PJSS Vol. 80, No. 1, January-June, 2025

PJSS PHILIPPINE JOURNAL OF SURGICAL SPECIALTIES

Metastatic Axillary Lymphadenopathy from a Triple-Negative Occult Breast Carcinoma in a Male Patient: A Case Report

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Occult Breast Carcinomas (OBCs) are rare. History and physical examination alone may lead to misdiagnosis hence inappropriate investigative and treatment modalities. Diagnosis is difficult without tissue biopsy and extensive immunohistochemical staining. Presented here is a 74-year-old Filipino male with a 2-month history of axillary mass with erythematous skin, initially assessed as hidradenitis suppurativa failing to resolve with antibiotics. An excision biopsy revealed adenocarcinoma within the lymph nodes. Immunohistochemical stains confirmed a breast primary. Radiologic imaging showed no breast lesions and no distant metastasis. Axillary node dissection done showed metastasis to 5 in 14 nodes harvested, classifying him as OBC Stage IIIA (cT0pN2M0). He completed whole breast radiotherapy and chemotherapy. No tumor recurrence was documented thereafter. Although misdiagnosis is common, OBC is a condition to consider in male patients presenting with axillary lymphadenopathy.

Key words: case report, occult breast carcinoma, axillary nodes, lymphadenopathy, male

Axillary adenocarcinomas are often metastases from the ipsilateral breast.[1] If physical examination and imaging such as breast ultrasound, mammogram, MRI or PET CT showed no identifiable breast tumors, Occult Breast Carcinoma (OBC) becomes the consideration. OBCs are rare with only 0.3 to 1% incidence among breast cancer patients.[2] Male patients with OBC are rarer and are only accounted for through various case reports.[3] The rarity of the disease may lead to misdiagnosis and the condition may be entirely overlooked in male patients. This case report discusses a triple-negative OBC in a male patient, his diagnostic assessment, and subsequent surgical and medical interventions.

This case report has been written in line with the SCARE 2020 Guideline: Updating Consensus Surgical Case Report (SCARE) Guidelines.[6]

The Case

The patient is a 74-year-old male, married, Filipino businessman who owns a construction company. He has a BMI of 21 and an ECOG performance score of 0. He is a non-smoker, non-alcoholic beverage drinker, and has no known allergies. He is hypertensive and non-diabetic, with no previous surgeries. He denies any history of malignancy in the family. The patient consulted at the clinic because of a 2-month history of a slowly enlarging left axillary mass.

On physical examination, the mass was 4 cm in size, firm, non-fluctuant, slightly erythematous, non-tender, with noticeable sinus tract but no discharge noted. There were no palpable neck and breast lesions. There were no other lesions on the skin and upper extremities. Contralateral breast and axilla were also unremarkable.

Patient initially consulted a general physician who treated the patient as a case of hidradenitis suppurativa. He was treated with a 10-day course of Clindamycin. Upon completion, although a decrease in erythema was noted, the left axillary mass was still palpable. On consult with a general surgeon, the impression of hidradenitis suppurativa was maintained and an excision biopsy was planned.

A 3.5 cm x 2.0 cm x 2.0 cm specimen was excised (Figure 1). Cut sections revealed a 2.5 cm x 1.5 cm x 1.0 cm nodular white mass beneath the skin. Microscopic examination (Figure 2) revealed lobules of closely-packed glandular structures. Glands were lined by cuboidal epithelium with large nuclei and nucleoli. There were numerous mitotic figures within lymphatic tissue

and necrosis is present. The pathology was reported out as "adenocarcinoma – to consider an apocrine primary versus metastatic breast ductal carcinoma."

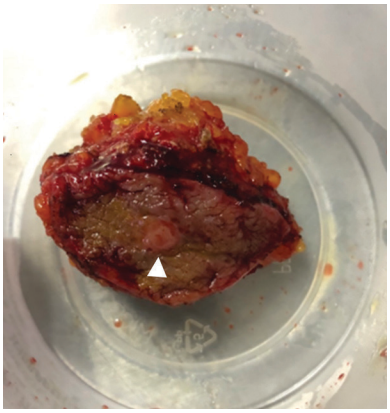

Figure 1. Axillary mass, left s/p excision biopsy; 3.5cm x 2.0cm x 2.0cm specimen. Cut sections revealed a 2.5cm x 1.5cm x 1.0cm nodular white mass (arrowhead).

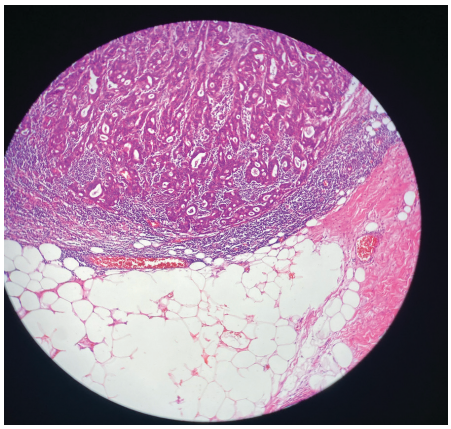

Figure 2. Axillary mass under high-power field microscopy.

