Breast tuberculosis: diagnosis, clinical features & management

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The significance of breast tuberculosis is due to rare occurrence and mistaken identity with breast cancer and pyogenic breast abscess. Breast tuberculosis was scarcely reported even from endemic areas until lately when several reports have come up from South Africa and India. The incidence of tubercular mastitis although decreasing in the West, could show a resurgence with the global pandemic of AIDS. Breast tuberculosis has no defined clinical features. Radiological imaging is not diagnostic. Diagnosis is based on identification of typical histological features or the tubercle bacilli under microscopy or culture. Antitubercular therapy for 6 months with or without minimal surgical intervention forms the mainstay of treatment today. Over the years since the first description of tubercular mastitis in 1829, the incidence, clinical presentation, diagnostic and treatment methodology of breast tuberculosis has gradually changed. This review discusses the important issues relating to the diagnosis, clinical features, and management of breast tuberculosis.

Key words  Breast tuberculosis - clinical presentation - diagnosis - treatment

Breast tuberculosis is a rare form of tuberculosis. The first case of mammary tuberculosis was recorded by Sir Astley Cooper in 1829 who called it ‘scrofulous swelling of the bosom’. A literature review by Morgan in 1931, revealed 439 cases of tubercular mastitis with the incidence between 0.5 and 1.04 per cent. In 1944, Klossner reported 50 cases of breast tuberculosis in women, out of 75,000 women with pulmonary tuberculosis with lung involvement. Of approximately 8,000 breast specimens studied, Haagensen reported only five cases of breast tuberculosis between 1938 and 1967. Only 500 cases were documented from the world literature by Hamit and Ragsdale in 1982. Since then, case reports and reviews have been published at infrequent intervals mostly in western literature.

Breast tuberculosis is rare in the western countries, incidence being <0.1 per cent of breast lesions examined histologically. But, with the global spread of AIDS, mammary tuberculosis may no longer be uncommon in the developed world (as an AIDS-defining condition). Breast lesion caused by an atypical mycobacterium has recently been reported by Verfaillie G, et al.

The incidence of tuberculosis, in general, is still quite high in India and so is expected of the breast tuberculosis. But the disease is often overlooked and misdiagnosed as carcinoma or pyogenic abscess. Thus, reports on breast tuberculosis from India have been few. Less than 100 cases of breast tuberculosis were reported from India till 1987. The first 13 cases...
of breast tuberculosis from India were reported by Chaudhury in 1957\textsuperscript{14} from 433 breast lesions studied by her. This was followed by several reports from different parts of India\textsuperscript{15-19}. Several Indian series reported the incidence of breast tuberculosis amongst the total number of mammary conditions to vary between 0.64 and 3.59 per cent\textsuperscript{16,18}. In our own series (unpublished data), we have found 30 cases of breast tuberculosis of the 1180 breast lesions examined in the past 20 yr giving an overall incidence of 2.5 per cent (Table I).

\textit{Routes of infection:} Breast tissue is remarkably resistant to tuberculosis. This is due to the fact that, like skeletal muscles and spleen, it provides infertile environment for the survival and multiplication of tubercle bacilli\textsuperscript{18}. The theory of secondary involvement of the breast from a tuberculous lesion at some other site, was supported by Raw\textsuperscript{20} and Morgan\textsuperscript{4}. But, Mckeown and Wilkinson\textsuperscript{21} classified breast tuberculosis as primary when the breast lesion was the only manifestation of tuberculosis, and secondary when there was a demonstrable focus of tuberculosis elsewhere in the body. However, Vassilakos\textsuperscript{22} stated that primary breast tuberculosis was probably quite rare and was diagnosed because the clinician was unable to detect the true focus of the disease. Later on, breast tuberculosis was considered invariably secondary to a lesion elsewhere in the body. Primary form may rarely result from infection of the breast through abrasions or through openings of the ducts in the nipple.

The breast may become infected in a variety of ways\textsuperscript{21} \textit{e.g.,} (i) haematogenous, (ii) lymphatic, (iii) spread from contiguous structures, (iv) direct inoculation, and (v) ductal infection. Of these, the most accepted view for spread of infection is centripetal lymphatic spread\textsuperscript{18}. The path of spread of the disease from lungs to breast tissue was traced via tracheobronchial, paratracheal, mediastinal lymph trunk and internal mammary nodes\textsuperscript{21}. According to the Cooper’s theory, communication between the axillary glands and the breast results in secondary involvement of the breast by retrograde lymphatic extension\textsuperscript{23}. Supporting this hypothesis was the fact that axillary node involvement was shown to occur in

