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Breast tuberculosis in Jakarta: Review of 7 cases

Farida B. Sobri,¹ Odetta N. Halim^{2*}

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ABSTRACT

Introduction: Breast tuberculosis (TB) is a rare manifestation of extrapulmonary TB. It can present with various clinical appearances, mimicking pyogenic abscess or breast cancer. Radiological, laboratory, and histopathology results are often inconclusive. Correct diagnosis of breast TB is required as the treatment consists of mainly antitubercular therapy, with only minimal surgical intervention.

Cases Presentations: We report seven cases of breast tuberculosis that was diagnosed with several diagnostic methods. All patients

were treated with antitubercular therapy and showed a good response.

Discussion: The diagnosis of breast TB is difficult because it has variable clinical and radiological features, with a wide range of differential diagnosis. Also, the percentage of smear-positive for Acid-fast Bacilli (AFB) is low.

Conclusion: Breast TB should be considered as differential diagnosis of breast lesion, especially in TB endemic countries, which one of them is Indonesia.

Keywords: tuberculosis, breast, diagnostic methods, antituberculous treatment

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¹Department of Surgical Oncology, Metropolitan Medical Centre Hospital, Jakarta, Indonesia

²Department of Surgery, Pariaman General Hospital, West Sumatera, Indonesia

INTRODUCTION

The World Health Organization (WHO) declared tuberculosis (TB) as a global emergency.¹ There were 10.4 million new tuberculosis (TB) cases, equivalent to 142 cases per 100,000 population in 2015 worldwide. Six countries accounted for 60% of the global total are India, Indonesia, China, Nigeria, Pakistan and South Africa respectively. The first three countries alone accounted for 45% of global cases. In Indonesia, there were 1.02 million new TB cases in 2015.²

Mainly considered as a pulmonary disease; however, almost 17,9% of TB cases have extrapulmonary manifestations. Extrapulmonary involvement of the breast is quite rare. Breast TB, nearly 0.1-0.5% of all TB cases, is rare in developed countries, with an incidence of 0.025 to 0.1% of all breast lesions.¹ In developing countries where *Mycobacterium tuberculosis* (MTB) infection is endemic, it constitutes approximately 3-4% of all breast diseases.^{3,4}

Breast, like skeletal muscles and spleen, is relatively resistant to TB. Breast TB commonly affects females in reproductive age groups.⁵ Risk factors include multiparity, lactation, trauma, past history of suppurative mastitis and AIDS. It most commonly presents as a lump.⁴ The diagnosis is complicated, and it is often misdiagnosed as pyogenic abscess or carcinoma.³ Herein we reported seven cases of breast TB over a period of two years, with emphasis on the diagnostic aspect.

CASE PRESENTATIONS

All seven cases were a married woman, with the majority had a history of breastfeeding. Their age ranged from 29-52 years old. The eldest had reached menopause at the time of presentation.

Patients presented with lump, swelling, pain and nipple discharge. The right breast was predominantly involved. None of them had involvement of axillary lymph node. Breast ultrasound showed features of mastitis or abscess.

Initially, all patients were diagnosed with mastitis and treated empirically with surgical debridement and antibiotics. Three out of seven patients were diagnosed TB by three different tools after surgery. One patient had positive acid-fast bacilli (AFB) smear and culture from pus sample. The TB characteristic finding Langhans' giant cells and caseous necrotic area were found in one patient. One patient had positive interferon-gamma release assay (IGRA) result. Those three were given TB treatment right after.

The pathological examination of the remaining four patients showed granulomatous mastitis features. They were treated as common mastitis at first. However, no good response was achieved. Their surgical wounds could not heal well and kept producing pus. Concerning the clinical fact of the unhealed wound and granulomatous feature found in pathology specimen, we challenged these patients with antitubercular therapy by giving informed consent before.

*Correspondence to:
Odetta N. Halim, Department of
Surgery, Pariaman General Hospital,
West Sumatera, Indonesia
o_detta@yahoo.com

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By the time this report is written, five patients had completed their antitubercular therapy, while the remaining are still on medication. All patients have a good response, including healed wounds, better physical performance, and fitness. The most common side effects of the drugs are nausea and liver function disturbance.