The patient was referred to a medical oncologist and metastatic work-up was done. At this time, the main consideration was metastasis from a breast or other apocrine primary. The patient was advised ultrasound of the breasts and the axilla. No noted breast lesions were seen, but there were enlarged lymph nodes in the left axillary area, measuring 1.9 cm x 2.4 cm and 1.8cm x 2.0cm. A contrast-enhanced breast MRI also showed no mass lesions on both breasts but at least 2 contrast enhancing lobulated enlarged lymph nodes approximately 2.1cm x 1.8cm and 1.3cm x 1.5cm, respectively, were detected in the left axilla. CT scan of the Chest and Abdomen again showed no breast masses but at least two lobulated soft tissue enhancing nodules in the axilla measuring 2.1cm x 1.8cm x 2.8cm and 1.6cm x1.0cm x 2.0cm (Figure 3). No pulmonary masses were seen. Multiple hypodense hepatic nodules were identified scattered throughout the liver, with the largest at segments 6/7 measuring 0.9cm x 1.0cm x 1.0cm. These were thought to be multiple hepatic cysts though metastasis could not be completely ruled out. FDG PET CT scan done showed no tracer uptake on the hepatic nodules. Likewise, there was no tracer uptake in the brain and bone, the salivary glands and reproductive organs and prostate. The PSA (5.0 ng/mL; NV: 0.21-6.77ng/mL) is within normal limits.

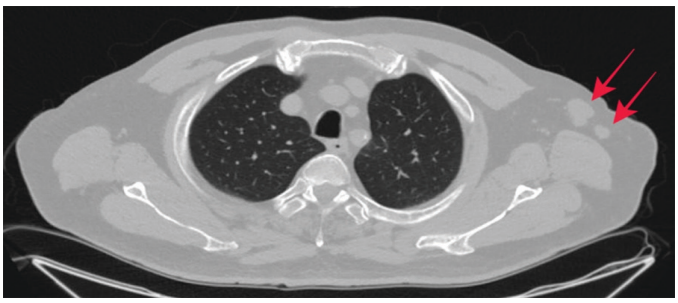

Figure 3. Transverse view of chest CT scan with IV contrast; enlarged axillary lymph nodes (arrows).

The axillary mass (Figure 1), paraffin block, and slides were sent to another tertiary hospital for review. Immunohistochemistry was positive for mammaglobin and negative for p63, CK5/6, ER, and PR. HER2/neu was equivocal while FISH was negative. The report revealed "lymph nodes with immunomorphologic findings consistent with metastatic carcinoma of breast primary." Additional immunohistochemical stains were done: GCDFP-15 and GATA3 were both positive. The report again revealed "immunomorphologic findings most compatible with invasive carcinoma of breast primary." After consultation and slide review with different pathologists, it was concluded that the axillary mass was carcinoma, particularly adenocarcinoma, non-apocrine (CK5/6 negative), metastatic from a breast primary (mammaglobin, GCDFP-15, and GATA3 positive), and was a triple-negative (ER -, PR -, HER2/neu -) breast cancer.

The patient was managed as a case of triple-negative OBC. Four weeks from diagnosis, the patient underwent axillary lymph node dissection under general anesthesia under the same surgeon (Figures 4, 5 and 6). Histopathology revealed metastasis compatible with breast carcinoma as primary, with 5 positive metastatic nodes out of the 14 harvested during the dissection. The oncologist advised chemotherapy and radiotherapy. Patient was able to complete a 6-cycle regimen with Cyclophosphamide, Doxorubicin, Docetaxel and Carboplatin. He also underwent radiotherapy sessions at a different institution. On the 3rd cycle of Docetaxel with Carboplatin, the patient lost approximately 9 kg after developing multiple aphthous ulcers. He was then admitted, given oral gel and mouthwash for the ulcers, and provided nutritional support with lipid emulsions and mechanically soft diet on top of parenteral nutrition. Patient was discharged in 2 weeks, after resolution of oral ulcers and a better appetite. These did not recur on subsequent chemotherapy sessions.

The patient was able to follow-up with the surgeon at 1st, 2nd and 4th week after the ALND. Wound was dry and well-coaptated with no lymphedema. Drain was removed on the 7th post-operative day (Figure 7). He also followed-up with his oncologist regularly, even upon completion of chemotherapy and radiotherapy after 1 and 3 months, then every 6 months with complete physical examination and blood tests, including a yearly mammography which showed no breast nor axillary lesions. After a follow-up 33 months post-ALND, there was no evidence of tumor recurrence. There was no lymphedema nor limitation of movement of the left upper extremity.

