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Synchronous Breast Cancer and Tuberculosis in Axillary Lymph Nodes: A Case Report and Review of Literature

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ABSTRACT

Axillary lymphadenitis in the setting of breast cancer raises suspicion for metastasis. However, there are other causes of lymphadenitis, which can present at the same time as breast cancer. In endemic countries particularly, tuberculosis should be considered in the differential diagnosis as it could lead to unnecessary and incorrect treatment.

In our report, a 75-year old Hispanic woman with a right breast lump and enlarged lymph nodes detected by ultrasound was diagnosed with infiltrating ductal carcinoma, while the axillary lymph nodes had caseation granulomas that were positive for acid-fast bacilli. While no definitive guidelines exist, it was decided that anti-tuberculosis treatment should preclude radiotherapy to avoid disease reactivation.

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CASE REPORT

Patient and evolution

A 75-year old Hispanic woman presented with a lump on her right breast. Her past medical history includes long-standing type 2 diabetes mellitus with microvascular complications (retinopathy, neuropathy, and microalbuminuria), dyslipidemia, peptic ulcer disease, unipolar depression, and restrictive lung disease with use of supplementary oxygen, attributed to a 60-year exposure to smoke from a wood stove. Current medications include metformin, subcutaneous insulin, salbutamol, fluticasone, and citalopram.

Additionally, three years prior she had an episode of community-acquired pneumonia characterized by productive cough with green sputum, oxygen saturation of 83%, and leukocytosis. An X-ray demonstrated a right basal consolidation with air bronchogram. It was classified as PORT IV, requiring hospitalization. Treatment included intravenous piperacillin/tazobactam and supplementary oxygen. It resolved without further complications. Two years after that she had pleuritic pain, which prompted her to go to the emergency department, where no specific diagnosis was delivered and she was sent home. During her workup, multiple X-rays were taken in the span of five years, none of which showed evidence suggestive of pulmonary tuberculosis (TB). A purified protein derivative skin test was never performed.

Physical examination revealed a mass of approximately 1 x 1 cm in the upper external quadrant of the left breast, hard in consistency, and not adhered to deep tissue. No other masses were palpable and there was no axillary adenopathy. No clinical evidence that suggested primary TB was found.

She was first evaluated with mammography and complementary ultrasound, which reported three irregular masses in the upper external quadrant, the largest measuring 13 mm, with architectural distortion and associated to regional pleomorphic calcifications. Retroareolar asymmetry was also noted, so the radiologist classified the images as Breast Imaging Reporting and Data System (BI-RADS) 5.

She was referred to the Oncologic Surgery department, which indicated an ultrasound-guided core-needle biopsy. The report was of an infiltrating ductal carcinoma non-specific, moderately differentiated, with a luminal B immunophenotype (ER+, PR+, HER2-, Ki67 20%). She was scheduled for a modified radical mastectomy with sentinel lymph node biopsy. However, her case was reviewed by the Functional Breast Clinic Unit, where the surgical risk was considered high and tamoxifen therapy was decided instead. She received this for six months, after which a progression of disease was noted so she was switched to letrozole. A follow-up ultrasound was performed 15 months later, where RECIST criteria was met for stable disease. Five months later, one of the three previously reported nodules was no longer found. However, previously unseen ipsilateral axillary lymphadenopathy involving three nodes was reported.

A month later her case was re-evaluated and she was considered fit for oncologic surgery. Thoracoabdominal computerized tomography and bone scintigraphy were negative for metastatic disease. Radical modified left mastectomy with axillary dissection was performed two months later, with a successful recovery.

Histopathological findings

The surgical specimen measured 20 x 13 x 3 cm, with no macroscopic alterations of the areola-nipple complex. On sectioning, a white solid tumor with infiltrative borders measuring 2.0 x 1.0 x 0.7 cm was identified in the superior quadrant midline. The rest of the parenchyma was irrelevant. Numerous

lymph nodes were identified. Histologically, an infiltrating ductal carcinoma not otherwise specific, moderately differentiated, was observed (Fig. 1). Of 21 analyzed lymph nodes, metastasis was found in four of them. Granulomatous lymphadenitis (Fig. 2), Ziehl-Neelsen positive (Fig. 3) was observed in one lymph node.