<p>| Table I. Cases of breast tuberculosis (n=30) of the 1180 breast lesions examined (between 1983 and 2003) in the Department of Surgical Oncology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India |</p>
<table>
<thead>
<tr>
<th>Presenting features</th>
<th>Diagnosis &amp; treatment</th>
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<tbody>
<tr>
<td><strong>Age (yr):</strong></td>
<td></td>
</tr>
<tr>
<td>&lt; 20</td>
<td>2 FNAC</td>
</tr>
<tr>
<td>20-40</td>
<td>24 Positive</td>
</tr>
<tr>
<td>40-60</td>
<td>3 Negative</td>
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<tr>
<td>&gt; 60</td>
<td>1 Core biopsy</td>
</tr>
<tr>
<td><strong>Clinical features:</strong></td>
<td></td>
</tr>
<tr>
<td>Lump only</td>
<td>7</td>
</tr>
<tr>
<td>Tubercular ulcer+lump</td>
<td>11 Open biopsy:</td>
</tr>
<tr>
<td>Sinus (es) + lump</td>
<td>4 Incisional</td>
</tr>
<tr>
<td>Tubercular breast</td>
<td>8 Excisional</td>
</tr>
<tr>
<td>abscess</td>
<td></td>
</tr>
<tr>
<td><strong>Axillary lymph node:</strong></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>18 Pulmonary Koch’s</td>
</tr>
<tr>
<td>Absent</td>
<td>12 Absent (old/active)</td>
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<tr>
<td><strong>Treatment:</strong></td>
<td></td>
</tr>
<tr>
<td>ATT only</td>
<td>2</td>
</tr>
<tr>
<td>ATT + aspiration</td>
<td>8</td>
</tr>
<tr>
<td>Primary excision</td>
<td></td>
</tr>
<tr>
<td>biopsy + ATT</td>
<td>8</td>
</tr>
<tr>
<td>ATT + excision of</td>
<td></td>
</tr>
<tr>
<td>residual lump</td>
<td>11 Simple mastectomy</td>
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Fine needle aspiration cytology; antitubercular chemotherapy

50 to 75 per cent of cases of tubercular mastitis\textsuperscript{24}. In our own series, ipsilateral axillary nodal involvement was present in 18 cases (60\%) (Table I).

Breast is resistant to tuberculous infection by bloodstream, even in debilitated patients of tuberculosis\textsuperscript{21}. Occasionally, direct extension from contiguous structures such as infected rib, costochondral cartilage, sternum, shoulder joint and even through the chest wall from a tuberculous pleurisy or via abrasions in the skin can occur\textsuperscript{25,26}. Coincidental tuberculosis of the faucial tonsils of suckling infants has been suggested as one of the common routes of spread of breast tuberculosis from the suckling infant to the nipple, and in turn, to the lactating breast via lacticiferous ducts\textsuperscript{19,27}. In all cases, bacilli infected the ducts and spared the lobules. This may be the sole example of primary breast tuberculosis relevant even today.
Clinical presentation: The history of the presenting symptoms in breast tuberculosis is usually less than a year but varies from few months to several years\(^\text{17,18}\). Breast tuberculosis commonly affects women in their reproductive age group\(^\text{28}\), between 21-30 yr, similar to the highest incidence of pulmonary tuberculosis reported in the same age group of females\(^\text{29}\). This may be because the female breast undergoes frequent changes during the period of activity and is more liable to trauma and infection\(^\text{18}\). In pregnant and lactating women, the breast is vascular with dilated ducts, predisposed to trauma making it more susceptible to tubercular infection\(^\text{13,28}\). It is uncommon in prepubescent females and elderly women\(^\text{7}\). Breast tuberculosis is rare in males\(^\text{30}\) and is reported in about 4 per cent of cases\(^\text{4}\). Bilateral involvement is uncommon (3\%)\(^\text{13}\).

Breast tuberculosis most commonly presents as a lump\(^\text{19,31}\) in the central or upper outer quadrant of the breast\(^\text{29}\). It is probably due to frequent extension of tuberculosis from axillary nodes to the breast. Multiple lumps are less frequent\(^\text{16}\). The lump is often indistinguishable from carcinoma breast being irregular, hard and at times, fixed to either skin or muscle or even chest wall\(^\text{28}\). But the lump is usually painful. Breast remains mobile unless involvement is secondary to tuberculosis of the underlying chest wall\(^\text{13}\).

