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Tuberculosis of Breast Masquerading as Malignancy

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Keywords: Tuberculosis; Mycobacterium tuberculosis; *Tuberculous mastitis*; Mammary tuberculosis

Abbreviation: BCG: *Bacillus Calmette-Guerin*; ESR: Erythrocyte Sedimentation Rate; FNA: Fine Needle Aspiration; HIV: Human Immunodeficiency Virus; PCR: Polymerase Chain Reaction TB: Tuberculosis

Introduction

Tuberculosis is caused by Mycobacterium tuberculosis and affects primarily the lungs. Breast tuberculosis is a rare disease with an incidence of <0.1% of all breast lesions in Western countries and 3-4% in tuberculosis endemic regions, such as India and Africa [1,2]. Most commonly the disease presents as a lump in the central or upper-outer quadrant of the breast while multiple lumps appear less frequently [3]. The 'triple assessment' of any breast lump is a well-established process to aid in the effective diagnosis of breast cancer [4]. It was only after having assessed the patient clinically, imaging the lump appropriately and subjecting it to cytological and histological analysis, that we were confidently able to exclude breast cancer.

Case Presentation

A 56-year-old female patient presented with painful swelling, multiple discharging sinuses of the left breast and a normal looking right breast. According to the patient the lump was present for the past six to seven months but the sinuses had developed recently (Figure 1). On physical examination, the left breast was very tender with a diffuse irregular mass being felt mainly involving the central quadrant. The overlying skin was reddish with multiple sinuses discharging a dirty yellow fluid. There was no nipple discharge or skin retraction. There was no axillary or cervical lymphadenopathy. The patient was treated with several non-specific antibiotics by her family physician but her breast symptoms remained the same.

She was febrile but there was no prominent history of fever or respiratory symptom. She had no family history of breast carcinoma, no HIV risk factor, no TB exposure. Examination of abdomen revealed no evidence of any intra-abdominal lump or ascites. Mantoux test was negative (14 mm). She had no history of BCG vaccination. Ultrasonography examination of the breast revealed a hypoechoic mass with thick internal collection and lymphadenopathy which suggested mastitis. Mammography showed increased density and coarsened trabeculation but no micro calcification nor any suspicious focal abnormalities. Her routine hematologic and biochemical parameters were in the normal range along with ESR of 10 mm.

FNA yielded cheesy material. The smears showed groups of lymphocytes along with epithelioid cells and Langhans giant cells (Figure 2). The same lesion was operated and sent for histopathological examination. Grossly lumpectomy specimen was received, solid hard whitish fibro fatty tissue measuring 3 × 3 cm with a foci of haemorrhagic

Figure 1: Swelling in the central quadrant [black circle] along with one sinus developed since 3 days [arrow head] and healed sinuses [two sided arrow].

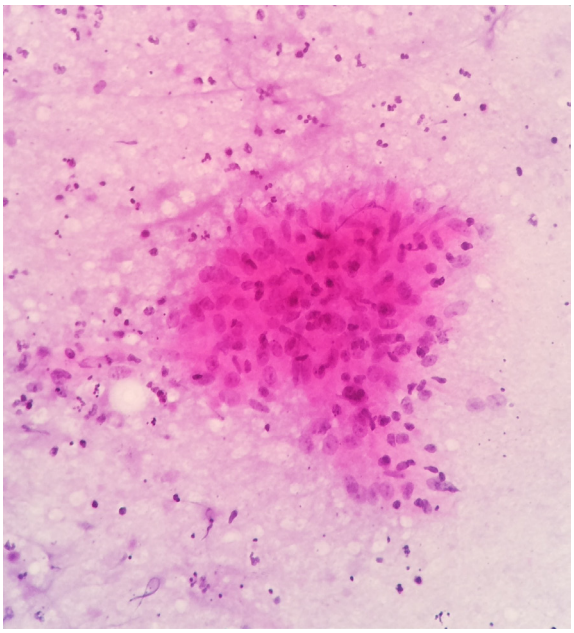

Figure 2: Cytosmears showed groups of lymphocytes along with epithelioid cells and Langhans giant cells in a necrotic background. [H& E 40X].

