



Multiple Lymph Node and Bone Metastases From An Occult Breast Cancer: A Case Report

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ABSTRACT

Cancer of unknown primary is defined as cancer with an unknown primary origin. Occult breast cancer (OBC) is a rare diagnosis in which physical examination, imaging methods, and even surgical procedures are insufficient to put on a primary tumoral site in the breasts. This definition leads to only 0.3-1% of all breast cancer cases. The diagnosis of OBC is usually obtained with an axillary lymph node biopsy. A 52-year-old female presented with right arm weakness and a neck lump. On the physical examination, multiple masses were palpated at the right axillary, right supraclavicular, and anterior cervical areas. Mammography, breast ultrasonography, breast magnetic resonance imaging, and 18-fluorodeoxyglucose positron emission tomography (18-FDG PET) scan could not show a suspicious tumoral area as the primary origin. 18-FDG PET scan put on the massive tumoral burden at multiple bones and lymph nodes, but there were no lesions to suspect as the tumoral origin. Finally, the supraclavicular lymph node biopsy result has revealed the diagnosis; hormone receptor-positive and C-erbB2 positive occult breast cancer. Cervical lymph node metastasis is also a scarce condition for breast cancer. The lymphatic drainage pathway is not clear in explaining the breast cancer involvement of the cervical.

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Introduction

Cancer of unknown primary (CUP) syndrome is referred to as a state whose primary site is unclear, but malignant cells have metastasized in a widespread. Occult breast cancer (OBC) is clinically recognizable axillary metastatic carcinoma from an undetectable primary breast tumour. With negative preliminary imaging and a biopsy-confirmed diagnosis of metastatic site, the patient is now classified as having OBC with an unknown primary site. The incidence of OBC is less than 1% of all patients who present with breast cancer (BC). OBC denotes the clinical status of axillary lymph node metastases consistent with a breast carcinoma arising in the absence of any identifiable primary breast tumour (pT0N+) in the staging system.¹

Mammography, breast ultrasonography, and chest x-ray are the first screening methods after detecting pathological axillary lymph nodes. Magnetic resonance imaging (MRI) of the breast, likely to reveal a suspicious lesion in 76% of patients, can identify the primary occult tumour

in 62% of this sub-group, with a false positive rate (FPR) of 29%. Although criticized for its high false-positive results in routine BC diagnosis, the role of MRI is crucial in the diagnostic dilemma of OBC.¹

The incidence of ipsilateral supraclavicular lymph node metastasis in BC is reported to be as low as 1-4.3% even though breast cancer is known as the most common primary cancer to metastasize to neck lymph nodes when primary head and neck cancers are excluded.^{2,3} Even though there is not a primary tumoral origin, in this case, extended tumoral spread with multiple metastases at lymph nodes and bones makes this case precious.

Case Report

A 52-year-old woman presented with persistent and progressive neck swelling and weakness in her right arm. On her physical examination, multiple masses were palpable on the right anterior cervical chain, right supraclavicular, and axillar areas. The largest one was at the right supraclavicular area, 4 cm in diameter. There was minimal restriction in

