



Breast Tuberculosis: A Disease not to be Forgotten

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Abstract

Introduction: Breast tuberculosis is a rare manifestation of extra-pulmonary tuberculosis which accounts for less than 0.1% of breast conditions in developed countries but reaches 3–4% in regions where the disease is endemic like India and Africa. It appears mostly in women of reproductive age who are multipara or lactating. The most common presentation is that of a tumor in the breast with or without ulcer or pus discharging sinus. Differential diagnosis includes breast cancer and chronic abscess.

Materials and Methods: We report a case series of breast tuberculosis that were treated in a tertiary center. After a diagnosis of breast tuberculosis based on FNAC and histological finding, all the patients received anti-tubercular treatment and followed monthly to see the response.

Result: On the triple assessment of breast lump, diagnosis of breast tuberculosis was confirmed by FNAC in two patient and Tru-cut biopsy and histological examination in four patients. One patient with biopsy report of necrotizing mastitis was labeled as breast tuberculosis on the basis of clinical suspicion. All patients showed a good response to ATT on monthly follow up.

Conclusion: Although breast tuberculosis is a rare disease and can be misdiagnosed as breast cancer, a high index of clinical suspicion should be kept in mind during evaluation of breast lump, non-healing breast ulcer, and chronic sinuses. Early diagnosis based on clinical features and supplanted by FNAC and Tru-cut biopsy is suggested. Anti-tubercular therapy is effective.

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1. Introduction:

Although breast tuberculosis is a rare disease, with the global pandemic of HIV, increased survival of immunocompromised patients and increased incidence of MDR-TB, there is increased incidence of extra-pulmonary tuberculosis including breast tuberculosis (Rieder et al., 1989; Fujii et al., 2003). This fact has motivated us to present our experience with breast tuberculosis, with the intention to increase awareness about this lesser-known entity. The incidence of this disease is around 3-4% of all breast lesions in the tuberculosis-endemic region, such as India and Africa, whereas less than 0.1% in Western countries (Luh et al., 2008). In India, the true incidence is not known as the disease is often misdiagnosed as carcinoma or chronic abscess.

Several Indian series reported the incidence to vary between 0.64 to 3.59% (Dharkar et al., 1968). The breast may become infected by various routes like hematogenous, lymphatic, spread from the contiguous structure, direct inoculation, and ductal infection.

Centripetal lymphatic spread from pulmonary Koch's is the most common route (Mukherjee et al., 1974) It commonly affects the female of reproductive age groups (Shinde et al., 1995). Patients with this disease usually present with a combination of symptoms like a breast lump, ulcer, cold abscess and discharging sinuses. Clinicopathologically, it has been classified as nodulocaseous mastitis, disseminated mastitis and breast abscess (Tewari & Shukla, 2005).



The gold standard for the diagnosis of breast tuberculosis is the detection of *M. tuberculosis* by Ziehl Neelson staining or by culture (Marinopoulos et al., 2012). The treatment of breast tuberculosis consists of primarily anti-tubercular drugs.

Surgical intervention is usually required for diagnostic purposes (e.g. tissue biopsy, excisional biopsy) and for drainage of abscesses, excision of residual sinus tracts and lumps (Elmrabet et al., 2002). We report our experience of seven patients diagnosed as a case of tubercular mastitis at our center.

2. Methodology:

Over a period of 16 months (from Jan-2015 till April-2016), seven cases of breast tuberculosis were encountered. Each case was evaluated by clinical, pathological (FNAC, Tru-cut biopsy, excisional biopsy), microbiological (AFB staining, pus/tissue culture) and radiological examination. After confirming the diagnosis, five patients were put on anti-tubercular treatment (ATT) of six months regimen, including two months intensive phase (HRZE) followed by a continuation phase of four months (HRE) whereas two patients who had history of previous treatment for tuberculosis were put on eight months regimen (2 HRZES+1 HRZE+ 5 HRE). All patients were followed monthly to document their treatment compliance and response to treatment.