Tubercular ulcer over the breast skin and tubercular breast abscess with or without discharging sinuses are other common forms of clinical presentation of breast tuberculosis\(^\text{29}\). Peau d’ orange is often seen in patients with extensive axillary nodal tuberculosis. Purulent nipple discharge or persistent discharging sinus may be the rare presenting feature. Twenty two of the 30 patients in our present series presented with lump in the breast, 11 of these had tubercular ulcer and 4 had multiple discharging sinuses in the overlying breast skin (Table I).

Classification of breast tuberculosis: Breast tuberculosis was first classified into five different types by Mckeown and Wilkinson\(^\text{21}\): (i) Nodular tubercular mastitis, (ii) Disseminated or confluent tubercular mastitis, (iii) Sclerosing tubercular mastitis, (iv) Tuberculous mastitis obliterans, and (v) Acute miliary tubercular mastitis. Since then this classification has been followed though the clinical scenario of breast tuberculosis has gradually changed over the years.

The nodulocaseous form of breast tuberculosis presents as a well circumscribed, slowly growing painless mass (es) that progresses to involve the overlying skin, may ulcerate, form sinuses and may become painful. In early stage it is difficult to differentiate from a fibroadenoma, while at later stages it mimics a carcinoma\(^\text{32,33}\). Sixteen of 20 patients of Dubey and Agarwal\(^\text{17}\) were found to have nodular tubercular mastitis and only 2 had sclerosing tuberculous mastitis. All four cases reported by Dharkar et al\(^\text{16}\) had nodular variety. Similarly, Mukerjee et al\(^\text{18}\) found 9 of the 14 cases with nodulocaseous variety and 3 had sclerosing tuberculous mastitis. Other reports also indicated that the nodulocaseous variety was still the commonest form of breast tuberculosis\(^\text{24,28,34}\).

Few reports described disseminated form of breast tuberculosis\(^\text{24,28}\). It is characterized by multiple foci throughout the breast that later caseate leading to sinus formation. The overlying skin is thickened and stretched with or without painful ulcers. The breast may be tense and tender. The draining axillary lymph nodes are enlarged and matted\(^\text{28}\). The sclerosing variety finds mention in old literature usually affecting involuting breasts of older females. Excessive fibrosis rather than caseation is the dominating feature. There is a hard painless slow growing lump with nipple retraction. Suppuration is rare. It may be misdiagnosed as a scirrhotic carcinoma\(^\text{28}\). Often the entire breast becomes hard because of dense fibrous tissue.

Tuberculous mastitis obliterans as described by Mckeown and Wilkinson\(^\text{21}\) is characterized by duct infection producing proliferation of lining epithelium and marked epithelial and periductal fibrosis. The ducts are occluded and cystic spaces are produced resembling ‘cystic mastitis’. In acute miliary tubercular mastitis breast disease is a part of a generalized miliary tuberculosis. However, no case of breast tuberculosis was found in a post-mortem series of 34 patients with miliary tuberculosis\(^\text{18}\) and is of little clinical significance\(^\text{21}\).

With the changes seen in presentation of tuberculosis over the period of time, miliary tuberculosis is rare today. Moreover, there are hardly
enough reports in the past two decades to merit the sclerosing tubercular mastitis, tuberculous mastitis obliterans and acute miliary tubercular mastitis in the classification of breast tuberculosis.

Tubercular breast abscess is often a common mode of presentation of breast tuberculosis, especially in young women. In a review of benign breast disorders in India, Shukla and Kumar found tubercular breast abscess to be a common presentation of breast tuberculosis. In our series we found eight patients presented with a fluctuant breast abscess (Table I).

Thus at present, breast tuberculosis may be reclassified as nodular, disseminated and abcess varieties. The sclerosing type, mastitis obliterans and miliary variety are of historical importance only (Table II).

Diagnosis: Breast tuberculosis is mostly misdiagnosed and the patient is often subjected to numerous investigations before a definitive diagnosis is made. It warrants a high index of suspicion on clinical examination and pathological or microbiological confirmation of all suspected lesions.

(i) Mantoux test - This test is usually positive in adults in endemic area for tuberculosis. It simply demonstrates that at some point of time the person was exposed to tubercle bacilli. It is, therefore of no diagnostic value for breast tuberculosis and today stands obsolete.

(ii) Radiological investigations - The modern radiological investigations help in defining the extent of the lesion rather than in diagnosis. Sophisticated radiological tools like mammography, computed tomography (CT-scan) and magnetic resonance imaging (MRI) of the breast have been extensively explored for the diagnosis of breast tuberculosis but of no avail. The chest X-ray may show evidence of active or healed tuberculous lesion in the lungs in a few cases, and may also reveal clustered calcifications in the axilla suggesting the possibility of lymph node tuberculosis in suspected patients.

