

Tuberculosis of the breast: report of 4 clinical cases and literature review

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سل الثدي: تقرير عن أربع حالات سريرية واستعراض للأدبيات المنشورة
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الخلاصة: هناك حوالي 18% من حالات السل لا تحدث مظاهرها إلا خارج الرئة. ويُعدُّ سل الصدر أحد أنواع السل التي يندر حدوثها خارج الرئة. وتقدّم هذه الدراسة تقريراً عن أربع حالات لسل الثدي مع تأكيد إصابتها بالسل الباثولوجي، أو المتفطري، أو كليهما. وأوضحت هذه التقارير أنه يتعيّن دائماً أخذ إمكانية الإصابة بالسل، بعين الاعتبار أولاً، لدى إجراء التشخيص التفريقي في حالات التهاب الثدي الورمي الحبيبي، في المناطق الموطونة بالسل. واشتملت المعالجة على الأدوية المضادة للسل لمدة ستة أشهر على الأقل، والجراحة في الحالات التي استدعت ذلك.

ABSTRACT Nearly 18% of tuberculosis (TB) cases have only extrapulmonary manifestations. Breast tuberculosis is a rare type of extrapulmonary TB. This paper reports 4 cases of breast TB confirmed either pathologically or mycobacteriologically or both. These reports showed that TB should always be considered first in the differential diagnosis of granulomatous mastitis in TB-endemic areas. Therapy included at least 6 months of anti-TB medication and surgery when indicated.

Tuberculose mammaire : étude de 4 cas cliniques et synthèse de la littérature

RÉSUMÉ Près de 18 % des cas de tuberculose ne s'accompagnent que de manifestations extrapulmonaires. La tuberculose mammaire est une localisation rare de la tuberculose extrapulmonaire. Le présent article rapporte 4 cas de tuberculose mammaire, confirmée par l'anatomopathologie ou l'examen mycobactériologique ou les deux ensemble. Ces observations montrent que la tuberculose doit toujours être envisagée d'emblée dans le diagnostic différentiel de la mastite granulomateuse dans les zones d'endémie tuberculeuse. Le traitement a consisté en l'administration d'antituberculeux pendant un minimum de 6 mois et la chirurgie si indication.

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Introduction

Tuberculosis (TB) has traditionally been regarded as a pulmonary disorder. However, nearly 17.9% of TB cases have only extrapulmonary manifestations [1]. Breast and skin are considered to be rare sites of extrapulmonary mycobacterial infection, comprising 0.1% to 0.5% of all TB cases, respectively [2]. Tuberculous mastitis is an uncommon lesion [1] even in countries where the incidence of pulmonary and extrapulmonary TB is still very high [3]. The clinician may confuse TB of the breast with either breast carcinoma or abscess [4–6]. Although the usual form of the disease is unilateral, it occasionally presents bilaterally [7].

We summarize here 4 cases of tuberculous mastitis presenting to the National Research Institute of Tuberculosis and Lung Disease over a 5-year period at Shaheed Beheshti Medical Science University.

Case presentations

Case 1

A 37-year-old female was referred to this centre for management of left breast pain. There was no history of recent pregnancy or

lactation or a history of breast trauma. She first noticed a painful mass in her left breast 1.5 years ago, 20 days later she noticed a visible lesion on the breast skin with purulent discharge. Subsequently, sinus tracts with purulent discharges appeared in a total of 6 locations. She received at least 8 courses of antibiotic therapy with no therapeutic effect before she was referred to our centre.

On physical examination, a painful nodular mass was detected in the medial half of the breast. A surgical scar, more than 6 healed sinus tracts, and a region containing exudate were detected (Figures 1 and 2). Sonography showed a well-defined 20 × 12 × 14 mm mass in the medial portion of the left breast.

Based on the sonography and mammography results, the patient underwent biopsy with a suspicion of malignancy. Diagnosis of granulomatous mastitis was established from biopsy. A second biopsy of the new sinus tract also confirmed a granulomatous lesion and there was no sign of malignancy. The fine-needle aspiration (FNA) smear was negative for acid-fast bacilli (AFB). FNA was negative on polymerase chain reaction testing for mycobacterium TB and culture-negative for actinomycetes and fungi. The angiotension converting enzyme



Figures 1 and 2 Multiple breast sinus tract and erythematous skin lesions

level was in the normal range. Complete blood counts and liver function tests were all normal. The patient's purified protein derivative (PPD)/Mantoux skin test was 16 mm in diameter. Chest radiography was intact and there were no changes compatible with TB or sarcoidosis. High resolution computerized tomography of the lung was normal.

