

## CASE REPORT

# COEXISTENCE OF BREAST CANCER METASTASES AND TUBERCULOSIS IN AXILLARY LYMPH NODES - A RARE ASSOCIATION AND REVIEW OF THE LITERATURE

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**Abstract.** The coexistence of metastatic breast cancer and tuberculosis in axillary lymph nodes is very rare. We present the case of a 57-year-old woman with multifocal invasive ductal breast carcinoma in whom the resected axillary nodes were found to harbor both metastatic cancer and tuberculous lymphadenitis. Thorough investigation revealed no evidence of primary tuberculosis elsewhere. A quantiFERON TB-Gold test was positive, indicating latent tuberculosis. The patient was treated with adjuvant chemotherapy antituberculous therapy, radiation and hormonal therapy with aromatase inhibitors. We conclude the possibility of coexistent latent tuberculosis should be kept in mind when granulomatous lesions are identified in axillary lymph nodes with metastatic breast cancer, especially in patients from endemic regions.

**Key words:** axillary lymph nodes, breast cancer, metastasis, granuloma, tuberculosis

### INTRODUCTION

The coexistence of breast cancer and tuberculosis is rare. It was originally described in 1899 (Warthin, 1899) and may pose a challenge in the diagnosis and treatment of patients with breast cancer (Tulasi *et al*, 2006; Alzarara and Dalal, 2008). We describe here a rare case of a multifocal invasive ductal breast cancer where the histopathology of the resected axillary nodes revealed concomitant metastasis and tubercular lymphadenitis. Diagnostic

evaluation and management of the patient are discussed along with a review of the literature.

### CASE REPORT

A 57-year old woman presented to our breast clinic with a lump in her right breast which she first noticed 10 days ago. Her past medical history was notable for rheumatoid arthritis. She had no family history of breast cancer and had experienced menopause 5 years previously. On clinical examination, an irregular hard lump measuring approximately 2x2 cm was palpated 5 cm superior to her right nipple. Enlarged lymph nodes were palpable in the right axilla. The contralateral breast and axilla, including the supraclavicular

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and cervical nodes, were unremarkable. Mammography revealed the presence of 4 irregular masses in the right breast (Figs 1, 2). Routine blood examinations, including carcinoembryonic antigen (CEA) and carbohydrate antigen (CA15-3), were within normal limits. Fine needle aspiration cytology revealed breast carcinoma. The patient subsequently underwent a right modified radical mastectomy. The specimen consisted of an overlying elliptical skin flap and nipple-areola complex measured 23 x 14 x 6.5 cm. Thorough sectioning revealed the presence of 4 tumors measuring from 2.3 to 0.6 cm in diameter. Histopathological examination showed a multifocal invasive ductal breast carcinoma, grade II using Bloom and Richardson modified classification, associated with ductal carcinoma *in situ*. Four of the 13 resected lymph nodes showed metastatic deposits of carcinoma. All 4 metastatic nodes also contained granulomatous lesions in the form of epithelioid cell granulomas, with Langhans-type giant cells, associated with central necrosis (Figs 3, 4). Two other enlarged nodes free of metastases contained extensive granulomatous lesions associated with central necrosis (Fig 5). Histological examination of the remaining 7 lymph nodes showed non-specific reactive lymphadenitis. On immunohistochemical analysis, the tumor cells were highly positive for estrogen and progesterone receptors; expression of c-Erb-B2 was not detected. Further clinical and laboratory investigations did not reveal any evidence of other metastases or tuberculosis. The QuantiFERON TB-Gold test [QuantiFERON®-TB Gold (QFT-G, Cellestis, Carnegie, Victoria, Australia)] was strongly positive, indicating latent tuberculosis. The patient was from a tuberculosis endemic region. She was treated with adjuvant chemotherapy along with

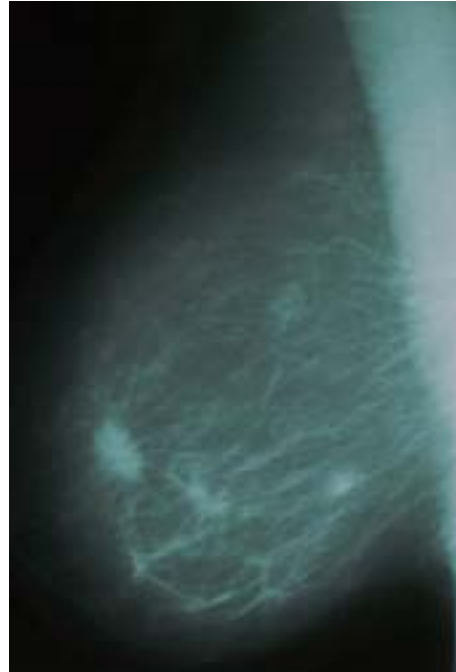


Fig 1, 2—Mediolateral oblique (MLO) and craniocaudal (CC) mammograms showing 4 irregularly-shaped masses in the right breast.