Because of this, her case was again presented to a multidisciplinary panel. The conclusion agreed upon was to give four weeks of intensive anti-TB treatment consisting of rifampin, isoniazid, pyrazinamide, and ethambutol; after this adjuvant chemotherapy would be initiated, along with four more weeks of intensive anti-TB treatment followed by a maintenance phase of seven months. The primary risk to be assessed is considered liver toxicity, along with reactivation of TB as a side effect of the chemotherapy.

REVIEW

A PubMed search yielded 36 cases in which both breast cancer and axillary TB were diagnosed, plus our own report. Ages varied from 21 to 82 years, with a mean of age of 52. Of the 37 cases, 17 had left sided tumors while 16 were right sided. Four cases did not specify side of tumor[1-24]. Seven patients also had TB in the breast itself[3,14,18,23,25], and 28 had palpable lymph nodes at presentation. Only five of these were biopsied, either by fine needle aspiration cytology (FNAC) or excisional methods. The rest were analyzed after surgery was performed.

The most common method of breast cancer diagnosis was FNAC (10 patients), followed by core-needle biopsy (five patients), and excisional biopsy (five cases). Twenty-nine patients underwent modified radical mastectomy and four underwent breast-conserving surgery; one patient did not undergo any kind of surgery.

There were 19 cases of metastatic breast cancer detected in the lymph nodes, of which nine had

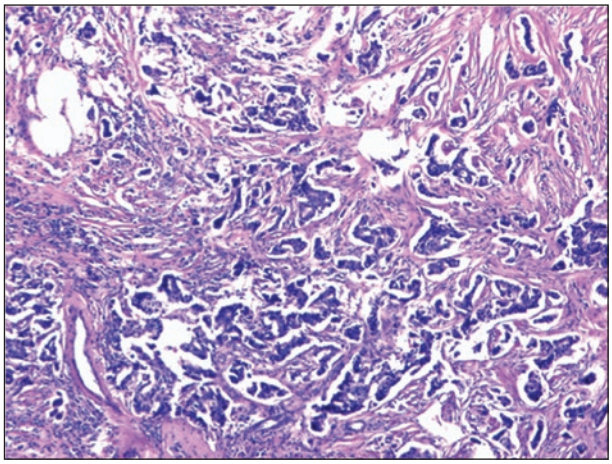

Figure 1. Infiltrating ductal carcinoma (hematoxylin and eosin stain).

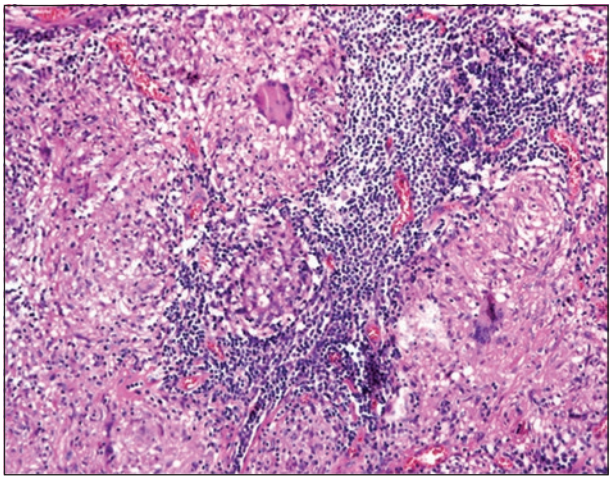

Figure 2. Granulomatous lymphadenitis with multinucleated giant cells, Langhans' type, in the subcapsular area (hematoxylin and eosin stain).

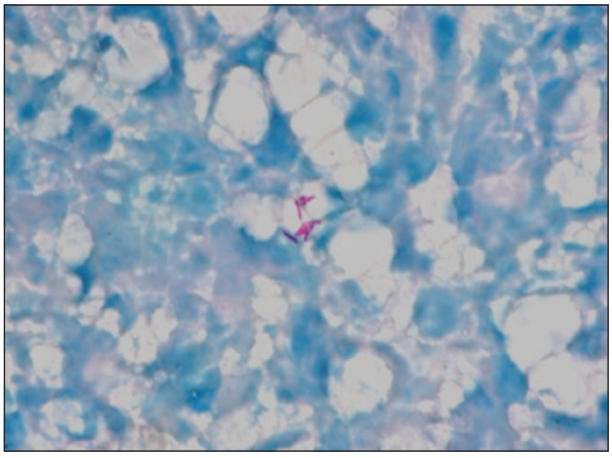

Figure 3. Ziehl-Neelsen stain positive for micobacteria.