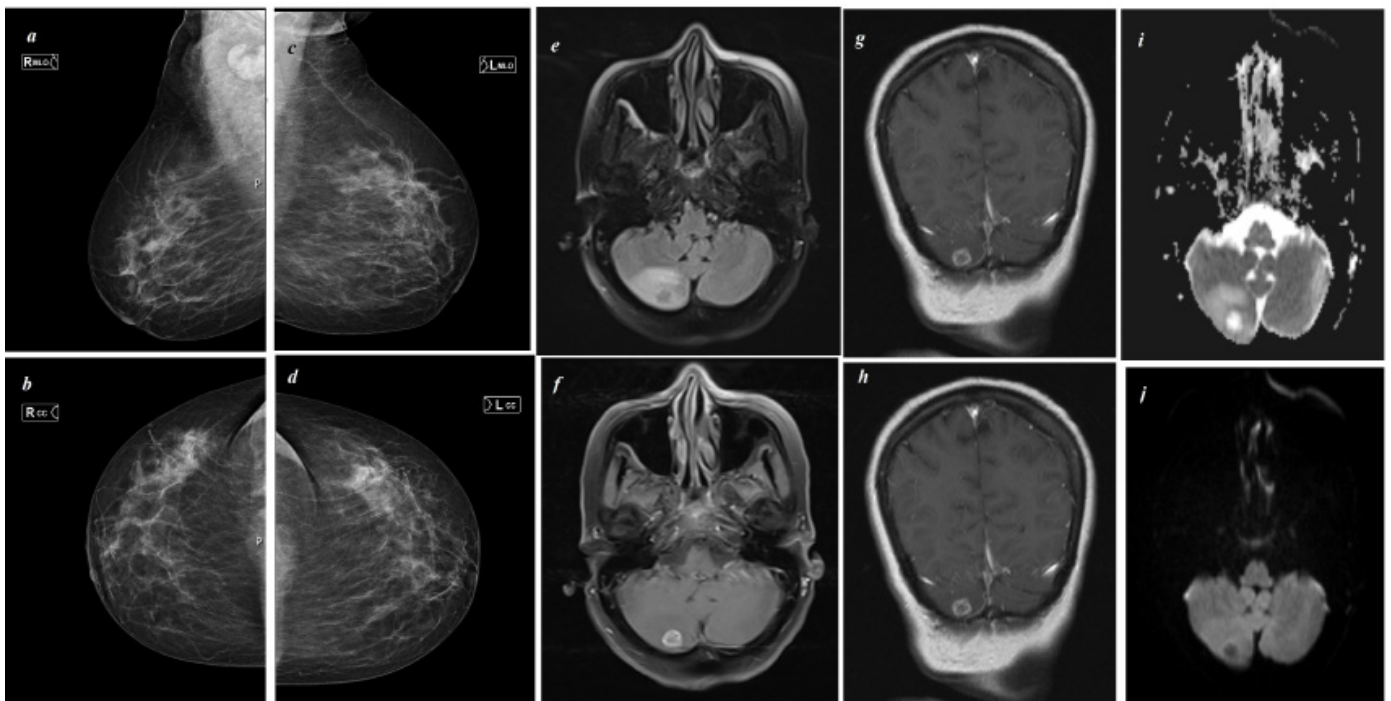


Figure 1. BIRADS-3 findings were observed in the mammography imaging (a,b,c,d). In cranial MR imaging; right cerebellar hemisphere posteromedial section has T2-Flair A (e) peripheral hyperintense edema area measuring approximately 10x12 mm in its widest dimension, showing intense contrast enhancement in T1 hypointense postcontrast T1 series (f,g,h) and causing mild limitation in diffusion examination (i,j) mass lesion observed.

right shoulder abduction and flexion movements, tenderness, and weakness in the right arm. Each of the largest ones in axillary and cervical masses was approximately 3 cm in diameter. There was no palpable mass in both of the breasts. Her right arm muscle strength examination was 3/5. She had only a beta-thalassemia minor in her medical history. She was not under any medications except the nonsteroidal anti-inflammatory drugs she used for her right arm pain.

In the laboratory tests, haemoglobin was 10.4 g/dL, MCV 65 fL, and LDH 321 IU/L. There were no other abnormal results at routine biochemistry tests. With the suspicion of breast

cancer, as she had an axillary mass, we performed mammography and breast ultrasonography. Both of them could not find a tumoral site in the breasts with the Breast Imaging Report and Data System (BIRADS) 3 (*Figure 1*). Electroneuromyographic electrophysiological findings were consistent with the lesion where the medial and lateral cord of the brachial plexus was severely affected, and the posterior cord was moderately affected. In cranial magnetic resonance imaging (MRI), the right cerebellar hemisphere posteromedial section has T2-Flair a peripheral hyperintense oedema area measuring approximately 10x12 mm in its broadest dimension, showing intense contrast

