Original Investigation

Breast tuberculosis: a diagnosis not to be forgotten

Hammami et al. Breast tuberculosis

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Abstract

Objectives: To study the clinical particularities and imaging features of breast tuberculosis and to describe treatment.

Material and Methods: We conducted a retrospective study including all patients hospitalized in the infectious diseases department for breast tuberculosis between 1997 and 2018.

Results: We encountered 22 women with a mean age was 39±12 years. In total, 18 patients were multiparous (81.8%). Both lump and mastalgia were the revealing symptoms in 19 cases (86.3%). Ipsilateral axillary lymphadenopathy was noted in 14 cases (63.6%). The most common finding on ultrasound was a well or poorly defined mass lesion, noted in 17 cases (77.2%) followed by fistulous tracts in seven cases (31.8%). Mammography showed focal asymmetric breast density in 17 cases (89.5%) and diffuse in two cases (10.5%). The diagnosis was confirmed based on the presence of epithelioid cell granulomas and caseous necrosis in 13 cases (59.1%). Patients received antitubercular therapy for a mean duration of 11±5 months. The disease evolution was favorable in 20 cases (91%). There were two relapsing cases (9%).

Conclusion: Breast tuberculosis should be considered in front of young patients presenting palpable lump with axillary lymphadenopathy, especially in endemic regions. The diagnosis confirmation usually requires an excision biopsy providing histological or bacteriological evidence.

Keywords: Breast, tuberculosis, ultrasonography, mammography, lymphadenopathy
Introduction
Tuberculosis (TB) remains a public health issue, with an estimated 10 million new cases annually, worldwide (1). It’s a multisystem disease that might involve all sites. Breast TB is a rare disease, even in developing countries (2). Its incidence reaches 4% of all breast lesions in endemic regions (3). Patients usually consult for an isolated lump, without constitutional symptoms of TB, which are present in 20% of the cases (4). The diagnosis is often delayed due to the low index of suspicion and similarities with other breast pathologies. Breast TB is often mistaken for pyogenic abscesses or breast cancer (5). Imaging findings are often helpful in order to guide clinicians. However, breast TB has no specific ultrasonographic findings, which might present as heterogeneous, hypoechoic, irregularly bordered mass with internal echoes or thick-walled cystic lesions (6).
Although Tunisia is an intermediate endemiocity country for TB (7), breast TB remains a very rare disease, representing 0.2% of extrapulmonary TB cases (8). In this perspective, the aim of this work was to study the clinical particularities and imaging features of breast TB and to describe treatment.

Materials and Methods
Study design
We conducted a retrospective study including all patients hospitalized in the infectious diseases department for breast TB over a 22-year period between 1997 and 2018.

Data collection and case definitions
We collected data from the patient’s medical record. The age, gender, urbanity of residence and previous medical history of patients were recorded. Clinical symptoms, laboratory investigations, microbiological and histopathological results, and imaging features were reviewed. The treatment received, its duration and the disease evolution were also reported. Patients included in the study had microbiological or histopathological confirmed breast TB. In default, patients had clinical and radiological signs suggestive of the diagnosis which were followed by an adequate response to antitubercular therapy.
According to the clinical presentation, fine needle aspiration or excision biopsy were performed in order to obtain specimen for histological and microbiological (Ziehl-Neelsen staining) examination. Written informed consent was obtained from all patients.

Statistical Analysis
Statistical analysis was performed using the SPSS 20 software. Categorical variables were expressed as numbers and percentages. Continuous variables were presented as means and standard deviations, if they were normally distributed. Median and interquartile ranges were used for non-normally distributed data.

