MASTITIS TUBERKULOSIS PRIMER GAMBARAN KLINIS MENYERUPAI FIBROADENOMA MAMMAE

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ABSTRAK

Pendahuluan: Tuberkulosis payudara (mastitis TB) merupakan gambaran tuberculosis ekstra paru yang jarang terjadi ditandai secara patologis dengan keterlibatan mamma lobules secara ekstensif, yang disebabkan oleh infeksi *Mycobacterium tuberculosis*. Banyak studi epidemiologi menyatakan bahwa insiden mastitis TB lebih umum di negara berkembang daripada negara maju. Mastitis TB terjadi terutama pada wanita reproduktif.

Kasus: Seorang wanita, usia 32 tahun datang ke poli Bedah dengan keluhan utama benjolan payudara di kuadran kanan atas teraba sejak 4 bulan yang lalu. Pada pemeriksaan fisik payudara kanan ditemukan nodul tunggal, diameter ±3cm x 3cm x 2.5cm di kuadran superior, mobile, lunak, batas tegas, teraba seperti kelereng, kulit kemerahan, teraba hangat, tidak ada retraksi kulit dan sekret yang keluar dari puting payudara. Skala nyeri 2. Mammosonogram dilakukan dan kesan mastitis di kuadran superior payudara kanan. Aspirasi jarum halus didapatkna sel ganas negatif dan peradangan granulomatosa dan supuratif. Evaluasi histopatologi jaringan dari eksisi mammae didapatkan sel datia langhans dan kesan mastitis granulomatosa. Pasien dirujuk ke poli Paru. Pada pemeriksaan TB paru foto thorax normal dan tes basil tahan asam (BTA) normal. Pasien didiagnosis dengan mastitis TB primer. Pasien diberikan terapi obat anti tuberkulosis (OAT) dan memberikan respons yang baik tanpa ada efek samping.

Diskusi: Berdasarkan International Standart for Tuberculosis Care (ISTC) penegakan diagnosis mastititis TB dipastikan melalui anamnesis, pemeriksaan fisik, dan pemeriksaan penunjang seperti pencitraan sonomammografi, aspirasi jarum halus atau spesimen bedah untuk pemeriksaan patologi jaringan, kultur atau BTA dengan pewarnaan Ziehl-Neelsen. Dalam Pedoman Nasional Pengendalian TB, mastitis TB diobati dengan menggunakan oral anti tuberculosis (OAT), pada fase intensif 2 bulan pertama menggunakan 4 FDC dan fase lanjutan selama 4 bulan selanjutnya menggunakan 2 FDC. Pada kasus dievaluasi selama 2 bulan, kondisi pasien membaik dan disarankan untuk melanjutkan perawatan

Kesimpulan: Mastitis TB jarang terjadi sekalipun di negara dengan endemis TB. Penegakan diagnosis mastitis TB primer berdasarkan klinis, radiologis, patologi dan mikrobiologi. Terapi mastitis TB dengan OAT selama 6 bulan, terdiri dari fase intensif dan fase lanjutan.

Kata Kunci: mastitis tuberkulosis, diagnosis, pengobatan

PRIMARY MASTITIS TUBERCULOSIS CLINICALLY MIMICKING FIBROADENOMA MAMMAE

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ABSTRACT

Introduction: *Breast tuberculosis (mastitis TB) is a rare extrapulmonary presentation of tuberculosis that marked pathologily with involvement extensively mamma lobules, which because of infection of Mycobacterium tuberculosis. Many epidemiology studies stated that the incidence of mastitis TB is more common in developing countries than developed countries. Mastitis TB occurs mainly in reproductive woman.*

Case: *A 32-year-old woman came to Surgery Department with chief complaint right upper quadrant palpable breast lump for 4 months. Mammae dextra physical examination confirmed single nodule, size ± 3cm x 3cm x 2.5cm in superior quadrant, mobile, tender, well defined shape, feel like marble, reddish skin, warm, no skin retraction and no nipple discharge. VAS score 2. Mammosonogram was performed and indicated mastitis in the superior quadrant of mammae dextra. Fine needle aspiration revealed negative malignant cells and granulomatous with suppurative inflammation. The histopathological evaluation from mammae excision confirmed datia langhans cells and indicated granulomatous mastitis. Then patient referred to the Pulmonary Department. On TB pulmonary examination confirmed normal chest x-ray and negative acid fast basil (AFB). Patient was diagnosed with primary mastitis TB. Patient was treated with anti-tuberculosis drug (OAT) and gave good response and no side effects.*