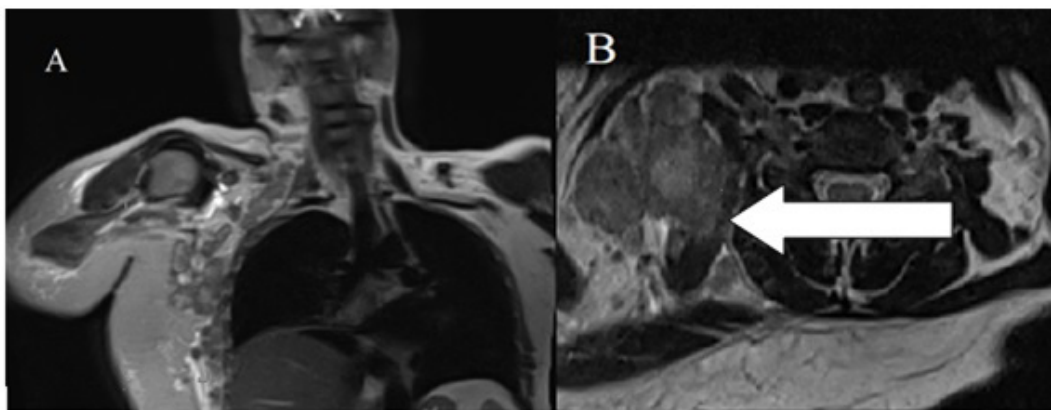


Figure 2. MRI images showing extensive involvement of the right brachial plexus. In A (coronal) and B (axial) T1-weighted sequences showing an infiltrating mass encasing the right brachial plexus.

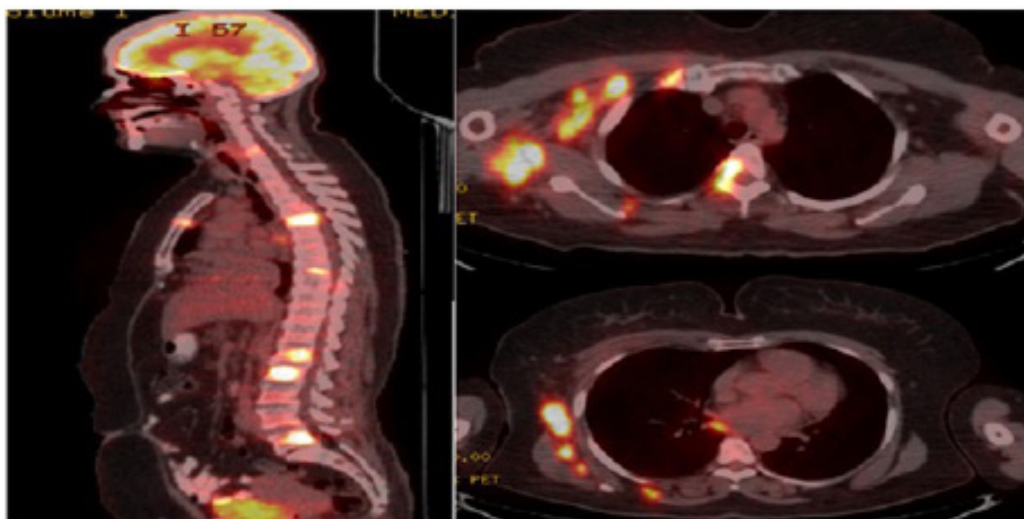


Figure 3. 18 FDG whole body positron emission tomography (PET) findings.

enhancement in T1 hypointense postcontrast T1 series and causing mild limitation in diffusion examination mass lesion observed (*Figure 1*).