3. Results:

In our study, data from seven patients having a diagnosis of breast tuberculosis were collected. All the patients were females of reproductive age group (15-45 years). Two patients had a previous history of ATT for tubercular mastitis and abdominal Koch’s respectively. Two patients had a history of incision and drainage of breast abscess. Except for one nulliparous patient, other six were multiparous (Table 1). All patients presented with a painless breast lump except in one who was having a painful lump. Three patients, in addition, had associated ulcer or discharging sinus. Out of seven patients, only four presented with constitutional symptoms like low-grade fever, malaise, and loss of weight. On breast examination, all patients had firm to hard, non-tender mobile lump with three patients having pus discharging sinus and/or ulcer over it. Two patients had nipple retraction. Palpable axillary lymph node was present in two patients (Table 2).

On the triple assessment of breast lump, diagnosis of breast tuberculosis was confirmed by FNAC in two patient as smear and stain was positive for AFB. Diagnosis of tubercular mastitis in four patients was confirmed by tru-cut biopsy and histological examination by the presence of caseating necrosis along with granulomatous inflammation. One patient with biopsy report of necrotizing mastitis was labeled as breast tuberculosis on the basis of clinical suspicion. All patients showed a good response to ATT on monthly follow up (Figure 1; Table 3).

Table 1: Demographic profile of patients.

Case	Age & Sex	Recent pregnancy or lactation	Risk factors for Tubercular infection
A	30 yrs/ F	No	None
B	36 yrs/ F	No	#ATT intake for Right Tubercular Mastitis 2 years back.
C	36 yrs/ F	No	None
D	22 yrs/ F	Nulliparous	Left Breast abscess and I & D, 3 years back
E	45 yrs/ F	No	None
F	31 yrs/ F	No	Right Breast abscess, I & D, 6 months back.
G	25 yrs/ F	No	#ATT intake for abdominal Koch’s 2 years back

#ATT: Anti Tubercular Treatment, I&D: Incision and drainage.

Table 2: Clinical Profile

Case	Presentation & Duration	Constitutional symptoms	Breast Examination
A	Painless left breast lump x 3 months Discharging sinus x 20 days Ulcer x 10 days	Low-grade fever, Malaise	Firm, non-tender, mobile lump Pus discharging sinuses and Ulcer + Peaud’ orange, Nipple retraction+ Ipsilateral Axillary LN+
B	Painless right breast lump x 1 month Ulcer x 15 days	Low-grade fever, Malaise	Firm, non-tender, mobile lump, ulcer+
C	Painless left breast lump x 6 months	None	Hard, non-tender, mobile lump, fixed to the skin, Retracted nipple+
D	Painful right breast lump x 12 months	Malaise Weight loss	Firm, diffuse, nodular, non-tender, mobile lump, Skin edematous
E	Painless left breast lump x 1 month	None	Hard, non-tender, mobile lump Ipsilateral Axillary LN+
F	Painless right breast lump x 6 months Discharging sinus over the previous scar of incision and drainage	None	Firm, non-tender, mobile lump Discharging sinus over the previous scar.



G	Painless left breast lump X 2 months	Low-grade fever Malaise	Firm, non-tender, mobile lump
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Figure 1. clinical pictures of three cases: before starting and after 4 months of ATT.

Table 3: Diagnostic evaluation and response to ATT

Case No.	Imaging	Pathological Test		Response to ATT
		FNAC	TRU-CUT BIOPSY	
A	*CXR – normal #MGF- BIRADS CAT-0 CECT- malignant Mass	? Ca left breast	Tubercular mastitis	Good
B	*CXR – normal #MGF- BIRADS CAT-II	Tubercular mastitis Stain for AFB- positive	Not done	Good
C	*CXR – normal #MGF- BIRADS CAT-V	Caseating necrosis Fungal stain- negative	Tubercular mastitis	Good
D	*CXR – normal USG-Irregular hypoechoic lesion	Acute on chronic Inflammation with necrosis Fungal stain- negative	Necrotizing mastitis	Good
E	*CXR – normal #MGF- BIRADS CAT-III	? Ca breast	Tubercular mastitis	Good
F	*CXR – normal #MGF- BIRADS CAT-IV	Granulomatous Mastitis Fungal stain- negative	Tubercular mastitis	Good
G	*CXR – normal USG -Irregular hypoechoic lesion	Tubercular mastitis Stain for AFB- positive	Not done	Good