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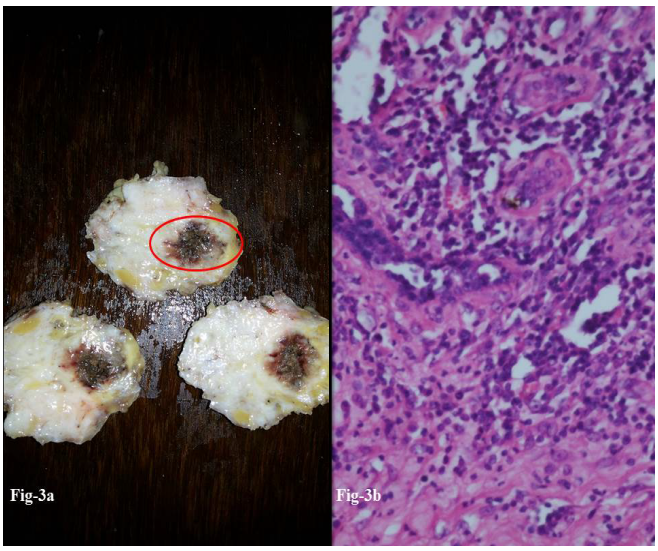

Figure 3a: Lumpectomy specimen solid hard whitish fibro-fatty tissue measuring 3 × 3 cm with a foci of haemorrhagic area 1cm diameter [red circle]. Figure **3b:** Microscopy showing epithelioid granuloma with Langhans giant cells and lymphohistocytic aggregates along with caseating necrosis. [H&E 40X].

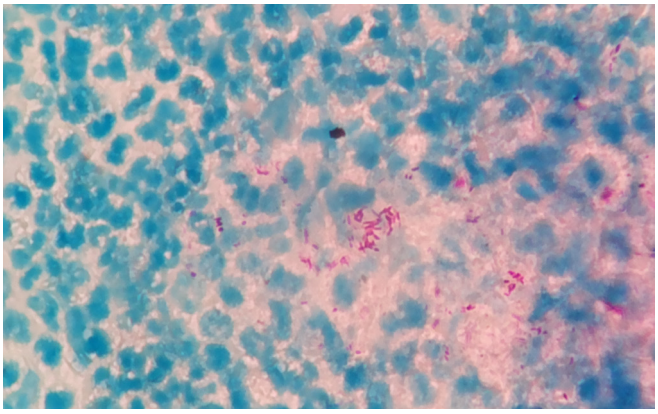

Figure 4: Special Stain showed the red rod shaped mycobacterium bacilli. [AFB 40X].

area 1 cm diameter (Figure 3a). Histosections revealed epithelioid granuloma with Langhans giant cells and caseating necrosis (Figure 3b). AFB stain on the tissue showed red rod shaped Mycobacterium tubercle bacilli (Figure 4). A diagnosis of Tuberculous Mastitis was made.

The intensive therapy with anti-tubercular drugs (Isoniazid 300 mg, Rifampicin 450 mg, Pyrazinamide 1500 mg and Ethambutol 1000 mg per day) was initiated for 2 months and continued with the addition of Rifampicin and Isoniazid therapy for an additional four months. With treatment, her breast lesion and tenderness steadily improved.

Discussion

The first case of breast tuberculosis was recorded by Sir Astley Cooper who described it as "scrofulous swelling of the bosom" [1]. Tuberculosis of the breast is a rare disease mostly because organs or tissues like the breast, skeletal muscle and spleen are more resistant to infection making the survival and multiplication of the tubercle bacilli difficult [2-6]. Tuberculosis mastitis is usually unilateral, seldom infects male patients and should be considered in immunodeficiency states like HIV infection [4]. Lactating women appear to be at higher risk, probably due to the increased blood supply to the breasts and to dilated ducts, making them more vulnerable to lacerations and infection [3].

