

Case Report

Tuberculosis of the breast: a rare extra-pulmonary presentation of tuberculosis

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Abstract

Introduction: Breast tuberculosis (TB) is a rare extra-pulmonary presentation of tuberculosis. In the western world, this accounts for less than 0.1% of breast conditions (all breast conditions, not limited to TB or extra-pulmonary TB), but can be up to 3-4% in regions endemic for TB such as in Africa and Asia.

Case presentation: We report a case of a 54-year-old human immunodeficiency virus (HIV)-positive lady who presented with six months history of multiple masses on the left breast which were initially suspected to be cancer of the breast. However, histology report of the mass confirmed TB of the breast.

Conclusions: Presentation of TB can be non-specific and atypical in patients with HIV infection, especially when it presents in extra-pulmonary forms.

Key words: HIV; mastitis; tuberculosis; breast.

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Introduction

Sir Astley Cooper recorded the first case of breast tuberculosis (TB) in 1829, which he described as “scrofulous swelling of the breast” [1]. TB is caused by the bacterial pathogen *Mycobacterium tuberculosis*. TB mastitis is a rare presentation of extra-pulmonary TB accounting for less than 0.1% of all breast conditions in the western world, but could be as high as 3–4% in areas endemic for TB [2].

TB mastitis is commonly seen in young lactating women in their reproductive age, but is uncommon in prepubescent and elderly woman [3,4]. This could be a result of the frequent changes the breast undergoes during the period of childbearing activity, and hence makes it more susceptible to trauma and infection [5]. There have also been reported cases of TB mastitis in prepubescent males and elderly women [6,7].

TB mastitis commonly presents as a lump in the central or upper-outer quadrant of the breast, and multiple lumps appear less frequently [7]. It is often suspected to be carcinoma or abscess [8,9].

This case study is presented to further emphasize on the need to include TB of the breast as a differential

when considering breast cancer and abscess, especially in human immunodeficiency virus (HIV)-infected patients living in TB endemic regions.

Case presentation

We present a case of a 56-year-old female HIV patient who was referred from the general outpatient clinic to the surgical outpatient clinic with a six month history of a slowly growing breast lump. Physical examination confirmed a symmetrical breast, and normal nipple areolar complex.

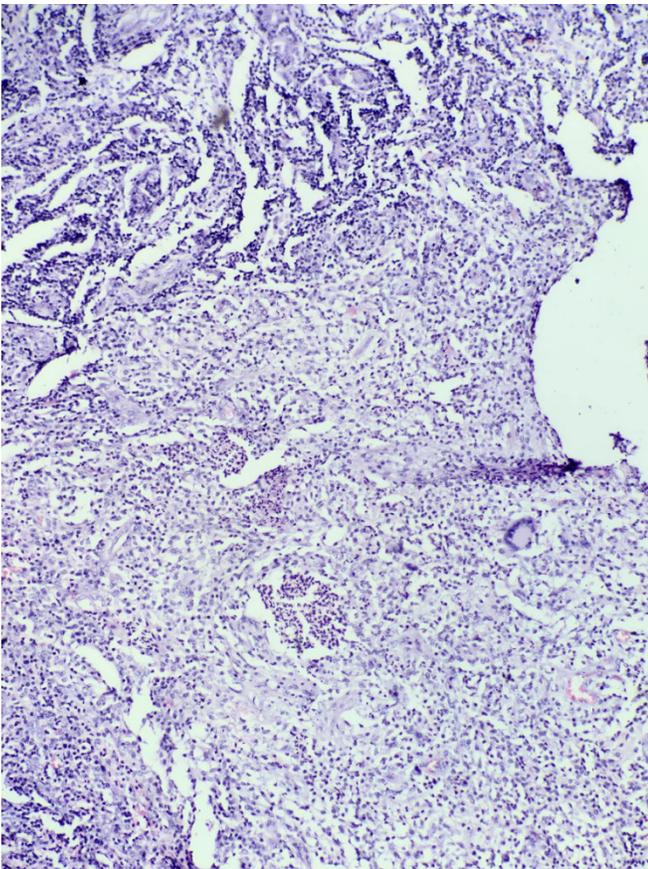
The patient had multiple left breast lumps. The first lump was a subareolar hard mass at the upper outer quadrant, not fixed to the skin or pectoralis, measuring 3 cm x 3 cm, and the mass was not fully defined. The second mass measured 2 cm x 2 cm, regular, firm at the upper outer quadrant and 8 cm from the areolar margin. There was no clinical manifestation of the disease on the nipple areolar area or signs of breast discharge. No palpable peripheral lymphadenopathy was noted. There was no history of cough, weight loss, drenching night sweat, fever, or history of contact with anybody with prolonged cough.