Table 1. Patient characteristics

Variable	(n)
Age, years (mean)	52.2 (28-81)
Tumor size (mean)	4.7 (0.9-22)
Diagnosis method (BC)	
FNAC	10
Core-needle biopsy	5
Excisional	5
Diagnosis method (ATb)	
Post-surgical	29
FNAC	1
Core-needle biopsy	1
Excisional	3
X-ray	2
Type of surgery	
MRM	24
SM	5
Lumpectomy	4
Axillary dissection	4
None	1
BC histology	
IDC	25
Other	7
Axillary lymph nodes	
BC metastasis	19
TB	37
Both	9
Medical treatment	
CT	17
RT	9
Anti-TB	24
CT + Anti-TB	16
Follow-up (mean)	23 (2-82)

ATb: active tuberculosis; BC: breast cancer; CT: chemotherapy; FNAC: fine needle aspiration cytology; IDC: invasive ductal carcinoma; MRM: modified radical mastectomy; RT: radiotherapy; SM: simple mastectomy; TB: tuberculosis.

both breast cancer and TB in the same nodes. Five patients had no palpable lymph nodes, but all of them were positive for TB (two of them also had breast cancer metastasis) and were diagnosed after surgery was performed. Additional patient characteristics are shown in table 1.

DISCUSSION

According to the World Health Organization (WHO), 9.6 million people became ill with TB in 2013, and 1.5 million died. The highest rates of TB are in sub-Saharan Africa, India, and Southeast Asia[26].

Breast cancer, on the other hand, accounts for 230,000 cases and is responsible for over 40,000 deaths a year in the USA[27]. In Latin America, there are over 596,000 new cases and 142,100 deaths a year[28]. In Mexico, breast cancer is the second largest cause of mortality by a malignant tumor, accounting for 14.8% of deaths[28].

Tuberculous lymphadenitis is one of the most common presentations of extrapulmonary tuberculosis (EPTB). It is responsible for 43% of all EPTB worldwide. While the cervical nodes are the most commonly affected sites, it is also observed in axillary, supraclavicular, and inguinal sites, among others.

The synchronous affectation of TB and breast cancer is an uncommon event. Kaplan, et al. in 1927 published a series of 201 patients that had TB along with neoplastic disease. The most frequent association was TB with lung cancer, followed by head and neck, with breast cancer in third place[29]. Only a handful of cases have been reported of patients with breast cancer along with tuberculous lymphadenopathy masquerading as metastatic disease. Warthin published the first two in 1899, from which he suggested that the occurrence of these two diseases together, although rare, is purely coincidental[23]. Kim, et al. reported 73 patients with axillary lymphadenopathy identified on breast sonography; of these only three were TB[30].

To understand the implications of this coexistence, it is important to consider the mechanism of disease for axillary TB: after establishing a pulmonary infection focus, macrophages phagocytize bacilli and can disseminate via the lymphatic vessels and/or hematogenously. If the immune response is intact, the bacterial growth is contained and granulomatous encapsulation occurs, which contains viable organisms. Reactivation of this latent focus may occur whenever an underlying

condition affects the immune response, such as malignancy or diabetes, both of which were observed in our patient. Although our patient showed no signs of disease reactivation, it is important to consider the possibility of a primary foci reactivating as a result of chemotherapy or substandard treatment of diabetes[31].

Generally, when axillary lymphadenopathy presents along with breast cancer, the clinical suspicion for TB is very low as most of the time there are no clinical symptoms of TB present and other, more urgent, diagnoses, such as metastasis, must be ruled out. Tuberculosis in the axillar lymph nodes is diagnosed by pathological analysis of tissue samples obtained from biopsies or surgical remnants such as breast tissue from a mastectomy. In countries with endemic TB, such as Mexico, the possibility of infectious disease in these nodes must be considered beforehand in order to properly stage the disease and avoid unnecessary treatment.