*CXR- chest x-ray, #MGF-mammography

4. Discussion:

Tuberculosis of breast is rare, as it has been suggested that mammary gland tissue offers resistance to the survival and multiplication of tubercle bacilli (Da Silva et al., 2009). Breast tuberculosis commonly affects females in the reproductive age group as the female breast undergoes frequent change during this period of hormonal activity and is thus more liable to trauma and infection

(Mukherjee et al., 1974). In our experience, all of the seven patients were females within the reproductive age group (15- 45 years) with a mean age of 32 years which is similar to average age of 33.71 years reported by Puneet et al. (2005). Breast tuberculosis commonly affects multiparous, lactating women. A study done by Uzma et al. reported 70% of their patients were parous including 52% multiparous and 18% primiparous (Jalali et al., 2005) In our study, six patients (86%) were multiparous and one was nulliparous. None of the patients were pregnant or lactating at the time of presentation.

Breast tuberculosis most commonly presents as a lump which may sometimes be irregular and hard and mimic as carcinoma breast (Gupta et al., 1982; Shinde et al., 1995). Other common presentations include tubercular ulcer and abscess with or without discharging sinus (Shukla & Kumar, 1989). In this study, all patients presented with painless breast lump of 1 to 12 months of duration, except one who presented with a painful lump. In our study, breast lump alone was present in 4 patients which is comparable with a study done by Uzma et al in which 59% of patients presented only with a breast lump (Jalali et al., 2005).

Three of the patients also had an associated ulcer or discharging sinus. Studies have reported that constitutional symptoms of breast tuberculosis like fever, malaise, night sweats and weight loss are present in less than 20% of the

cases of breast tuberculosis (Mirsaeidi et al., 2007).

In our study, 4 (57%) patients had constitutional symptoms like low-grade fever, malaise, and loss of weight. Tuberculosis of breast is usually secondary to a primary focus somewhere else in the body (Khanna et al., 2002). In this study, we could not find clinical symptoms suggestive of tuberculosis of any other organ system as a primary focus. However, in two patients, past history of

ATT was present for tubercular mastitis and abdominal tuberculosis respectively. Ipsilateral axillary lymph nodes were palpable in two patients. It is debatable whether the axillary lymph nodes were involved secondary to mammary tuberculosis or these were the primary site of tubercular infection.

Various tests are useful in diagnosis and further evaluation of patients with breast tuberculosis. Mantoux test is usually positive in an endemic area for tuberculosis, therefore, has no role indefinite diagnosis of tuberculosis, but only confirms the exposure (Tewari & Shukla, 2005).

Fine needle aspiration cytology (FNAC) from breast lesion is an important diagnostic tool for breast tuberculosis. Approximately 73% of the cases can be diagnosed on FNAC when both epithelioid cell granuloma and necrosis are present (Kakkar et al., 2000). In our study diagnosis of two patients was confirmed on the basis of FNAC as smear shown the above mentioned both characteristic features and stain was positive for AFB (Figure 2). A tru-cut biopsy was done in rest five patients. The subsequent histopathological finding of granuloma (composed of histiocytes, Langhans giant cells, lymphocytes and rare plasma cells) and caseous necrosis were found in four patients which are the characteristic features of breast tuberculosis. (Figure 3&4) In one patient, HPE was suggestive of necrotizing mastitis, and on the basis of high clinical suspicion, this patient was also labeled as tubercular mastitis.

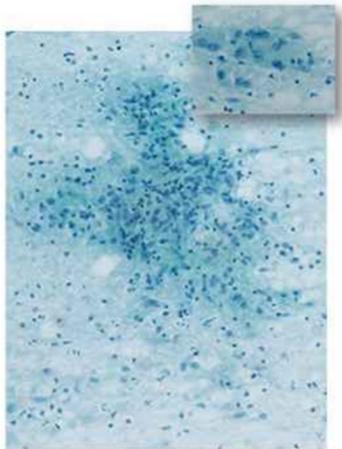


Figure 2. Papanicolaou Stain (wet fixed): showing granuloma with epithelioid cells and Langhans giant cells in the inset.