Mammary tuberculosis may be primary when no other focus of tuberculosis is detectable or secondary when a source can be identified mainly located pulmonary. The routes of spreading to the breast are hematogenic, lymphatic, by direct extension from the thoracic wall, the axillary lymph nodes spread, by inoculation through traumatized skin or ducts [5,7,8]. The commonest clinical presentation is that of a lump with or without a duct painful or not most often located in the central or upper outer quadrant of the breast. The lump can mimic breast carcinoma being hard with irregular border fixed to either the skin or the muscle or even to the chest wall [8,9]. Fistula formation may occur much as nipple or skin retraction but breast discharge is uncommon. The lump may be followed by inflammation and abscess formation, skin ulceration and diffuse mastitis. Recurrent inflammation and abscess of the breast that do not respond to surgical drainage and standard antibiotic therapy in young women should raise suspicion of malignancy. Symptoms like fever, malaise, night sweats and weight loss are present in less than 20% of the cases [4].

Based on radiological and clinical characteristics the disease can be described by three forms: nodular, diffuse and sclerosing. The nodular form is well circumscribed, slow growing with an oval tumor shadow on mammography which can hardly be differentiated from breast cancer. The disseminated form is characterized by multiple lesions associated with sinus formation. This form mimics inflammatory breast cancer on mammography. The sclerosing form of the disease is seen in elderly women and is characterized by an excessive fibrotic process [3,6,10].

Various tests are useful in the diagnosis and further evaluation of patients with breast tuberculosis. Mantoux testing does not offer definitive diagnosis but confirms exposure of the patient to tubercle bacilli. Radiological imaging modalities like mammography or ultrasonography are unreliable in distinguishing tuberculosis mastitis from carcinoma because of its nonspecific features [11]. Similarly computed tomography and magnetic resonance imaging are not diagnostic without histological confirmation. Fine needle aspiration cytology may not be able to detect the responsible pathogen itself but can detect the presence of epithelioid cell granulomas and necrosis leading to definitive diagnosis in up to 73% of cases. Histopathology of the lesion identifies a chronic granulomatous inflammation with caseous necrosis and Langhans type giant cells, contributing to diagnosis in the majority of the cases. The gold standard for the diagnosis of breast tuberculosis is detection of M. tuberculosis by Ziehl Neelsen staining or by culture but with some limitations due to the delay in obtaining the final result and the possibility of false-negative results in pauci-bacillary samples. PCR is highly sensitive for the diagnosis of breast tuberculosis. Although seldom used, it is recommended in cases with negative culture results or for differential diagnosis between other forms of granulomatous mastitis.

The principal differential diagnosis is that of breast carcinoma. Clinical examination often fails to differentiate carcinoma breast from tuberculosis and high index of suspicion is necessary. Factors predictive but not diagnostic of breast tuberculosis include constitutional symptoms, mobile breast lump, multiple sinuses and an intact nipple and areola in young, multiparous or lactating females. Nipple retraction, peau d'orange, and involvement of axillary lymph nodes are more common in malignancy than in tuberculosis. A mammography

is not of much help as the findings in carcinoma in advanced stage are similar to that of tubercular lesion. Carcinoma and tuberculosis of the breast occasionally co-exist. Similar finding in the axillary lymph nodes may also be seen. In assessing diagnosis it is therefore important to remember that recognition of tuberculosis does not exclude concomitant breast cancer [12]. Other diseases of the breast such as fatty necrosis, plasma cell mastitis, peri-areolar abscess, idiopathic granulomatous mastitis and infections like actinomycosis and blastomycosis are to be considered [13].

Anti-tubercular therapy with four drugs is the primary line of treatment. The six-month regimen comprises of a two-month intensive phase with four drugs used orally followed by a continuation phase of four months with two drugs. [6,10]. Surgical intervention in the form of an excisional biopsy is necessary mainly for diagnostic purposes and is required for drainage of breast abscesses, excision of residual sinus tracts or lumps after poor response to anti-tubercular therapy.

Conclusion

Breast tuberculosis is extremely rare and in absence of well-defined clinical features the true nature of the disease remains obscure, often mistaken for carcinoma or pyogenic breast abscess. Diagnosis is best achieved by the 'triple approach' i.e. imaging (usually mammography and ultrasound), clinical examination and needle sampling for cytology or histology. The disease is eminently curable with the modern anti-tubercular chemotherapeutic drugs with surgery playing a role in the background only.

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