Discussion: *Based on the International Standards for Tuberculosis Care (ISTC) diagnosis of mastitis TB can be confirm by anamnesis, physical examination, and also some additional diagnostic test such as sonomammographic imaging, fine needle aspiration or surgical specimens for pathology examination and culture or AFB with Ziehl-Neelsen staining. In Indonesian National Guidelines for TB Control, mastitis TB was treated with fixed drug combination (FDC), intensive phase in 2 months using 4 FDC and advanced phase in 4 months using 2 FDC. In case followed up in 2 months, patient recovered very well and advised to continue the treatment.*

Conclusions: *TB mastitis is rare even in countries with TB endemic. Diagnosis of primary mastitis TB based on clinical, radiological, pathological and microbiological. Treatment of mastitis TB with FDC for 6 months consists of an intensive phase and an advanced phase in this patient gave good outcome.*

Keywords: *mastitis tuberculosis, diagnosis, treatment*

BACKGROUND

TB is an infectious disease caused by the bacillus Mycobacterium tuberculosis. TB typically affects the lungs (pulmonary TB) but can also affect other sites (extrapulmonary TB). Extrapulmonary TB represented 15% of the 6.1 million incident cases that were notified, ranging from 8% in the WHO Western Pacific Region to 23% in the Eastern Mediterranean Region.[1]

Breast tuberculosis (mastitis TB) is a rare extrapulmonary presentation of tuberculosis that marked pathologily with involvement extensively mamma lobules, which because of infection of Mycobacterium tuberculosis. Mastitis TB is rare clinical entity, often mimicking fibroadenoma mammae, breast cancer or abscess of benign or malignant origin. Many epidemiology studies stated that the incidence of mastitis TB is more common in developing countries than developed countries. Mastitis TB occurs mainly in reproductive woman.[1,2]

This report is to detail our experience of the difficulties in diagnosing breast tuberculosis, especially in the absence of other specific clinical sign and to emphasize the anti tuberculosis therapy.

CASE PRESENTATION

A 32-year-old female came to Surgery Departement Bethesda Hospital with chief complaint a palpable breast lump in right upper quadrant. She revealed a 4 months history of gradually growing breast lump, which was initially palpated during breast self-examination. Mammae dextra physical examination confirmed single nodule and tender mass was palpable in the superior quadrant of the right breast. These measured about ± 3cm x 3cm x 2.5cm respectively. It was mobile, not attached to the overlying skin, well defined shape, feel like marble. No nipple discharge. Areola were normal. Overlying skin were reddish, warm, no skin retraction. Visual analogue score (VAS) 2. The right axillary lymph nodes were normal. The left breast was normal. No history of lactating.

Patient was motivated to perform mammosonogram examination. The result of the mammosonogram was widening of the lactiferous ductus. On the color flow mapping, dominant vascular flow in the superior quadrant was seen. No lympadenopathy found in both axilla. Thus, the patient diagnosed suspect mastitis in the superior quadrant of mammae dextra (Figure 1). The patient is recommended to do a fine needle aspiration (FNA). FNA in the right mammae performed after 4 days. From cytologic result, malignant cells were negative and there was inflammation of granulomatous with suppurative inflammation. The patient diagnosed with mastitis mammae dextra. The patient treated with oral antibiotic and some analgesics.

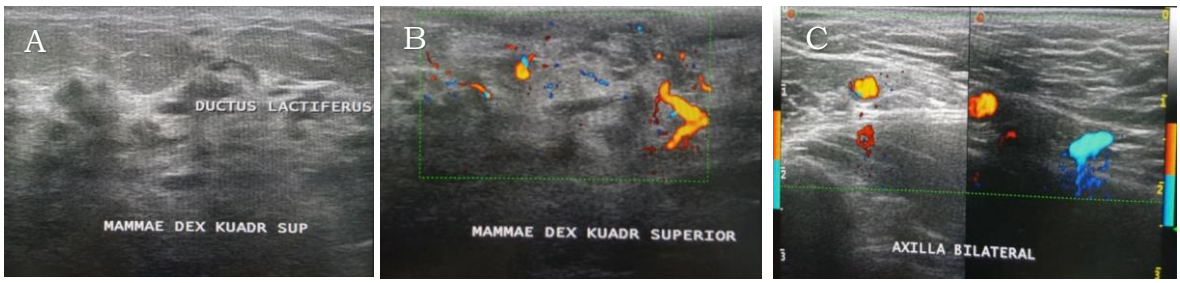

Figure 1: A. Dextra mammosonogram appears dilation of the lactiferous ducts; B. Color flow mapping appears to be the dominant vascular flow in the superior quadrant; C. Bilateral axillar is not seen lympadenopathy.