The patient had no family history of breast or ovarian cancer in any first degree relative. Her past surgical history was an appendectomy. She received her Bacillus Calmette-Guérin (BCG) vaccination and had a scar on her left arm to show for that. She was 3 years post-menopausal, and did not smoke or drink alcohol.

Laboratory work up showed anemia, Packed Cell Volume (PCV) 33%, and hemoglobin concentration (HB) 10.7g/dL (reference ranges for PCV and HB in women are 36–46%; and 12–15g/dL, respectively). Laboratory results also showed lymphocytosis with lymphocyte count of 48.6% (reference range of 20–40%). Erythrocyte sedimentation rate was markedly elevated to 130 mm/hour (reference range for women: < 19mm/hour). Her viral load was 10^7 copies/mL and CD4 count was 232 cell/ μ L. Liver and kidney functions were essentially normal. An initial diagnosis of carcinoma of the breast was entertained.

Chest X-ray was normal. A high resolution ultra sound scan of the breast showed an ovoid-shaped predominantly hypoechoic lesion in the upper quadrant of the left breast. No calcification was seen within it. It measured 2.35×1.08 cm in size. The remaining aspect

Figure 1. Histology of breast tissue shows sheets of epithelioid histiocytes, lymphocytes, plasma cells, and giant cells; with areas of necroinflammation. $\times 10$ magnification.



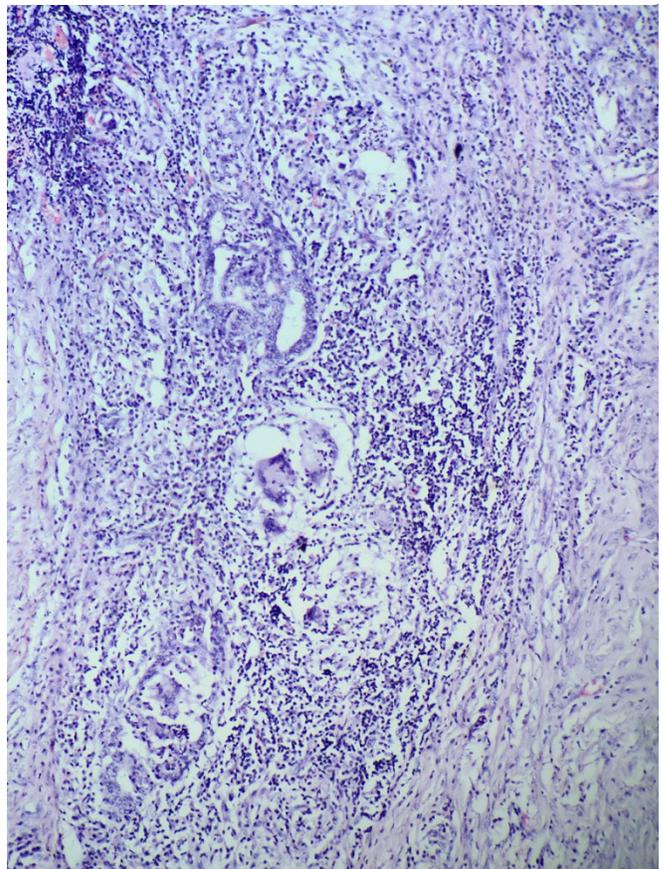
of the left breast, pectoralis muscles shadow, axillary tail, subareolar area, and the right breast were within normal limits.

Tru-cut biopsy was taken but the sample was inadequate for the pathologist to make an assessment.

An excisional biopsy was taken and macroscopic sample examination showed that the specimen consisted of nodular masses each measuring 5.0×4.0 cm. Cut section showed variegated surfaces with mottled appearance and pockets of pus. Microscopic examination of sections of breast tissue (showed granulomata composed of epithelioid histiocytes and giant cells with extensive areas of tissue necrosis (Figure 1) and reactive nuclear changes (Figure 2) No malignancy was seen.