The mammogram in breast tuberculosis is of limited value as the findings are often indistinguishable from carcinoma breast. The mammographic picture of nodular tuberculosis is usually of a dense round area with indistinct margins seen without the classic halo sign found in fibroadenoma. The mammographic size of the tuberculous lesion correlates well with its clinical size, unlike that of a carcinoma. Disseminated variety mimics inflammatory carcinoma and the radiographs show dense breast with thickened skin. Sclerosing tubercular mastitis reveals a homogenous dense mass with fibrous septa and nipple retraction. However, as breast tuberculosis is found in young women of 20-40 yr of age, dense breasts makes interpretation of mammogram difficult. Moreover, this facility might not be available and economical to many patients from the less developed world where the disease is very common.

Ultrasonography of the breast is cheap, easily accessible and helps in characterizing the lesion better (especially cystic from solid lesions) without exposure to radiation. In nodular form of the disease, lesions are either hypoechoic with ill-defined margins or complex cystic masses. In diffuse breast tuberculosis, ill-defined hypoechoic masses are seen whereas in patients with sclerosing breast tuberculosis, increased echogenicity of the breast parenchyma often with no definite mass is seen. At times, a beak like fistulous connection between retromammary abscess and thoracic wall is seen in sonogram. Ultrasound-guided
Fine needle aspiration decreases the failure rate and obviates the need for multiple punctures. The mammographic and sonographic features of tubercular mastitis as stated by a recent study include a mass lesion mimicking malignant tumours (30%), smooth bordered masses (40%), axillary or intramammary adenopathy (40%), asymmetric density and duct ectasia (30%), skin thickening and nipple retraction, macrocalcification (20% each), and skin sinus (10%). On ultrasound, 60 per cent had hypoechoic masses, 40 per cent focal or sectorial duct ectasia, and 50 per cent axillary adenopathy.

CT scan seldom adds to the diagnostic yield other than in defining the involvement of thoracic wall in patients presenting with deeply adhered breast lump. Tubercular breast abscess may be seen as smoothly marginated, non homogeneous, hypodense lesion with surrounding rim on contrast CT. A direct fistulous tract with the pleura or a destroyed rib fragment in the abscess can also be seen. Percutaneous drainage of a tubercular breast abscess under CT guidance is feasible. CT can show area(s) of lung destruction beneath the pleural disease, and is a valuable tool in demonstrating the extent of disease, in planning of surgery and also in assessment of response to treatment.

MRI of the breast may reveal a smooth or irregular bright signal intensity lesion on T2-weighted images suggesting a breast abscess. Again the findings are non specific and reports on MRI of the breast suggest its usefulness only in demonstrating the extramammary extent of the lesion.

(iii) Fine needle aspiration cytology - Fine needle aspiration cytology (FNAC) from the breast lesion continues to remain an important diagnostic tool of breast tuberculosis. Approximately 73 per cent cases of breast tuberculosis can be diagnosed on FNAC when both epitheloid cell granulomas and necrosis are present. Failure to demonstrate necrosis on FNAC does not exclude tuberculosis in view of small quantity of the sample harvested and examined. The demonstration of acid-fast bacilli (AFB) on FNAC is not mandatory, since for AFB to be seen microscopically, their number must be 10,000-100,000/ml of material. In tubercular breast abscess, FNAC may be inconclusive and the FNA picture may be dominated by acute inflammatory exudates. AFB-negative breast abscess that fail to heal despite adequate drainage and antibiotic therapy, and those with persistent discharging sinuses should raise suspicion of underlying tuberculosis. Biopsy of the abscess wall and demonstration of characteristic histological features or culture are essential to confirm the diagnosis of breast tuberculosis.

(iv) Culture - Though mycobacterial culture remains the gold standard for diagnosis of tuberculosis, the time required and frequent negative results in paucibacillary specimens are important limitations. Moreover, culture is not always helpful in the diagnosis of breast tuberculosis. During the last two decades several rapid techniques for detection of early mycobacterial growth (5-14 days as compared to 2-8 wk with conventional methods) have been described which helped in obtaining the culture and sensitivity reports relatively early. Prominent among such methods are BACTEC, mycobacterial growth indicator tube (MGIT), Septi-chek, MB/BacT systems.