Results
Patient characteristics
During the study period, we encountered 22 patients with breast TB. All our patients were females. The mean age was 39±12 years. Twelve patients were aged between 20 and 40 years (54.6%). Eleven patients were from rural areas (50%). Three patients had a previous medical history of treated TB (13.6%). One patient had a family history of pulmonary TB (4.5%). At the time of diagnosis, five patients were pregnant (22.7%), and three patients were lactating (13.6%). In total, 18 patients were multiparous (81.8%) and four patients were nulliparous (18.2%) (Table 1).
Both lump and mastalgia were the revealing symptoms in 19 cases (86.3%). Ipsilateral axillary lymphadenopathy was noted in 14 cases (63.6%) and breast abscess in 11 cases.
(50%). Location was reported as unilateral in 21 cases (95.5%) and bilateral in one case (4.5%). The mean size of the lump was 5.1±2.8 cm. It was located in the upper outer quadrant of the breast in 10 cases (45.5%). Associated with breast TB, other foci of TB were noted in four cases (18.2%), represented by cervical lymph node TB in four cases (Table 1). The median delay in seeking medical care was 40 [27-75] days. Elevated C-reactive protein level was noted in 10 cases (45.5%) with a median level of 42 [25-53] mg/L. An accelerated erythrocyte sedimentation rate was noted in seven cases (31.8%). Tuberculin skin test was positive in 13 cases (59.1%). All patients were tested negative for human immunodeficiency virus.

**Imaging features**

Ultrasound was performed in all cases. The most common finding was a well or poorly defined mass lesion, noted in 17 cases (77.2%). Fistulous tracts were noted in seven cases (31.8%), and ductal dilatation with echogenic component in six cases (27.2%). The disseminated form was noted in two cases (9%) with multiple collections mostly containing debris.

Mammography, performed in 19 cases (86.3%), showed focal asymmetric breast density in 17 cases (89.5%) and diffuse in two cases (10.5%) (Figure 1). Skin thickening was noted in five cases (26.3%), multiple mass lesions in two cases (10.5%) and microcalcifications without suspect grouping in three cases (15.7%).

Magnetic resonance imaging (MRI) was performed in three cases (13.6%). One patient presented a bilobed mass enhancement with intermediate intense T2, surrounded by an hypointense, regular and fine halot hypointense T1, and an early and heterogenous enhancement (curve type 2). Multiple confluent mass enhancement with irregular margins was noted in one case. One of these masses presented a rim enhancement pattern, classified therefore ACR5 (Figure 2). Non-mass enhancement was noted in one case.

**Intervention and therapeutic procedure**

Excision biopsy was performed in seven cases (31.8%). In order to exclude a possible breast cancer, lumpectomy was indicated in 10 cases (45.5%) and mastectomy in two cases (9%). Drainage of the abscess was indicated in one case (4.5%).

The diagnosis was confirmed based on the presence of epithelioid cell granulomas and caseous necrosis in 13 cases (59.1%). The presence of epithelioid cell granulomas without caseous necrosis was noted in seven cases (31.8%). The detection of *Mycobacterium tuberculosis* in smear or culture confirmed the diagnosis in four cases (18.2%) (Table 1).

Patients received antitubercular therapy for a mean duration of 11±5 months. Side effects of antitubercular therapy were noted in 10 cases (45.5%). The disease evolution was favorable in 20 cases (91%). There were two relapsing cases (9%). The median length of hospital stay was 7 [4-13] days.

**Discussion**

The diagnosis of breast TB can not only rely on imaging results, which may be non-specific. High index of suspicion followed by clinical, radiological examination and appropriate biopsies are mandatory in order to confirm the diagnosis of breast TB. It remains a rare disease affecting commonly young, multiparous and lactating women (9). Its rarity is explained by the resistance of breast tissue to the infection, making therefore, survival and multiplication of *Mycobacterium tuberculosis* difficult (10). However, during lactation, the breast is highly vascularized, and the ducts are dilated which explains the susceptibility to TB infection (11). A previous study including 65 cases of breast TB reported a rate of 10.6% of lactating patients (8), which was similar to our results.
Breast TB was initially classified as primary when no other focus of TB was detectable, and secondary when it was associated with other focus of TB elsewhere in the body (12). Later, it was reported that breast TB is usually secondary even if no other focus of TB was clinically or radiologically noticeable (13). We found other sites of TB associated with breast TB in 18.1% of the cases, while a previous study reported a rate of 67.9%, which was mostly represented by pleural and pulmonary TB (14). This discordance might be explained by the misdiagnosed of other sites of TB in our study.