DISCUSSION

Breast TB, even in the endemic area of TB infection, is a rare disease, mostly because breast, like skeletal muscles and spleen, is relatively resistant to the tubercle bacilli, as they do not provide a suitable environment for the survival and multiplication of the organism.⁵ Also, there is also under-reporting cases due to lack of awareness of clinical symptoms, misdiagnosis, and inadequate laboratory facilities.⁶

The majority of our patients were in their reproductive age and had a history of breastfeeding. Lactating women are more susceptible to getting breast TB because the breast is more vascularized with dilated ducts, predisposed to trauma and infection.⁷

Breast TB is classified into primary etiology when no demonstrable TB focus exists, or secondary to a co-existing lesion present elsewhere in the body, mainly located pulmonary.⁷ Primary disease occurs through abrasions or openings of the ducts in the nipple. While the more common, secondary form spreads through hematogenic, lymphatic, or by contiguous seeding from the ribs, pleural space, or rectus sheath from an intraabdominal source.⁸ Our patients were most probably cases of primary breast TB as they had no other organ involvement. However, Vassilakos stated that primary breast TB was quite rare and was diagnosed because the clinician could not detect the true TB focus.⁵

Four of our patients presented with lump, while others had pain, swelling, and nipple discharge. The lump is the commonest manifestation of breast TB, with the predilection location is the central or upper quadrant of the breast. It is probably due to a frequent extension of TB from axillary nodes to the breast.^{4,5} The lump is often indistinguishable from breast cancer, as it is irregular, hard and could be fixated to the skin or muscle even chest wall.⁵ The lump may progress to inflammation and abscess formation, skin ulceration and diffuse mastitis that resembles pyogenic abscess feature. Only less than 20% of cases present with generalized symptoms like fever, night sweats, malaise and weight loss.⁷ Purulent nipple discharge may rarely present.⁵ However, we had one patient with this uncommon complaint.

The diagnosis of breast TB is difficult because it has variable clinical and radiological features, with a wide range of differential diagnosis. Also, the percentage of smear positive for AFB is low.³ Detection of AFB in a smear requires more than 10,000 organisms/mL.⁴ A report from India stated that the rate of positive Ziehl-Neelsen smears for AFB was around 2%.³ Culture of *Mycobacterium tuberculosis* is the gold standard for diagnosing TB. However, it is not practical due to the time required and the possibility of false-negative results in paucibacillary specimens.⁵ We had only one patient with a positive result for AFB smear and culture.

Nucleic acid amplification test (NAAT) such as polymerase chain reaction (PCR) could be beneficial for detecting *M. tuberculosis* in nonrespiratory samples, which have a lower frequency of positive AFB smear.⁸ This is a rapid and specific method, but its sensitivity is quite low, as low as 50% in some series, especially in AFB smear-negative cases.⁴ PCR is recommended in cases in which culture is negative or for differential diagnosis between other forms of granulomatous mastitis.¹ A negative PCR result does not exclude TB disease with certainty.⁹ The role of PCR in the diagnosis of breast TB is less reported.^{8,9} We did not perform PCR to our patients.

Fine needle aspiration cytology (FNAC) is another method for diagnosis. Although FNAC from the breast lesions cannot determine the etiologic agent, the finding of both epithelioid cell granulomas and necrosis is enough for breast TB diagnosis, making a definitive diagnosis in almost 73% of cases. Failure to find necrosis on FNAC does not exclude breast TB.¹ In TB-endemic countries, finding of granuloma in FNAC could be the basis of starting empirical treatment for TB even in the absence of positive AFB and without culture results.^{8,10} We performed FNAC to one patient only, and the result revealed acute inflammatory cells with no sign of malignancy.

Histologically, breast TB is a form of granulomatous inflammation. It is an inflammatory process which could be caused by multiple etiologies, such as sarcoidosis, various fungal infections, and fat necrosis.⁵ To differentiate granulomatous mastitis from *M. tuberculosis* is very difficult and sometimes they can not be identified separately.¹⁰ A biopsy is mandatory for confirmation of diagnosis and also to rule out a co-existing malignancy.¹¹ The majority histopathological examination of our patients revealed granulomatous features.