When pulmonary TB is suspected, the diagnosis is typically made through chest x-rays, tuberculin skin test, and sputum for acid-fast smear and cultures. In the case of tuberculous lymphadenitis, tissue samples must be obtained by way of fine-needle aspiration (FNA) or excisional biopsies, which have the highest diagnostic yield. Lee, et al. described 47 patients with cervical lymph node TB in whom FNA was able to detect 62% of cases, while excisional biopsies detected all cases of TB[32]. Newer techniques such as polymerase chain reaction (PCR) provide further aid in diagnosing TB on tissue samples. Khurram, et al., in a series of 22 patients with breast cancer and associated granulomatous inflammation of the axillary lymph nodes, reports that Ziehl-Neelsen stain was not able to detect TB in any of the lymph node samples, whereas Mycobacterium tuberculosis-PCR assays detected 11 (50%) cases of TB, adding another, more sensitive, diagnostic option[33].

As with our patient, most cases are diagnosed postoperatively from pathologic analysis of the surgical samples. Although there is no clear consensus defining the timing and relationship of anti-TB therapy in these patients, it is generally thought that preoperative administration is preferable so as to reduce complications related to TB, such as wound infection, and to facilitate axillar dissection[1]. In patients in whom TB is not treated preoperatively, Broughton, et al. recommend that anti-TB therapy be given for at least four weeks before chemotherapy (CT) and radiotherapy (RT) begin to avoid reactivation of the disease[5].

In Mexico, standard TB treatment for EPTB is an induction phase of two months consisting of isoniazid, rifampin, pyrazinamide, and ethambutol. Following this is a maintenance phase of seven months of isoniazid and rifampin. For our patient, it was decided that the first four weeks of the induction phase would be administered before the start of CT and RT. After this, the induction phase would be continued along with CT and RT for another month, followed by seven months of maintenance therapy.

The synchronous appearance of breast cancer along with axillary TB is an important, albeit rare, event that can confuse and complicate the diagnosis, staging, and treatment of the disease. It is important for physicians in endemic countries, such as Mexico, to consider the possibility of a granulomatous disease masquerading as axillary metastasis in order to correctly address both diseases.

REFERENCES

1. Akbulut S, Sogutcu N, Yagmur Y. Coexistence of breast cancer and tuberculosis in axillary lymph nodes: a case report and literature review. Breast Cancer Res Treat. 2011;130:1037-42.
2. Avninder SP, Saxena S. Infiltrating ductal carcinoma of the breast, metastatic to axillary lymph nodes harboring primary tuberculous lymphadenitis. Pathol Oncol Res. 2006;12:188-9.
3. Balasubramanian S. Coexisting mammary tuberculosis and malignant disease. African J Emerg Med. 2013;3:140-1.
4. Baslaim MM, Al-Amoudi SA, Al-Ghamdi MA, Ashour AS, Al-Numani TS. Case report: Breast cancer associated with contralateral tuberculosis of axillary lymph nodes. World J Surg Oncol. 2013;11:43.
5. Broughton A, Galant C, Hainaut P. Simultaneous occurrence of metastatic breast cancer, Hodgkin's disease and tuberculous lymphadenitis in