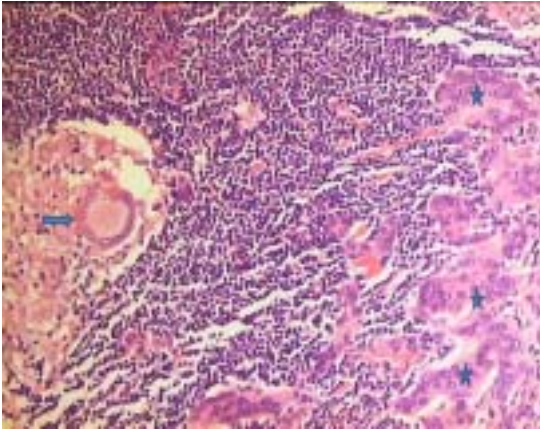


Fig 3–Histomicrograph of lymph node showing epithelioid granuloma with a Langhans-type giant cell (*arrow*) and metastatic deposits of invasive breast adenocarcinoma (*stars*). (H&E, x 100).

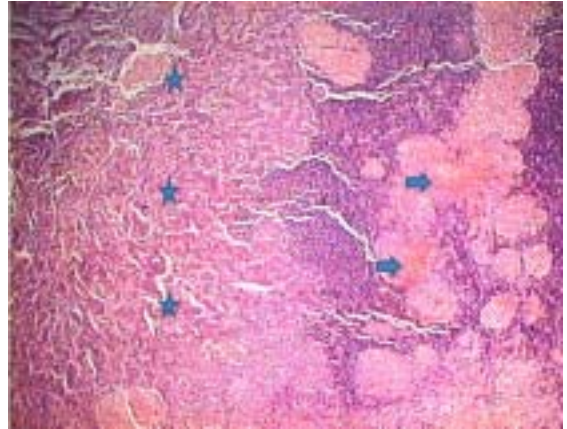


Fig 4–Histomicrograph of lymph node showing confluent epithelioid granulomas, some with central necrosis (*arrows*), and metastatic deposits of invasive breast adenocarcinoma (*stars*). (H&E, x 25).

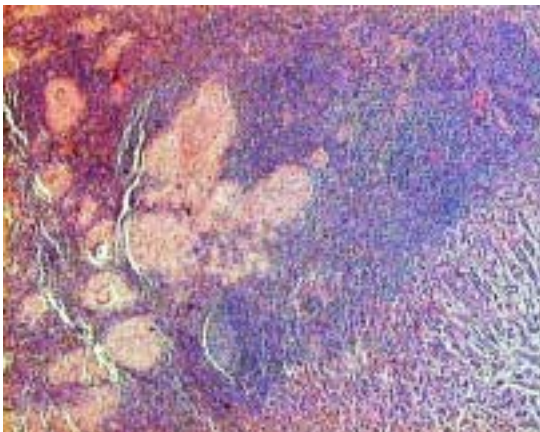


Fig 3a–Lower power of Fig 3 (H&E, x 25).

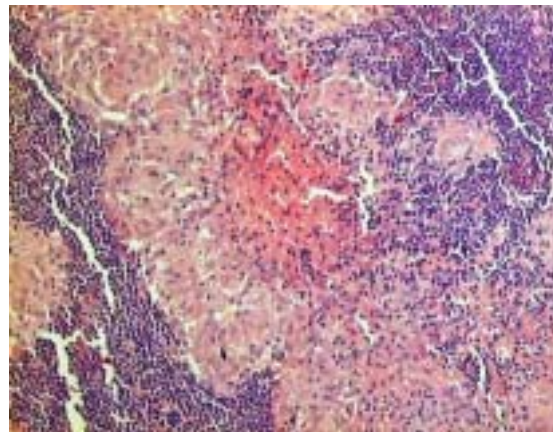


Fig 4a–Higher magnification of Fig 4 (H&E, x 100).

antituberculous treatment with isoniazid and radiotherapy. Chemotherapy consisted of 4 cycles of FEC 75 (Fluorouracil: 500 mg/m<sup>2</sup>, Epirubicin: 75 mg/m<sup>2</sup>, and Cyclophosphamide: 500 mg/m<sup>2</sup>), followed by 4 cycles of Docetaxel. After completion of adjuvant radiotherapy she started hormonal therapy with an aromatase inhibitor and is currently well 12 months after surgery.