Subsequently, an assessment of tuberculous mastitis was made. The patient was immediately started on anti-Koch's — a daily dose of 300 mg isoniazid, 600 mg rifampicin, 1500 mg pyrazinamide, and 800 mg ethambutol. She took her anti-Koch's for six months; two months of intensive phase and four months of continuation phase. Her anti-retroviral medications

Figure 2. Photomicrograph of the breast showing sheets of epithelioid histiocyte, giant cells and breast acini lined with cuboidal cells that show reactive nuclear changes. $\times 10$ magnification.



were adjusted to accommodate for drug interaction. Her anti-retroviral medications included tenofovir 300 mg daily, lamivudine 300 mg daily, and dolutegravir 50 mg daily; as a one pill combination. In order to accommodate for drug interaction between rifampicin and dolutegravir, the dosage of dolutegravir was increased to 50 mg twice daily.

Discussion

TB is caused by *Mycobacterium tuberculosis*. It primarily affects the lungs, but could affect other tissues resulting in extra-pulmonary TB [10]. However, TB of the breast is extremely rare because breast tissue is more resistant to infection, which hinders multiplication and survival of the tubercle bacilli [11]. Mckeown and Wilkinson classified breast TB into 5 pathological types: nodular tubercular mastitis, disseminated tubercular mastitis, sclerosing tubercular mastitis, tuberculous mastitis obliterans, and acute miliary tubercular mastitis [12].

Breast TB may be primary when no other focus of TB is detected, or secondary when an alternate focus can be located [12]. No primary focus was identified in our patient. However, we exercised caution in reaching this conclusion because she was immunosuppressed (HIV-positive) and resident in a TB endemic country (Nigeria). However, in more recent publications, authors have considered almost all cases of breast TB to be secondary; rare primary breast TB have been reported to occur through duct openings in the nipple and breast abrasions [10]. TB spreads to the breast through haematogenic and lymphatic routes, direct extension from the thoracic wall or axillary lymph nodes, and by inoculation through traumatized skin or ducts.

Breast TB is usually unilateral and the commonest clinical presentation is that of a lump, with or without a duct, painful or not, most often located in the upper outer quadrant of the breast. The lump can mimic breast carcinoma; since it is hard; irregular in shape and fixed to the skin, muscle or chest wall [14,15].

Risk factors for breast TB are HIV infection, lactation, multiparity, trauma, and past history of suppurative mastitis; and it commonly occurs in the 20 to 50 years age group [17,18]. Our patient however was not within the age group, but she was diagnosed as HIV-positive eight months prior to presentation, and had commenced anti-retroviral medications immediately. Additional symptoms such as fever, malaise, weight loss, night sweat are reported to be present in less than 20% of cases [16].

Pathological examination is more valuable than bacteriological examinations and preferred for the accurate diagnosis of breast TB [19]. The gold standard diagnosis of breast TB is by bacteriological culture of breast culture or by Ziehl Neelsen (ZN) stain [17]. However, the bacilli are isolated in only 25% of cases and acid-fast bacilli (AFB) are identified only in 12% of the patients. Hence, demonstration of caseating granulomas from the breast tissue and involved lymphnodes may be sufficient for the diagnosis [20-22].

Approximately 73% of the cases of TB mastitis can be diagnosed with fine needle aspiration cytology (FNAC) when both epithelioid cell granulomas and necrosis are present [23,24]. In TB endemic countries, the finding of granuloma in FNAC warrants empirical treatment for TB even in the absence of positive AFB and without culture results [23,25]. Khanna *et al.* reported that in 52 patients with breast TB, FNAC was 100% reliable in making the diagnosis of breast TB [26].

Radiological tools like mammography, computed tomography (CT) scan, and magnetic resonance imaging (MRI) of the breast have been used in diagnostic work up of breast lumps, but are unreliable in distinguishing TB mastitis from carcinoma because of its non-specific features [27]. Hence CT scan and MRI cannot be used as diagnostic tools, and histological confirmation is needed [19]. Nucleic acid amplification tests, such as polymerase chain reaction (PCR), are rapid and specific but have low sensitivity [28].

BCG provides some protection against all forms of TB, independent of the HIV status. BCG is particularly protective against extrapulmonary TB among HIV-negative individuals. However, studies have shown that HIV seems to abrogate this protective effect against extra-pulmonary TB [29].

Conclusions

Immunosuppressive conditions like HIV infection increase the chance of TB presenting atypically with rare extra-pulmonary manifestations like breast TB. A high index of suspicion is essential when treating non-specific breast abnormalities, particularly in TB endemic areas of the world. Diagnosis can be established by FNAC or histology, and anti-TB drug therapy is the mainstay of treatment. Surgery is recommended only for selected refractory cases.

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