With the ongoing suspicion of breast cancer, we performed a breast MRI. There was no focus to maintain our suspects at both breasts, but the right supraclavicular, retro pectoral, and right deep axillary lymph nodes were seen in the MRI scan. Besides, T2 hyperintense, T1 hypointense, and T1-T2 hypointense irregular-shaped heterogeneous multiple lesions (*Figure 2*) were observed in the vertebral column and sacral bone. In the 18-fluorodeoxyglucose positron emission tomography (18-FDG PET) scan, which was performed to choose the best site for taking the biopsy sample and for staging the disease, multiple hypermetabolic lymph nodes were observed at the right supraclavicular fossa with the largest one 41x38 mm in dimensions, the interpectoral area with the most prominent one 35x35 mm in sizes, right retro pectoral area with the largest one 40x36 mm in dimensions, right axillary fossa, right parasternal and subcarinal area, left axillary fossa and right jugular area. Also, multiple metastatic lesions were seen in all the bones of the pelvic arch, both femurs, sternum, 3rd cervical-, 3rd, 4th, 8th, and 9th thoracic, 1st, 4th, and 5th lumbar vertebral corpus and 2nd, 3rd lumbar vertebral pedicles. However, there was no pathological FDG uptake in both breasts or any other solid organ (*Figure 3*).

Excisional biopsy was performed from the supraclavicular Lymph node because it was easy to reach and one of the highest SUV max and most prominent lymph nodes detected with an 18-FDG PET scan. With positive estrogen receptor (ER) and progesterone receptor (PR) results of enzyme immunoassay and positive C-erbB2 gene mutation proven by PCR analysis, lymph node biopsy was reported as breast cancer metastasis. The follow-up and treatment of the patient are proceeding at the clinical oncology department with the diagnosis of OBC.

Discussion

Here, we described an occult BC patient with progressive enlargement of axillary, supraclavicular, and retro pectoral lymph nodes

that have involved the brachial plexus in a 52-year-old woman. Advanced neuropathic findings and aggressive enlargement of the involved lymph nodes made us suspicious of malignancy, especially breast cancer. Mammography, breast ultrasonography, and chest x-ray were not enough to give a clue about the primary site of the tumour. MRI of the breasts also failed to expose any lesions to the suspect as the primary origin. 18-FDG PET scan was also unable to put on a primary focus on the breasts or any solid organ, but multiple metastatic lesions at the bones and the lymph nodes in a widespread pattern. After all, an excisional supraclavicular lymph node biopsy was taken. The histopathological assessment of the biopsy sample was reported as breast cancer metastasis with positive ER, PR, and CerbB2.

Breast cancer may be specifically suspected when axillary nodes are involved in women. Even if the ultrasonography and mammography are negative, a breast MRI is recommended if the findings are like CUP syndrome.^{4,5} The use of MRI identifies a lesion which may be the primary focus in 72% of patients whose mammography and ultrasound results are negative. Over 85% of the suspected lesions shown by MRI are proven as the primary breast carcinoma upon biopsy.⁶ In our case, MRI was also helpless to determine a malignant focus in breasts. MRI is also the distinguished image modality for evaluating the brachial plexus and its pathological involvement. Among 104 cases with non-traumatic brachial plexopathy, radiation fibrosis (31% of cases), metastatic BC (24%), and primary or metastatic lung cancer (19%) were the most common causes.^{7,8}

It is well known that OBC includes various subtypes, from hormone receptor-positive tumours to human epidermal growth factor receptor 2 (HER2) positive and triple-negative tumours. Negative ER/PR immunohistochemistry results do not exclude breast cancer diagnosis. Still, they are not enough for the diagnosis as different malignancies can synthesise hormone receptors, such as colon, ovarian, and endometrium. Blood tumour marker studies such as CEA and CA 15-3 can provide a more reliable diagnosis. Immunohistochemical stains for lactalbumin, CEA, ER, and PR are recommended for diagnosing breast cancer when in doubt.⁹⁻¹¹

Conflict of Interests

The authors declare that they have no conflict of interest.

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Informed Consent

Written consent was obtained from the patient.

Authors' Contribution

Literature Review, Critical Review, Manuscript preparing held by all authors.

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