Interferon-gamma release assays (IGRAs) are new TB diagnostic tools based on detection of a T-cell immune response to the TB antigens.

Table 1 Demographic and clinical data of the breast TB (n=7)

Characteristics	n
Age (in years)	
26-30	1
31-35	3
36-40	1
41-45	1
46-50	0
51-55	1
Marital status	
Single	0
Married	7
History of lactation	
Present	5
Absent	2
Sign and symptom	
Lump	4
Pain	1
Swelling	1
Nipple discharge	1
Involved breast	
Left	1
Right	5
Bilateral	1
Methods of diagnosis	
AFB* smear and culture	1
Histopathology Langhans' cells	1
IGRA*	1
Clinical judgment	4
Histopathological features	
Mastitis with abscess formation	3
Granulomatous mastitis	3
Langhans' giant cells and caseous necrosis	1

*AFB: Acid-fast bacilli; #IGRA: Interferon-gamma release assay

Currently, two commercial IGRAs are available: the QuantiFERON-TB® Gold in-tube assay (QFT-GIT) which measure interferon-gamma (IFN- γ) concentration by enzyme-linked immunosorbent assay (ELISA) and the SPOT® TB test (T-Spot) test which measure the number of IFN- γ -producing T cells (spot).¹²

IGRAs may be slightly superior to the tuberculin skin test (TST) in detecting latent TB infection. However, IGRAs cannot distinguish latent TB infection from active TB. Neither QFT-GIT nor T-Spot can provide enough sensitivity and

specificity for the diagnosis of extrapulmonary TB (EPTB), especially for patients from high TB burden countries. Pooled sensitivity for the diagnosis of EPTB was 72% [95% confidence interval (CI) 65-79%] for QFT-GIT and 90% (95% CI, 86-93%) for T-Spot; in high-income countries the sensitivity of QFT-GIT (79%, 95% CI 72-86%) was much higher than that (29%, 95% CI 14-48%) in low/middle-income countries. Pooled specificity for EPTB was 82% (95% CI 78-87%) for QFT-GIT and 68% (95% CI 64-73%) for T-Spot.¹² Therefore, these methods have no utility in the diagnosis and treatment in highly endemic countries.¹³ A negative IGRA result does not exclude TB disease. IGRAs should be considered as an adjunct, not to replace the clinical evaluation of those suspected of having TB.¹⁴ We had one patient with positive IGRA result.

Treatment of breast TB consists of antitubercular drugs with limited surgical intervention. The success rate of medical therapy reaches 95% in most cases with six months antitubercular treatment (two months of isoniazid, rifampicin, pyrazinamide, and ethambutol, followed by four months of isoniazid and rifampicin). Some authors prefer the 9-month regimen due to lower relapse rate in general. Surgery is performed for biopsy to help in diagnosis, aspiration, and drainage of abscess, and excision of residual sinuses and masses. Simple mastectomy is reserved for cases with extensive disease, causing a significant painful ulcerated mass involving the entire breast.^{5,7,8}

Breast TB is a diagnosis of exclusion. The differential diagnosis of breast lesions breast TB should be included especially for patients from high-risk populations and endemic regions. The trial of antitubercular therapy is recommended in case of high clinical suspicion of TB.¹⁰

CONCLUSION

Despite its rare incidence, breast TB should always be included in the differential diagnosis of breast lump, abscess or fistula with poor response to empiric antibiotic treatment, especially in TB endemic countries like Indonesia. Routine diagnostic procedures such as AFB smear, culture and PCR do not have the same diagnostic utility as they do in pulmonary TB. FNAC and biopsy may also be inconclusive. Diagnosis is usually based on a high index of suspicion, finding of a granulomatous lesion with Langhans giant cells and excellent response to antitubercular drugs. Treatment of choice consists of antitubercular medications and minimal surgical intervention.

CONFLICT OF INTEREST

All authors declare there is no conflict of interest regarding publication of this manuscript and have got patient's permission in this article.

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