In fact, secondary breast TB is commonly due to retrograde lymphatic spread from axillary lymph nodes, less commonly from cervical or mediastinal lymph nodes (15), which explains the frequent ipsilateral axillary lymphadenopathy associated to breast TB. Other sources of infection were reported including hematogenous, or contiguous spread from the pleura or the chest wall (16).

Three Types of breast TB have been reported, based on the clinical, radiological and pathological aspect of the disease. The nodular is the most common type, followed by the disseminated and the sclerosing form (17). Previous studies reported that the elderly present commonly the nodular form, which mimics breast carcinoma clinically and radiologically (18,19), while younger patients usually present pyogenic abscess (19,20). Imaging features confirm the presence of three form of the disease, found during the clinical examination. The nodular form is presented, on mammography, as an ill-defined density, which mimic breast cancer (21). The disseminated form is characterized by the sinus formation secondary to multiple foci of TB (22). The irregularity of its margin might represent the tunneling of the abscesses and the associated blurring of the fat due to inflammatory reaction and edema (23), which mimic inflammatory carcinoma (15). The sclerosing form is seen when there is extensive fibrosis rather than caseation and the entire breast became hard with a retracted nipple (4). A strongly suggestive aspect of tuberculous abscess is rarely found on mammography, which is represented by a dense sinus tract connecting an ill-defined breast mass to a localized skin thickening (24).

Imaging findings are of great interest in defining the extent of the lesion. However, differentiating breast TB from breast cancer remains usually difficult (25). The simultaneous occurrence of breast cancer and TB is rarely noted, this diagnosis helps in down staging of carcinoma of breast and further management of the case (26). An excision biopsy, obtaining adequate tissue samples, is strongly recommended, which is not usually the case of fine needle aspiration (17). Demonstration of bacilli by microbiological, cytopathological or histopathological proof confirm the diagnosis of breast TB (2). This disease can present a diagnostic problem on radiological and microbiological investigations, and thus a high index of suspicion is needed.

The cornerstone of the treatment remains antitubercular therapy prescribed for a minimum of six month (11). In order to prevent recurrence (27), or in front of slow clinical response (24), a prolonged treatment duration was reported, like the case of our patients. In fact, the associated site of TB may also interfere in the treatment duration, such as patient who presented tuberculous meningitis. Along with medical therapy, surgical intervention might be required, in front of the lack of response to antitubercular therapy or due to the presence of lesions involving the entire breast (17).

Conclusion
In our country, breast TB remains a rare and overlooked disease. The disease should be considered in front of young patients presenting palpable lump with axillary lymphadenopathy, especially in endemic regions. Although, imaging results were non-specific, they might guide the clinicians. However, the diagnosis confirmation usually requires an excision biopsy providing histological or bacteriological evidence.
Conflict of Interest: The authors declare that they have no conflicts of interest.

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References

Table 1. Characteristics of patients with breast tuberculosis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number</th>
<th>Percentage (%)</th>
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<tr>
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<tr>
<td>20-40</td>
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<td>41-60</td>
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<td>36.4</td>
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<td>&gt; 60</td>
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<td><strong>Clinical symptoms</strong></td>
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<td>Lump</td>
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<tr>
<td>Mastalgia</td>
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<tr>
<td>Breast abscess</td>
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<td>Breast fistula</td>
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**Diagnosis confirmation**

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<tr>
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<td>Bacteriological proof: detection of <em>Mycobacterium tuberculosis</em></td>
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**Disease evolution**

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<td>Relapse</td>
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*: In microscopic smear or culture

**Figure 1.** Standard craniocaudal view of the right and left breast shows an asymmetric density in the upper quadrant of the right breast (arrow)
**Figure 2.** Breast magnetic resonance imaging shows multiple mass enhancement and a mass (encircled) with a rim enhancement.