation treatment to regional lymph nodes and ipsilateral whole breast. Her recurrent nodal disease was subsequently managed by surgical resection followed by radiation therapy to surgical bed. **Conclusion:** This case report emphasizes the diverse locations where metastatic breast cancer can manifest and underscores the advancements in diagnostic tools that have enhanced the detection of these metastatic sites.

© 2024 The Author(s).
Published by S. Karger AG, Basel

Correspondence to:
Fawzi Abuhijla, fhijle@khcc.jo

Introduction

Common regional nodal spread from primary breast cancer includes axillary, internal mammary and supraclavicular lymph nodes. Common sites for distant metastases are lungs, liver, bone, and lymph nodes [1]. However, breast cancer's metastatic potential extends beyond these conventional sites and can occasionally involve unusual locations. These unusual metastatic sites, although not universally defined, occur in less than 1% of the cases [2]. According to Di Micco et al. [2], the most reported unusual metastasis sites for breast cancer are the stomach (185 reported cases), meninges (125 reported cases), and pituitary gland (104 reported cases). Specifically, breast cancer metastasis to the stomach accounts for more than 0.3% of stomach resections, as reported by Rodrigues et al. [3]. While the stomach is the most commonly reported site for rare metastases of breast cancer, it remains a relatively uncommon consideration in the broader context of surgical resections performed for such cases.

In this report, we present a case of an occult right breast cancer, with spread to regional axillary lymph nodes and an unusual metastatic site in retro-scapular lymph node. To our knowledge, this case represents the first description of breast cancer metastasis to the retro-scapular area.

Case Presentation

A 45-year-old female patient presented with a history of rheumatoid arthritis on methotrexate and steroids for 3 years, and hypothyroidism on levothyroxine. She had an excisional biopsy-proven metastatic right axillary lymph node originating from breast cancer and was referred to our tertiary cancer center for further investigations and management.

Histopathology review of initial biopsy was performed and confirmed metastatic adenocarcinoma consistent with breast origin. Hormonal receptor status was as follows: estrogen receptors were positive and moderately expressed in 30% of tumor cells, and progesterone receptors were positive and strongly expressed in 40% of tumor cells. Immunohistochemistry revealed human epidermal growth factor receptor 2 (HER2) overexpression with score (3+) as shown in Figure 1.

Prior breast ultrasound (U/S) and mammogram performed outside before the biopsy identified two oval, well-defined masses in the upper lateral tail of the right breast, the larger mass measured 2.4 × 2.9 cm and the smaller one 1.2 × 1.6 cm. These were suggestive of fibroadenomas. In contrast, breast mammogram and U/S performed at our center demonstrated postoperative changes of previous biopsy in the right axilla, with mildly prominent bilateral axillary lymph nodes, more on the right side, showing preserved fatty hilum and homogenous cortical thickening. Breast magnetic resonance imaging (MRI) showed postoperative changes in the right axilla with residual abnormal-looking nodes (Fig. 2). No suspicious right intramammary findings were noted. An oval-enhanced mass was visualized in the mid-inner left breast with prominent left axillary nodes, leading to U/S-guided biopsies. These biopsies revealed no malignancy in either left breast or left axilla. Staging chest, abdomen, and pelvis (CAP) computed tomography (CT) scan, along with a bone scan, showed no evidence of distant metastasis.