Although we found no laboratory evidence for TB mastitis, due to the Mantoux skin test and strong clinical suspicion, the patient was put on standard anti-TB regimen of isoniazid, rifampin, pyrazinamide and ethambutol. In the subsequent 6-month period no other sinus tracts appeared and the breast mass showed an apparent remission on multiple sonography.

Case 2

A 41-year-old woman presented with pain and swelling of the left breast. She was a known case of TB from 18 years before and had received a complete 6-month period of anti-TB treatment. The patient's symptoms had started one year after discontinuation of breast feeding with pain and a mass in the superolateral portion of the left breast. The symptoms progressed over a few months and no associated constitutional symptoms were found.

After ultrasound examination, a biopsy was taken with the suspicion of breast carcinoma. The result was reported as granulomatous mastitis and after ruling out other diagnoses, the patient underwent anti-TB treatment with an excellent response; however, she discontinued medication after 3 months. Two weeks later, the left breast mass reappeared, associated with multiple lymph nodes in the left axillary pit. Sonography supported the prior diagnosis of granulomatous mastitis. This time, a 6-month course of anti-TB therapy was started with a standard regimen and no mass or abscess

was reported on ultrasound examination during the course of treatment. After 6 months of follow-up, starting from the end of treatment, no mass or lymphadenopathy appeared and the patient complained only of minor pain.

Case 3

A 19-year-old female was referred to this centre with a complaint of breast pain and retraction of the right nipple with yellowish discharge. She was nulliparous with no history of breast trauma. Her symptoms began 1 year before referral and gradually progressed. She took various different kinds of antibiotics during this period. On physical examination, painful masses were palpated in the centre and superolateral quadrant of the right breast. An enlarged lymph node in the right axilla, dimension 20 × 20 mm, was also palpable on physical examination. Full nipple retraction and purulent yellowish discharge from the same nipple was detected (Figures 3 and 4). At least 4 openings of sinus tracts were visible with no purulent discharge at the time.

On sonography, there was thickening of the breast skin in the superolateral and supercentral portion. This abnormality along with several hypoechoic lesions suggested abscess formation. There was evidence of left pleural effusion on chest radiography. The PPD/Mantoux skin test was 11 mm. Complete blood count and liver function tests were all normal. Sputum smears were negative; however, direct smear of breast discharge was 1+ positive for AFB, compatible with World Health Organization criteria. Aspiration of pleural fluid was not performed because of the patient's dissent.

Considering AFB secretions and concomitant pulmonary and pleural involvement, a diagnosis of TB was suggested and a standard anti-TB drug regimen of isoniazid,



Figures 3 and 4 Full nipple retraction and purulent yellowish discharge from the same nipple was detected

rifampin, pyrazinamide and ethambutol was prescribed.

After beginning anti-TB medication, the breast discharge and pain decreased significantly after 2 months. Direct smear of breast discharge became negative after 2 months although discharges continued. After 6 months of chemotherapy, a decision for surgical intervention was made to alleviate persistent discharges; however, the patient left the country and the treatment remained interrupted.

Case 4

A 49-year-old woman presented with suppurative secretions from her left breast. She had suffered from pain and a mass in the left breast for 4 years. An ultrasound-based diagnosis of suppurative abscess had been suggested and she underwent antibiotic therapy plus aspiration. Due to recurrence, repeated courses of antibiotic therapy were given. A sinus tract appeared in the left breast, superior to the nipple with suppurative secretions 8 months previously. Bacteriologic studies at different periods from abscess and sinus tract secretions gave negative results. Mycologic studies led to negative results. The PPD/Mantoux skin test was also negative. Liver function tests

and other tests were normal and lung computerized tomography scan gave no abnormal findings. Smear and culture from sinus tract secretions were sent for bacteriological evaluation which showed negative-smear results. However, AFB colony growth in the culture was confirmed and using differential tests, *Mycobacterium tuberculosis* was eventually identified.

Discussion

The first case had a granulomatous lesion in her breast. Granulomatous mastitis is a descriptive and non-specific term which encompasses many specific lesions such as TB, fungal infections, sarcoidosis and granulomatous reactions in carcinoma [8]. Several diagnoses must be ruled out to establish TB mastitis.