Patient came again to Oncology Department after 3 months with same complaints, no improvement and getting worse. Tumor marker analysis revealed that Ca125 slightly elevated, while a-FP and CEA level were all within normal limits. Patient was advised to do an excision biopsi. Biopsi was thereafter performed and sent for pathological examination. This revealed an unencapsulated, irregularly shaped fibro fatty soft tissue measuring 8.0 x 6.0 x 3cm. Histology, however, showed numerous granulomas tissue, tubercle, surrounded by inflammatory response typical epithelioid macrophages and lymphocytes (Figure 1A). There were a few Langhans type multinucleated giant cells in between the macrophages (Figure 1B). Malignant cells were negative.

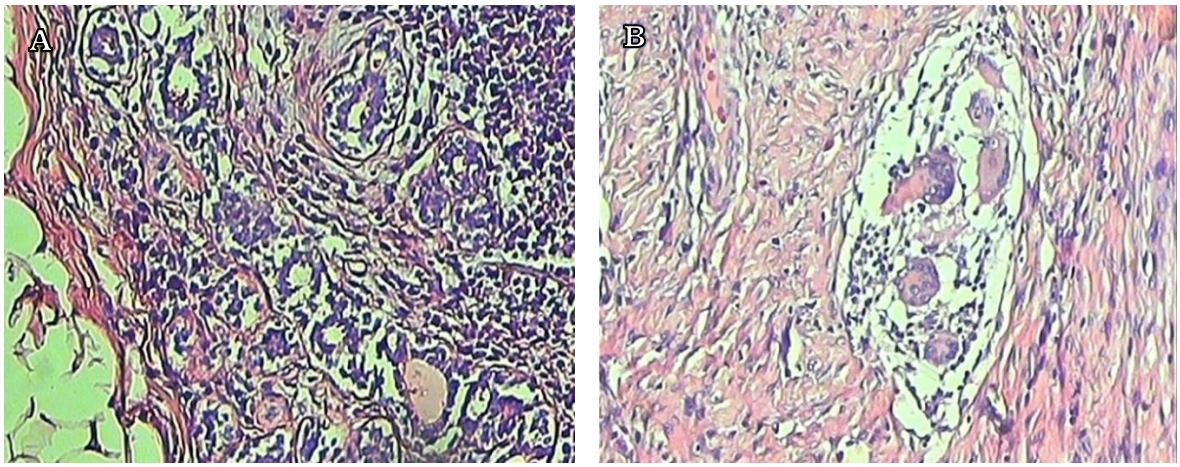

Figure 2: A. Numerous granulomas tissue, tubercle, surrounded by typical epithelioid macrophages and lymphocytes; B. Langhans type multinucleated giant cells in between the macrophages

The patient is referred from Oncology Department to Pulmonary Department. She denied had cough more than 2 weeks, coughing up blood, chest pain, shortness of breath, night sweats, and weight loss. Patients also denied any history of smoking, asthma, heart disease, diabetes, family history of TB and breast cancer, and previous consumed anti-tuberculosis treatment (OAT). The vital signs were afebrile and normal blood pressure. General physical examination of lung did not get abnormalities. Laboratory workup, complete blood lab test results were normal. The sputum test with Ziehl Neelsen staining was done and the result is negative. Her chest x-ray performed bronchovascular pattern increase, minimal air bronchograms.

Patient was commenced on fixed drug combination (FDC) 5 tabs/ day (rifampicin 750 mg, isoniazid 375 mg, pyrazinamide 2000 mg and ethambutol 1375 mg per day) (Weight: 71 kg). She started intensive therapy for 2 months using 4 FDC. There are no clinical side effects. Scars and excision in right breast got dried. After that the treatment is currently continued with the advanced phase in 4 months using 2 FDC 5 tabs, 3 times per week (rifampicin 750 mg, isoniazid 375 mg). Patient observed in 2 month. Patient recovered very well and advised to continue treatment. No side effects from treatment.