After completing the workup, the case was reviewed at multidisciplinary breast tumor board (MDT) as an instance of occult right breast cancer with positive axillary involvement. The decision was made to proceed with neoadjuvant chemotherapy (NACT) and dual anti-HER2 therapy. The patient received NACT consisting of six cycles of TCHP: trastuzumab (8 mg/kg in cycle 1, reduced to 6 mg/kg in subsequent cycles), pertuzumab (840 mg/kg in

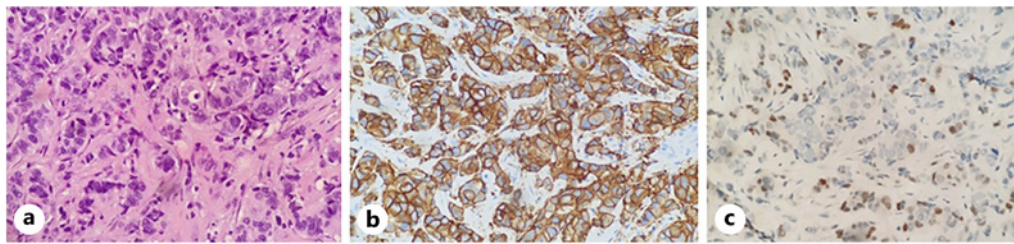


Fig. 1. **a** H&E (×40). **b** HER-2/neu (×40). **c** ERs (×40). ER, estrogen receptor; H&E, hematoxylin and eosin stain.

cycle 1, reduced to 420 mg/kg in subsequent cycles), docetaxel (75 mg/kg), and carboplatin (AUC 6). All agents were administered as intravenous infusion on day 1 of a 21-day cycle, for a total of six cycles [4].

Post-NACT, restaging with breast MRI revealed only a few small right axillary lymph nodes, and CAP CT confirmed the absence of distant metastasis. MDT recommended completing axillary dissection (AD), which was performed. The dissection revealed metastatic carcinoma in all eight dissected lymph nodes (8/8), with the largest deposit measuring 7 mm. Extra-nodal extension and lympho-vascular invasion were present, and one extra-nodal tumor deposit was observed. No treatment effect was noted in the examined lymph nodes. Consequently, the MDT decided to proceed with adjuvant radiotherapy and endocrine therapy and to continue trastuzumab.

She subsequently underwent adjuvant external beam radiotherapy (EBRT) to right breast and regional nodes, including the supraclavicular and axillary areas, at dose of 40.05 Gray over 15 fractions. The treatment involved tangential beams to the breast and axilla, and anterior-posterior beam to the supraclavicular fossa. Hormonal therapy was initiated and was planned to be continued for a minimum of 5 years, and trastuzumab was given for 1 year.

During follow-up, a CAP CT scan conducted 1 year after completing EBRT revealed no significant interval changes, except for an enlarging, nonspecific subcutaneous nodule in the right retro-scapular region, which was neither reported by the patient nor detected during physical exam. Bone scan showed no evidence of osteoblastic metastases. A biopsy of the subcutaneous retro-scapular nodule confirmed metastatic carcinoma consistent with primary breast cancer. A positron emission tomography (PET)/CT scan was done to rule out additional metastatic lesions which identified the retro-scapular lesion as hypermetabolic, measuring approximately 1.4 cm in its most active component with an SUV of 10. No evidence of hypermetabolic local tumor recurrence or other metastatic lesions was found (Fig. 3).

Breast MRI revealed no lesions; however, a shoulder MRI provided further details, identifying a soft tissue nodule on the dorsal aspect of the right shoulder, approximately 1.5 cm in diameter. This nodule was located within the fascial planes of the dorsal right shoulder, with focal concern for deep muscular invasion. As a result, the patient proceeded with a wide local excision. Histopathology showed metastatic invasive breast carcinoma in a lymph node, with extra-nodal extension and lympho-vascular invasion; both hormonal receptors were as follows: estrogen receptor and progesterone receptor were negative, while HER2 was positive (3+) by immunohistochemistry. The Ki67 proliferative index was 40%, and margins were clear of tumor.