Idiopathic granulomatous mastitis was first described in 1972 [9], for which TB mastitis should always be considered as a differential diagnosis in women with a positive history of exposure to TB patients [10]. This kind of exposure occurs very frequently in endemic countries. A similar granulomatous reaction has also been described in actinomycosis of the breast which

was ruled out by culture of the patient's discharge obtained by FNA in our patients [11].

The best description of TB mastitis is by Shinde et al. in India [12]. They showed that a lump in the breast with or without ulceration was the commonest presentation in TB of the breast, the other less common forms being diffuse nodularity and multiple sinuses. Concomitant axillary lymph nodes were found in one-third of the patients. Our second case had similar symptoms. This suggests that a young, multiparous, lactating woman with a similar lesion should always raise the suspicion of TB mastitis, although pre-therapeutic pathologic confirmation of benign conditions is mandatory. Similar results were reported by Al-Marri et al. from 13 multiparous women with TB of the breast from Qatar [13]. All of them presented with a lump, 2 had nipple discharge and 1 had a palpable axillary node on the same side. In that study all diagnoses were confirmed histologically.

In both these previous studies the type of breast lesion was similar to what we found in our cases; in our second case, the breast lesion emerged as an abscess, corresponding to Daali's report [14].

According to different studies, the age of patients with breast TB ranges between 20 and 40 years, which corresponds to the age of our patients. However, many other investigators have also reported breast TB in post-menopausal ages [4,6,15-17].

With regard to pathogenesis, the route of entry of mycobacterial TB to the breast varies. Spreading of infection from other TB foci via haematogenic path during primary infection is a common route [18].

TB mastitis should also be considered in immunodeficiency states in which pathogenesis is also via the haematogenic route [19,20]. There is also much controversy about the diagnostic criteria for TB mastitis

and different surgical biopsies and FNA have been recommended [13]. However, in several studies it has been shown that the overall rate of positivity of AFB in nipple discharge, FNA and tissue samples was 12.0%–22.7%. [12,16,21]. Although we obtained samples for smear and direct visualization from breast discharge samples and FNA for all our patients, only patient 3 was AFB-positive.

The differential diagnoses include duct ectasia, foreign-body giant-cell reaction with fat necrosis, foreign material or an abscess, idiopathic granulomatous mastitis, sarcoidosis, syphilitic gumma and Wegener's granulomatosis [16,22], all of which must be ruled out using proper diagnostic tests.

Various modes of therapy ranging from chemotherapy alone to mastectomy have been suggested for tuberculous mastitis [12]. In a study by Shinde et al., 14% of patients required simple mastectomy due to either lack of response to chemotherapy (10%) or large painful, ulcerative lesions involving the entire breast (4%). Axillary dissection was performed in only 8% of patients with large ulcerated axillary nodes. Al-Marri recommends that incisional or excisional biopsy together with anti-TB drugs is the most successful treatment [13]. Daali et al. recommend anti-TB chemotherapy for 9 months [14]. The clinical course was favourable at 6 months. They recommend that anti-TB antibiotic therapy might be accompanied by surgery in case of extension, therefore several authors suggest that anti-TB antibiotic therapy in combination with aspiration or surgical drainage are usually associated with an excellent outcome [4,6,7,23,24]. We recommend at least 9 months of anti-TB therapy and surgery in cases with unsatisfactory treatment results.

Although TB of the breast is a rare entity, it should always be considered in the

differential diagnoses of granulomatous mastitis in endemic areas. It seems that empirical therapy might be effective when primary evaluations for other causes lead to no definite conclusion. Diagnosis is based

on histopathology and it is less probable that a microbiological diagnosis be made. Therapy includes at least 6 months of anti-TB medication, and surgery when indicated.

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Diagnostic and treatment delay in tuberculosis

This document presents an in-depth analysis of the health-seeking behaviour of patients and the health system response in 7 countries of the Eastern Mediterranean Region. This study was conducted in order to obtain reliable information about the extent of diagnostic and treatment delay and the factors implicated in the Eastern Mediterranean Region. It is a detailed analysis of the health-seeking behaviour of tuberculosis patients from onset of symptoms until reaching the health system, final diagnosis and treatment. It also provides a thorough analysis of the health system in relation to tuberculosis.

It is envisaged that the information provided by this study could assist health policy-makers in devising suitable interventions in order to increase case detection and reduce transmission of infection in the community, and hence achieve proper tuberculosis control.

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