Figure 4. Left axilla, prior to ALND; note of previous excision biopsy scar (labelled)

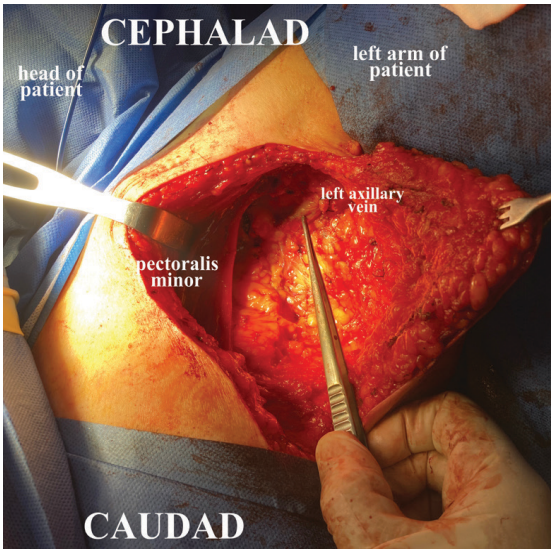

Figure 5. Axillary lymph node dissection; intraoperative photo showing the left axillary vein and left pectoralis minor muscle.

Figure 6. Axillary lymph node dissection; post-operative site; Jackson-Pratt drain placed.

Figure 7. Left axilla, 7th post-operative day; dry and well-coaptated wound, drain removed

Discussion

Occult Breast cancer is indeed rare, with only a 0.3-1% incidence.[1] It is even rarer to find a triple-negative breast carcinoma in a male patient.

Given an occult primary, if axillary nodes reveal adenocarcinoma, the National Comprehensive Cancer Network (NCCN) Guidelines recommend neck/chest/abdomen/pelvic CT, immunohistochemical stains, a mammogram, or a breast MRI if a mammogram is nondiagnostic, and serum PSA for patients above 40 years old.[4]

Various immunohistochemical stains can help accurately diagnose different tumors by detecting specific protein markers. Squamous epithelium and urothelium stain for p63. CK5/6 are positive in mesotheliomas, strongly staining in apocrine carcinomas (80% sensitivity), and negative in adenocarcinoma lesions[7]. GCDFP-15 is positive in ~60% of breast carcinomas and 10% of triple-negative breast cancers (TNBCs) while mammoglobin stains positive in 60% of breast malignancies and 15% of TNBCs. However, mammoglobin is still more sensitive than GCDFP-15 in identifying metastatic breast lesions.[7] Mammoglobin has been shown to be positive in 25-94% of invasive breast carcinomas, 11-76% of endometrial carcinomas, 37-100% of ovarian carcinomas, and 0-36% of prostatic adenocarcinomas.[8] GATA3 is another marker which is highly expressed in metastatic lesions of breast origin. In a study from India on breast carcinoma specimens, mammaglobin was expressed in 68% of primary, 56.6% of metastatic and 25% of triple negative breast carcinomas while GATA-3 was expressed in 92% of primary, 80% of metastatic and 60% of triple negative breast carcinomas, showing the superiority of GATA3 in detecting the tumor of origin of metastatic lesions.[9]

Treatment options may vary. These include Axillary Lymph Node Dissection (ALND) alone, ALND with mastectomy, or ALND with whole breast radiation therapy (WBRT). A study by Walker, et al in 2010 compared these treatment modalities with an observation group wherein no ALND, RT, nor mastectomy was done. Based on the study's multivariate analysis, "either mastectomy or RT improves overall survival in patients with occult breast cancer" after ALND.[5] Currently, NCCN Guidelines for Occult Primary recommends that OBC patients with axillary masses showing adenocarcinoma should be treated per NCCN Guidelines for Breast Cancer. Axillary lymph node dissection is recommended for those with a prostate, to include radiotherapy and systemic therapy as indicated.[4] Preferred regimens for systemic therapy include Carboplatin and Paclitaxel, Cisplatin and Gemcitabine.[4] The investigative measures performed in this patient to detect the primary and course of treatment taken were aligned with recommendations from NCCN.

There are various studies comparing the recommended treatment for OBCs mentioned in NCCN. Walker, et al, performed a population-based analysis comparing the cause-specific survival (CSS) and overall survival (OS) of 750 patients diagnosed as OBC among 770,030 patients diagnosed with breast carcinoma.[5] Patients who underwent ALND with mastectomy and ALND with Whole Breast Radiation Therapy had a 10-year OS rate of 63.5% and 67.1%, respectively, compared to 58.5% for those who underwent ALND alone and 47.5% for those who just observed. The CSS rate was found to be 73.9% for those who had ALND with mastectomy, 75.7% for those who underwent ALND with WBRT,

while 71.2% for those who underwent ALND alone. The study concluded that in OBC patients, the addition of mastectomy or RT after ALND can improve OS.[5] The National Institutes of Health (NIH) recommends that patients be offered breast conservation therapy with ALND and RT whenever possible.[10]

This report illustrates the importance of cultivating a good clinical eye and establishing a thorough list of differential diagnoses in the case of axillary lymphadenopathy without an obvious primary. Decision-making can be a challenge. An open mind and the benefit of the input of a multidisciplinary team can make managing such patients more straightforward.

Additional Information

The case report has been presented at the PSGS-PALES Joint Convention on July 21, 2023 at Shangri-La Mactan Cebu, Lapu-Lapu City, Cebu, Philippines.

The case report was performed in accordance with ethical practices and was approved by the Research Committee of the Department of Surgery of Capitol Medical Center. The study was exempted from review by the Research Ethics Board of the hospital.

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