Based on histopathology results, the MDT recommended adjuvant T-DM1 for 1 year, continuing endocrine therapy and adjuvant radiation therapy. EBRT was delivered to the operative bed including the preoperative lymph node with 5-mm margin and postoperative changes to account for the clinical target volume followed by 5-mm margin expansion for the planned target volume at dose of 40.05 Gray over 15 fractions using volumetric modulated arc radiotherapy with no overlap of isodoses from the first radiotherapy plan. In retrospect, the

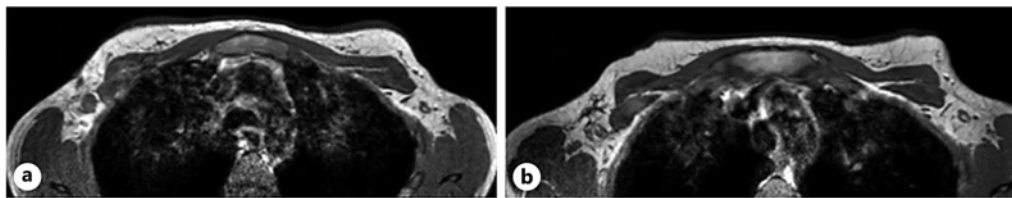


Fig. 2. **a** Initial axillary lymph nodes. **b** Post-neoadjuvant systemic treatment.

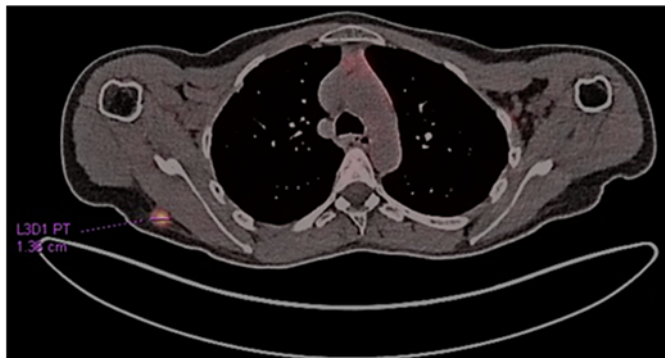


Fig. 3. Hypermetabolic metastatic right retro-scapular subcutaneous lymph node.

patient's initial images at the initial radiotherapy plan for the breast and regional nodes showed a hazy area at right retro-scapula, suggesting that this lymph node was potentially involved as shown in Figure 4.

Discussion

Occult breast cancer (OBC) is a rare form of breast cancer that typically presents as axillary lymphadenopathy without evidence of primary breast mass [5]. Its incidence is less than 1% of all breast cancer cases [2, 6]. OBC usually manifests with axillary lymphadenopathy, promoting a workup with clinical evaluation and biopsy for pathological and immunohistochemical classification. Imaging modalities used to detect primary disease include breast U/S, mammography, breast MRI [7, 8], and PET [9, 10].

Historically, OCB was treated with mastectomy and axillary lymph node dissection. However, current evidence regarding primary breast irradiation following AD is evolving [8, 11]. A meta-analysis has shown that loco-regional recurrence, distant metastasis, and mortality rates are similar between axillary lymph node dissections with either breast irradiation or mastectomy [12].

Surgical management of axilla typically involves removing all the nodes and fat in the anatomical boundaries of axilla: superiorly by the lower border of the axillary vein, medially by the chest wall, laterally by the axillary skin, anteriorly by the pectoralis major and minor, and posteriorly by the latissimus dorsi, teres major, and subscapularis. However, lymphatic pathways may be altered by prior surgical interventions such as previous AD, sentinel lymph node biopsy, or excisional biopsy [13–15], which may be relevant in our patient's case.

OBC is an unusual presentation of breast cancer that rarely metastasizes and generally has excellent outcomes [16, 17]. In our case, the initial presentation was atypical, and

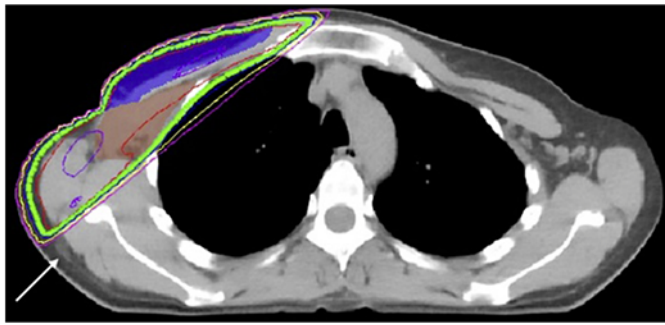


Fig. 4. Adjuvant radiation therapy to right breast and regional nodes, haziness at subscapular area labeled by arrow.

recurrence involved the right retro-scapular area, further illustrating the rarity of such occurrences.