Due to the high density of the breast tissue in young patients, mammography in breast tuberculosis is not helpful. Similarly, in elderly women, mammography findings are generally indistinguishable from breast carcinoma (Tewari & Shukla, 2005).

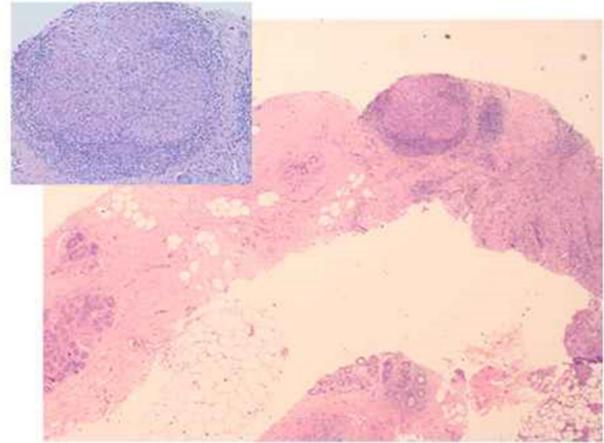


Figure 3. H&E (100 X): core biopsy showing granuloma and H&E (400 X) in inset showing granuloma with epithelioid cell around ducts.

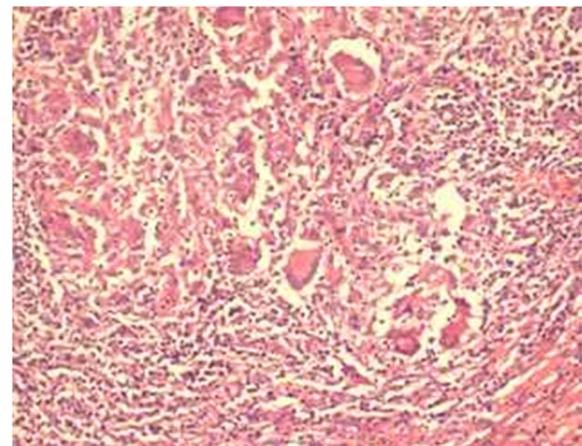


Figure 4. H&E (400 X): showing breast abscess with many neutrophils and Langhans giant cells.

Ultrasonography can detect a hypoechoic mass in 60% cases of tuberculosis mastitis. Other radiological imaging like CT and MRI are used to evaluate the extension of the lesion beyond the breast, in the planning of surgery and also in the assessment of response to treatment (Da Silva et al., 2009). In our study, 5 out of the 7 patients had a mammography did which was suggestive of varied BIRADS, ranging from “CAT 0-V”. The rest of the 2 patients in whom ultrasonography was done showed an irregular hypoechoic lesion.

The gold standard for the diagnosis of breast tuberculosis is the detection of *M. tuberculosis* by Ziehl Neelsen staining or by culture (Marinopoulos et al., 2012). Polymerase chain reaction (PCR) is recommended in cases with negative culture results or for differential diagnosis between other forms of granulomatous mastitis (Tse et al., 2004). All the patients were put on ATT and were followed monthly. Response to treatment was evaluated on the basis



of the resolution of symptoms. We observed the good response in all cases after completion of ATT.

5. Conclusion:

Breast tuberculosis is a rare disease that should always be suspected when evaluating cases of breast abscess, discharging sinuses and ulcers, if not responding to non-tubercular antibiotic treatments. The clinician may misdiagnose tubercular mastitis as carcinoma breast as both may appear similar on clinical examination and radiological imaging thus high index of suspicion acquires an important position in the diagnosis. Caseating epithelioid cell granulomas in the tissue sample, pus or tissue culture positive for AFB are diagnostic of tuberculosis. Nucleic acid amplification test (NAAT) can be done to differentiate it from other forms of granulomatous mastitis. This disease is curable with anti-tubercular drugs. Surgical intervention is usually required for the diagnostic purpose, drainage of abscesses and excision of residual sinus tract and lump.

Conflicts of Interest:

Authors declared no conflicts of interest.

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