homolateral axillary lymph nodes - A case report. Acta Clin Belg. 2008;63:391-3.
6. Bromberg SE, Amaral PG. Tuberculosis axillary lymph node coexistent breast cancer in adjuvant treatment: case report. Einstein (Sao Paulo). 2015;13:423-5.
7. Das DK, Mohil RS, Kashyap V, Khan IU, Mandal AK, Gulati SM. Colloid carcinoma of the breast with concomitant metastasis and a tuberculous lesion in the axillary lymph nodes: A case report. Acta Cytol. 1992;36: 399-403.
8. Gregl A, Kienle J. Axillary lymph node tuberculosis presenting lymphographic signs of metastasis from ipsilateral breast cancer. Radiology. 1969;93:1107-8.
9. Pandey P, Dixit A, Tanwar A, Mahajan NC. Infiltrating ductal carcinoma breast, metastatic to ipsilateral axillary lymph nodes harbouring primary tuberculous lymphadenitis: a case report. Pan Afr Med J. 2014;18:167.
10. Pandey M, Abraham EK, K C, Rajan B. Tuberculosis and metastatic carcinoma coexistence in axillary lymph node: A case report. World J Surg Oncol. 2003;1:3.
11. Robinson A, Horne C, Weaver A. Coexistence of axillary tuberculous lymphadenitis with lymph node metastases from a breast carcinoma. Clin Oncol. 2001;13:144-7.
12. Tulasi NR, Raju PC, Damodaran V, Radhika TS. A spectrum of coexistent tuberculosis and carcinoma in the breast and axillary lymph nodes: Report of five cases. Breast. 2006;15:436-8.
13. Wani B, Jajoo S. Ipsilateral axillary tubercular lymphadenopathy, contralateral osseous tuberculosis in a case of ductal carcinoma of breast. Indian J Cancer. 2008;45:182.
14. Alzaraa A, Dalal N. Coexistence of carcinoma and tuberculosis in one breast. World J Surg Oncol. 2008;6:29.
15. Chottanapund S, Wongtawatchai P. Patient with invasive ductal carcinoma of the breast : A case report. Thai J Surg. 2004;25:121-4.
16. Fujii T, Morihiko L, Yanagita Y, Koida T, Kuwano H. Tuberculosis of axillary lymph nodes with primary breast cancer. Breast Cancer. 2003;10:175-8.
17. Gaurav M. Concomitant tuberculosis and metastasis in axillary lymph nodes: a diagnostic surprise. ANZ J Surg. 2008;78:825-6.
18. Miller RE, York N, York N. The coexistence of carcinoma and tuberculosis of the breast and axillary lymph nodes. Am J Surg. 1971;121:338-40.
19. Mukhopadhyay T, Nandi M, Bhattacharya S, Khan E. Contralateral contiguous tuberculous lymphadenitis in a case of right breast carcinoma - Diagnostic dilemma. J Cancer Res Ther. 2015;11:1026.
20. Munjal K, Jain VK, Agrawal A, Bandi PK. Co-existing tubercular axillary lymphadenitis with carcinoma breast can falsely over-stage the disease - case series. Indian J Tuberc. 2010;57:104-7.
21. Pujani M, Khan S, Hassan MJ, Jetley S, Raina PK. Coexistence of metastatic breast carcinoma and primary tuberculosis in axillary lymph nodes: A report of a rare case. Breast Dis. 2015;35:195-8.
22. Salemis NS, Razou A. Coexistence of breast cancer metastases and tuberculosis in axillary lymph nodes--a rare association and review of the literature. Southeast Asian J Trop Med Public Health. 2010;41:608-13.
23. Warthin AS. The coexistence of carcinoma and tuberculosis of the mammary gland. Am J Med Sci. 1899;118:125.
24. Lee JW, Lee SM, Choi JH. 18F-FDG PET/CT findings in a breast cancer patient with concomitant tuberculous axillary lymphadenitis. Nucl Med Mol Imaging. 2011;45:152-5.
25. Bansal A, Sipayya V, Chintamani C, Saxena S. Carcinoma and tuberculosis of the breast coexisting in same breast with axillary lymphadenopathy: A rare association. Indian J Cancer. 2015;52:229.
26. World Health Organization. Global Tuberculosis Report 2014. 2015:1-20.
27. Seer.cancer.go. SEER Stat Fact Sheets : Soft Tissue including Heart Cancer Statistics at a Glance. 2015. Available Accessed January 2016.
28. Instituto Nacional de Estadística y Geografía. Estadística a propósito del día mundial de la lucha contra el cáncer de mama. Inst Nac Estadística y Geogr. 2015:1-15.
29. Kaplan MH, Armstrong D, Rosen P. Tuberculosis complicating neoplastic disease. A review of 201 cases. Cancer. 1974;33:850-8.
30. Kim SJ, Park YM. Clinical importance and sonographic features of nonpalpable axillary lymphadenopathy identified on breast sonography in patients without malignancy. J Ultrasound Med. 2015;34:2193-202.
31. Bernardo J. Epidemiology and pathology of miliary and extrapulmonary tuberculosis. UpToDate. 2015. Available at: http://www.uptodate.com/contents/epidemiology-and-pathology-of-miliary-and-extrapulmonary-tuberculosis?source=search_result&search=Epidemiology+and+pathology+of+miliary+and+extrapulmonary+tuberculosis&selectedTitle. Accessed January 2016.
32. Lee KC, Tami TA, Lalwani AK, Schecter G. Contemporary management of cervical tuberculosis. Laryngoscope. 1992;102:60-4.
33. Khurram M, Tariq M, Shahid P. Breast cancer with associated granulomatous axillary lymphadenitis: A diagnostic and clinical dilemma in regions with high prevalence of tuberculosis. Pathol Res Pract. 2007;203: 699-704.