Breast cancer tends to metastasize regionally to lymph nodes in 30–40% of cases [18], with axillary lymph nodes being the most common site. However, the increasing use of sentinel lymph node biopsy has led to the detection of non-axillary lymph nodes, sometimes necessitating changes in surgical and radiation management [19]. Detection of unusual lymph nodes may occasionally link to a history of vascular or inflammatory conditions [20], such as rheumatoid arthritis [21]. Notably, our patient had a history of rheumatoid arthritis and had been on methotrexate and steroids for 3 years prior to her cancer diagnosis.

In addition to regional metastasis, breast cancer has a propensity for distant metastasis, typically to the bone, lungs, liver, and skin [22]. Unusual metastatic sites in breast cancer have been documented, including inguinal [23], contralateral axilla [24] or intra-parotid [25]. OCB can also present with atypical metastatic sites; for example, Barbieri and colleagues [26] reported a case with a parietal skin lesion originating from OCB. Di Micco et al. [2] reviewed previously reported unusual sites of metastatic breast cancer, but the subscapular region was not mentioned. The retro-scapular region is a rare site for malignancy, whether as a primary site (e.g., sarcomas) or as a metastatic site. Mermershtain et al. [27] reported a single case of lung cancer with metastasis to the retro-scapular soft tissue, treated with neoadjuvant and adjuvant chemotherapy, surgery, and radiation therapy. Different subtypes of breast cancer tend to have different metastatic patterns; accordingly, HER2 neu-positive breast cancer tends to metastasize most commonly to bone and brain, and less commonly to atypical sites [28], and this is the first case in literature that describes a HER2 neu-positive breast cancer with retro-scapular lymph node metastasis.

As literature continues to describe emerging unusual sites of metastasis, there is an increasing need for more specific nuclear imaging techniques to detect such rare scenarios. In our case and other instances of rare breast metastases, 18F-fluorodeoxyglucose PET-CT has proven useful for identifying these atypical metastases. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see <https://doi.org/10.1159/000543346>).

Conclusion

Given the increasing evidence of unusual sites of breast cancer metastasis, it is crucial to maintain a lower threshold for suspecting such atypical involvement. Enhanced imaging techniques can aid in the earlier detection of these rare lesions, potentially leading to more

treatment options and improved outcomes for patients. Continued advances in imaging technology will be essential in identifying these unusual metastatic sites more effectively and providing timely, targeted interventions.

Statement of Ethics

This case report has been granted an exemption from requiring ethics approval, as per our Institutional Review Board policy. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

All authors declare no conflict of interest related to the material discussed in this manuscript.

Funding Sources

This project did not receive any fund.

Author Contributions

L.W. and F.A. designed the overall concept and outline of the manuscript; L.W., F.A., and H.A.-R. contributed data collection and review of literature. L.W., A.A., S.A., I.M., R.A., H.H., H.A.-R., and F.A. contributed to the writing, editing the manuscript, and final approval of the manuscript and believed that this manuscript will add useful information to existing literature.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