## DISCUSSION

The coexistence of breast cancer and tuberculosis is uncommon; the literature describes approximately 100 cases (Pandey *et al*, 2003). In a review by Kaplan *et al* (1974), 201 cases of tuberculosis were found among 58,245 patients with cancer. The highest prevalence of tuberculosis was seen in patients with Hodgkin's disease

(96/10,000), followed by lung cancer (92/10,000). Tuberculosis was seen in only 28 cases out of 14,742 patients with breast cancer (19/10,000).

Coexistence of tuberculous lymphadenitis and breast cancer in axillary lymph nodes is even rarer (Miller *et al*, 1971; Tulasi *et al*, 2006; Alzaraa and Dalal, 2008; Broughton *et al*, 2008; Wani and Jajoo, 2008). In our case, 4 lymph nodes were found to harbor both tuberculous lymphadenitis and breast cancer deposits. This association is extremely rare. We were able to find only 8 similar cases in the literature (Das *et al*, 1992; Robinson *et al*, 2001; Pandey *et al*, 2003; Avninder and Saxena, 2006; Khurram *et al*, 2007; Gaurav *et al*, 2008). Thorough investigation of our patient did not reveal any evidence of pulmonary or other extrapulmonary tuberculosis, similarly to a few cases reported previously (Robinson *et al*, 2001; Pandey *et al*, 2003; Avninder and Saxena, 2006; Gaurav *et al*, 2008). Since tuberculosis was not suspected preoperatively, microbiological cultures and polymerase chain reaction (PCR) were not performed. However, the QuantiFERON TB-Gold test result was positive for *Mycobacterium tuberculosis* indicating latent tuberculosis. The QuantiFERON TB-Gold Test is an *in vitro* test for diagnosing *Mycobacterium tuberculosis* infection. It detects the release of interferon-gamma (IFN- $\gamma$ ) in fresh heparinized whole blood from sensitized persons when it is incubated with mixtures of synthetic peptides representing two proteins present in *M. tuberculosis*: early secretory antigenic target-6 (ESAT-6) and culture filtrate protein-10 (CFP-10) (Mazurek *et al*, 2005). It may be used as a confirmatory test for tuberculin skin testing positive immigrants who are candidates for preventive therapy (Carvalho *et al*, 2007).

In cases like ours where no other source of infection can be identified during routine investigations, the only possible explanations for tuberculosis limited to the lymph nodes are either retrograde spread from the mediastinal nodes or hematogeneous spread from a subclinical focus (Avninder and Saxena, 2006).

Tuberculous lymphadenitis is the most common form of extrapulmonary tuberculosis (Avninder and Saxena, 2006) and should be differentiated from other clinical entities that may present with areas of granulomatous reaction in lymph nodes. Granulomatous inflammation is considered to be an immune mechanism against infections, nonneoplastic and neoplastic conditions (Brincker, 1986; Bhatia *et al*, 2009). Clinical entities that can cause granulomatous reactions include infective agents, such as mycobacteria, fungi, parasites, brucellosis, and noninfective entities, such as sarcoidosis, foreign bodies, Wegener's granulomatosis and traumatic fat necrosis (Alzaraa and Dalal, 2008; Bhatia *et al*, 2009). Certain types of tumors are known to be associated with granulomatous responses in primary tumor parenchyma, in lymph nodes draining from the region or in non regional tissues (Gregorie *et al*, 1962; Brincker, 1986; Oberman, 1987; Coyne, 2005). These lesions occur in 4.4% of carcinomas, 13.8% of patients with Hodgkin's disease and 7.3% of Non-Hodgkin's lymphomas; in some cases they may complicate the diagnostic evaluation (Brincker, 1986; Coyne, 2005).

Regarding breast cancer, epithelioid-cell and sarcoid-like granulomas have been observed in regional lymph nodes and tumor stroma in 0.7% and 0.3% of cases, respectively (Bässler and Birke, 1988). In areas with a high prevalence of tuberculosis in the general population, the presence of granulomatous axillary lym-



phadenitis in patients with breast cancer may lead to difficulties in interpretation and inappropriate treatment of both granulomatous disease and breast cancer (Khurram *et al*, 2007). In cases where morphological features are not diagnostic, PCR-based assays are relatively sensitive and rapid in the detection of *Mycobacterium tuberculosis* (Khurram *et al*, 2007). Tuberculous lymphadenitis coexisting with breast cancer should also be kept in mind when lymphadenopathy is noted and an X-ray shows clustered calcifications in the axilla (Fujii *et al*, 2003).

In summary, We present a rare case of multifocal invasive ductal breast carcinoma in a patient in whom the resected axillary lymph nodes were found to harbor both tuberculous lymphadenitis and metastatic breast cancer. The possibility of coexistent tuberculosis should be kept in mind when granulomatous lesions are identified in axillary lymph nodes with metastatic breast cancer, especially in patients from endemic regions. A thorough investigation is mandatory since the presence of tuberculosis may alter the postoperative management of the patient.

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