(v) Polymerase chain reaction (PCR) - Gene amplification methods (PCR as well as isothermal) developed for the diagnosis of tuberculosis are highly sensitive especially in culture-negative specimens from paucibacillary forms of disease. A variety of PCR techniques have been developed for detection of specific sequences of Mycobacterium tuberculosis and other mycobacteria. PCR has positivity rates ranging from 40 to 90 per cent in diagnosing tubercular lymphadenitis. PCR in the diagnosis of breast tuberculosis is less often reported, mostly as a tool to distinguish tubercular mastitis from other forms of granulomatous mastitis in selected reports. However, PCR is by no means absolute in diagnosing tubercular infection and false negative reports are still a possibility.

Most of these new techniques are too expensive and sophisticated to be of any practical benefit to the vast majority of TB patients living in underdeveloped countries like India for whom an early and inexpensive diagnosis remains as elusive as ever.

(vi) Histopathology of the specimen - Histological findings include epitheloid cell granulomas with caseous necrosis in the specimen. Core needle biopsy yields a good sample often yielding a positive
diagnosis. However, open biopsy (incision or excision) of breast lump, ulcer, sinus or from the wall of a suspected tubercular breast abscess cavity almost always confirms breast tuberculosis.

Histologically, tubercular mastitis is a form of granulomatous inflammation. There are many other conditions that are characterized histologically by a tuberculoid type of tissue reaction. These conditions include sarcoidosis, various fungal infections, and granulomatous reactions to altered fatty material. Sometimes the microscopical picture is indistinguishable from that of tuberculosis.

**Breast tuberculosis versus carcinoma breast:** 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. 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.

**Treatment:** The treatment of breast tuberculosis consists of anti-tubercular chemotherapy (ATT) and surgery with specific indications.

ATT is the backbone of treatment of breast tuberculosis. No specific guidelines are available for the chemotherapy of breast tuberculosis. The regimen generally followed in the treatment of breast tuberculosis is similar to that used in pulmonary tuberculosis. Extrapulmonary tuberculosis except for tubercular meningitis, can be treated with 6 months regimens comprising two months of intensive phase treatment (with 4-drug combination) followed by a continuation phase of 4 months (with 2-drug combination). The first line drugs being ethambutol (E) 1200 mg; streptomycin (S) 750 mg, rifampicin (R) 450 mg, isoniazid (H) 600 mg and pyrazinamide (Z) 1500 mg. The Revised National Tuberculosis Control Programme (RNTCP) of India recommends category III regimen (2HRZ/4HR) for less serious forms of extrapulmonary tuberculosis viz., lymph node tuberculosis, cutaneous tuberculosis, unilateral pleural effusion, and category I regimen (2EHRZ/4HR) for more severe forms of extrapulmonary tuberculosis.

Drugs are administered thrice weekly. The World Health Organization has recommended a 4-drug intensive phase (2EHRZ) in category III regimen as well. Patients resistant to standard 4-drug ATT will require second-line ATT drugs. Local streptomycin has been claimed to be useful. The overall prognosis is good with adequate medical treatment.

Multilating surgery like simple mastectomy for breast tuberculosis was in vogue in the past with the belief that the lesion tends to persist and reappear with conservative treatment even with chemotherapy. However, today minimal surgical intervention is required for drainage of breast abscess or biopsy from the abscess wall, scraping of sinuses in the breast, incisional or excisional biopsy. Small lesions are eminently treatable by an excision biopsy followed by a full course of ATT. Residual lump following ATT may require surgical removal. Simple mastectomy with or without axillary clearance is rarely required for extensive disease comprising large, painful ulcerated mass involving the entire breast and draining axillary lymph nodes rendering organ preservation impossible. For concomitant breast cancer, the form of surgery is dependant upon the stage of breast cancer.

In our series, FNAC was positive in 11 patients, core needle biopsy in 2, and an open biopsy was required in 17 patients. All 8 patients of tubercular breast abscess responded to repeat aspiration in conjunction with ATT. All patients were treated with ATT (2EHRZ/7HR) for a total of 9 months, and were free of recurrence in 12 to 200 months of follow up. Simple mastectomy was performed in one patient who defaulted after initial diagnosis and returned with a large ulcerated breast lesion and matted axillary nodes (Table I).
Conclusion

Extrapulmonary tuberculosis occurring in the breast is extremely rare. Breast tuberculosis is uncommon even in countries where the incidence of pulmonary and extrapulmonary tuberculosis is high. In the absence of well-defined clinical features, the true nature of the disease remains obscure and it is often mistaken for carcinoma or pyogenic breast abscess. It also presents a diagnostic problem on radiological and microbiological investigations and thus high index of suspicion acquires an important position. Caseating epitheloid cell granulomas in the tissue samples are diagnostic of tuberculosis. The disease is eminently curable with the modern antitubercular chemotherapeutic drugs with surgery playing a role in the background only.

References