References

- 1 Jimah BB, Amoako E, Ofori EO, Akakpo PK, Aniakwo LA, Ulzen-Appiah K, et al. Radiologic patterns of distant organ metastasis in advanced breast cancer patients: prospective review of computed tomography images. *Cancer Rep.* 2024;7(2):e1988. <https://doi.org/10.1002/cnr2.1988>
- 2 Di Micco R, Santurro L, Gasparri ML, Zuber V, Fiocco E, Gazzetta G, et al. Rare sites of breast cancer metastasis: a review. *Transl Cancer Res.* 2019;8(Suppl 5):S518–52. <https://doi.org/10.21037/tcr.2019.07.24>
- 3 Rodrigues MVR, Terciotti-Junior V, Lopes LR, Coelho-Neto JDS, Andreollo NA. Breast cancer metastasis in the stomach: when the gastrectomy is indicated. *Arq Bras Cir Dig.* 2016;29(2):86–9. <https://doi.org/10.1590/0102-6720201600020005>
- 4 Hurvitz SA, Martin M, Symmans WF, Jung KH, Huang CS, Thompson AM, et al. Neoadjuvant trastuzumab, pertuzumab, and chemotherapy versus trastuzumab emtansine plus pertuzumab in patients with HER2-positive breast cancer (KRISTINE): a randomised, open-label, multicentre, phase 3 trial. *Lancet Oncol.* 2018;19(1):115–26. [https://doi.org/10.1016/S1470-2045\(17\)30716-7](https://doi.org/10.1016/S1470-2045(17)30716-7)

- 5 Axillary node metastases with occult primary breast cancer - Uptodate Free [Internet]. [cited 2024 April 29]. Available from: <https://pro.uptodatefree.ir/Show/766>
- 6 Baron PL, Moore MP, Kinne DW, Candela FC, Osborne MP, Petrek JA. Occult breast cancer presenting with axillary metastases. Updated management. Arch Surg. 1990;125(2):210–4. <https://doi.org/10.1001/archsurg.1990.01410140088014>
- 7 de Bresser J, de Vos B, van der Ent F, Hulsewé K. Breast MRI in clinically and mammographically occult breast cancer presenting with an axillary metastasis: a systematic review. Eur J Surg Oncol. 2010;36(2):114–9. <https://doi.org/10.1016/j.ejso.2009.09.007>
- 8 Ofri A, Moore K. Occult breast cancer: where are we at? Breast Off J Eur Soc Mastology. 2020;54:211–5. <https://doi.org/10.1016/j.breast.2020.10.012>
- 9 Liu M, Liu B, Song Y, Ding L, Dong L. FDG PET/CT reveals the primary tumor in a patient with occult breast carcinoma undetected by other modalities. Clin Nucl Med. 2014;39(8):755–7. <https://doi.org/10.1097/RLU.0000000000000503>
- 10 Hu T, Zhang R, Zhang B, He S, Liu L, Zou Y, et al. Case report: uncommon multiple metastases from occult breast cancer revealed by 68Ga-DOTATATE PET/CT. Front Oncol. 2023;13:1106890. <https://doi.org/10.3389/fonc.2023.1106890>
- 11 Brill KL, Brenin DR. Occult breast cancer and axillary mass. Curr Treat Options Oncol. 2001;2(2):149–55. <https://doi.org/10.1007/s11864-001-0057-x>
- 12 Wang R, Yang HX, Chen J, Huang JJ, Lv Q. Best treatment options for occult breast cancer: a meta-analysis. Front Oncol. 2023;13:1051232. <https://doi.org/10.3389/fonc.2023.1051232>
- 13 Arıcan P, Peksoy İ, Naldöken S, Bozkurt B. The effect of the excisional biopsy in the detection of the sentinel lymph node by lymphoscintigraphy and intraoperative gamma probe in breast cancer. Mol Imaging Radionucl Ther. 2011;20(3):100–3. <https://doi.org/10.4274/MIRT.28>
- 14 Sato A, Sakai T, Iwase T, Kano F, Kimura K, Ogiya A, et al. Altered lymphatic drainage patterns in re-operative sentinel lymph node biopsy for ipsilateral breast tumor recurrence. Radiat Oncol. 2019;14(1):159. <https://doi.org/10.1186/s13014-019-1367-0>
- 15 Suami H, Koelmeyer L, Mackie H, Boyages J. Patterns of lymphatic drainage after axillary node dissection impact arm lymphoedema severity: a review of animal and clinical imaging studies. Surg Oncol. 2018;27(4):743–50. <https://doi.org/10.1016/j.suronc.2018.10.006>
- 16 Fayanju OM, Jeffe DB, Margenthaler JA. Occult primary breast cancer at a comprehensive cancer center. J Surg Res. 2013;185(2):684–9. <https://doi.org/10.1016/j.jss.2013.06.020>
- 17 Lloyd MS, Nash AG. “Occult” breast cancer. Ann R Coll Surg Engl. 2001;83(6):420–4.
- 18 Jatoi I. Management of the axilla in primary breast cancer. Surg Clin North Am. 1999;79(5):1061–73. [https://doi.org/10.1016/s0039-6109\(05\)70061-x](https://doi.org/10.1016/s0039-6109(05)70061-x)
- 19 Gherghe M, Bordea C, Blidaru A. Clinical significance of the lymphoscintigraphy in the evaluation of non-axillary sentinel lymph node localization in breast cancer. Chirurgia. 2015;110(1):26–32.
- 20 Schwager S, Detmar M. Inflammation and lymphatic function. Front Immunol. 2019;10:308. <https://doi.org/10.3389/fimmu.2019.00308>
- 21 Rahimi H, Bell R, Bouta EM, Wood RW, Xing L, Ritchlin CT, et al. Lymphatic imaging to assess rheumatoid flare: mechanistic insights and biomarker potential. Arthritis Res Ther. 2016;18:194. <https://doi.org/10.1186/s13075-016-1092-0>
- 22 Harrison’s Principles of Internal Medicine 21e. AccessMedicine McGraw Hill Medical [Internet]. [cited 2023 Nov 15]. Available from: <https://accessmedicine.mhmedical.com/book.aspx?bookId=3095>
- 23 Das Majumdar SK, Muraleedharan A, Mahapatra BR, Adhya AK. Inguinal lymph node metastasis in treated breast cancer: an extremely rare presentation and review of literature. BMJ Case Rep. 2022;15(6):e249152. <https://doi.org/10.1136/bcr-2022-249152>
- 24 Kim JY, Lee H, Kim TS, Kang HS, Kim SK. Unusual contralateral axillary lymph node metastasis in a second primary breast cancer detected by FDG PET/CT and lymphoscintigraphy. Nucl Med Mol Imaging. 2017;51(4):350–3. <https://doi.org/10.1007/s13139-017-0485-6>
- 25 Agrawal CR, Dutta K, Doval DC, Pasricha S, Gupta M. Breast cancer recurrence presenting as solitary intraparotid nodal metastasis detected by 18F-fluorodeoxyglucose positron emission tomography: a very unusual occurrence. Indian J Nucl Med. 2018;33(3):233–6. https://doi.org/10.4103/ijnm.IJNM_17_18
- 26 Barbieri E, Anghelone CAP, Gentile D, Raja CL, Bottini A, Tinterri C. Metastases from occult breast cancer. A case report of carcinoma of unknown primary syndrome. Case Rep Oncol. 2021;13(3):1158–63. <https://doi.org/10.1159/000510001>
- 27 Mermershtain W, Smolnikov A, Gusakova I, Rouvinov K. “Muscle like” metastasis of large cell undifferentiated carcinoma of the lung to the retroscapular soft tissue. Ann Clin Case Rep. 2019;4(1):1675.
- 28 Wang H, Zhang C, Zhang J, Kong L, Zhu H, Yu J. The prognosis analysis of different metastasis pattern in patients with different breast cancer subtypes: a SEER based study. Oncotarget. 2017;8(16):26368–79. <https://doi.org/10.18632/oncotarget.14300>