DISSCUSSION

Extra-pulmonary tuberculosis occurring in the breast is relatively rare despite one third of the world's

population being infected with tubercle bacilli. Tuberculosis of the breast was first documented in medical literature by Sir Astley Cooper in 1829. Though cases of tuberculous mastitis have been reported worldwide.[3]

Tabel 1: Notifications of TB, TB/HIV and MDR/RR-TB cases, globally and for WHO regions 2016.[1]

	Total Notified	New and Relapse	Pulmonary New and Relapse		Extra-pulmonary New and Relapse (%)	HIV Positive and Relapse	MDR/RR-TB	XDR-TB
			Number	Of Which Bacteriologically Confirmed (%)				
Africa	1.303.483	1.273.560	1.056.327	66%	16%	358.237	27.828	1.092
The Americas	233.793	221.008	186.940	77%	15%	20.528	3.715	112
Eastern Mediterranean	527.693	514.449	390.367	53%	24%	1.367	4.713	152
Europe	260.434	219.867	187.898	64%	15%	24.871	49.442	3.114
South East Asia	2.898.482	2.707.879	2.291.793	61%	15%	60.245	46.269	2.926
Western Pacific	1.400.638	1.372.371	1.268.798	38%	8%	11.526	21.152	618
GLOBAL	6.624.523	6.309.134	5.391.123	57%	15%	476.774	153.119	8.014

Epidemiologic studies have shown breast TB is a disease that occurs much more frequently in women of reproductive age between 20 and 50 years of age, especially among multiparous and lactating females where breast is more sensitive to infection and trauma.[2]

Tewari and Shukla suggested that breast tuberculosis be lumped into three categories base on clinical characteristics. They suggest lumping all cases into three types: Nodular variants, Disseminated variants, and Abscess variants.[4] *The nodular variants is well circumscribed; slow growing, with an oval tumor shadow on mammography. The disseminated variants is characterized by multiple lesions associated with sinus formation. The abcess/ sclerosing variant of the disease is seen in elderly women and is characterized by an excessive fibrotic process.*[4,5] *Our patient would be categorized as having a nodular variant. On examination, her presentation suggested palpable nodule tender mass, well defineded shape in the superior quadrant of the right breast, that after biopsy had showed numerous granulomas tissue, tubercle, surrounded inflammatory response by typical epithelioid macrophages and lymphocytes. There were a few Langhans type multinucleated giant cells in between the macrophages.*

Tuberculosis of the breast is a rare disease, mostly because organs or tissues like the breast, skeletal muscle and spleen are more resistant to infection, making the survival and multiplication of the tubercle bacilli difficult.[5] *Tuberculous mastitis may be primary, although this is extremely rare, or secondary.*[2,4,5] *Mastitis TB may be primary when no other focus of tuberculosis is detectable or secondary when a source can be identified, mainly located pulmonary. In many cases of mastitis TB, it is not known how the mycobacterium entered the breast tissue. The leading theory in most cases is that it spread to the breast via retrograde lymphatic flow from ipsilateral lymph nodes. However, other causes of spread include hematogenous, direct inoculation through traumatized skin or breast ductal system, and contiguous spread from the chest wall, pleura, and so forth.*[4,5]

Clinical presentation is extremely variable. The commonest clinical presentation is that of round nodular lump, single or multiple, with or without a duct, painful or not,

mainly located in the central or upper outer quadrant of the breast. In advance form mastitis TB can mimic breast carcinoma, lump being hard, with irregular border, fixed to either the skin or the muscle or even to the chest wall, invasion of the skin with skin and nipple retraction creating peau d'orange sign, but breast discharge is uncommon. The lump may be followed by inflammation and abscess formation, skin ulceration and diffuse mastitis. Symptoms like fever, malaise, night sweats and weight loss are present in less than 20% of the cases.[1,2,5]

Various tests are useful in the diagnosis and further evaluation of patients with breast tuberculosis. Based on the International Standards for Tuberculosis Care (ISTC) diagnosis of TB mastititis includes sonomammographic imaging, fine needle aspiration or surgical specimens for pathology examination, culture or AFB with Ziehl-Neelsen staining.[6]

In the case of our patient, clinical examination failed to differentiate mastitis TB with fibroadenoma mammae or carsinoma mammae. The gold standard for diagnosis remains detection of M. tuberculosis by Ziehl Neelsen staining or by culture, but a high index of suspicion is necessary in countries in which TB is not endemic.[2,4,5,7] *Fine needle aspiration remains an excellent tool for demonstrating histology compatible with tuberculosis. Fine needle aspiration cytology may not be able to detect the responsible pathogen itself, but is detecting the presence of epithelioid cell granulomas and necrosis, leading to definitive diagnosis in up to 73% of cases. Histopathology of the lesion identifies a chronic granulomatous inflammation with caseous necrosis and Langhans-type giant cells, contributing to diagnosis in the majority of the cases.*[2,5] *Distinguishing idiopathic granulomatous mastitis from tuberculous mastitis is extremely important as treatment options of the former may include steroids. Steroids may fl are up tuberculosis; and in tuberculosis-endemic regions, empiric antituberculous therapy may be warranted before considering steroids therapy.*[8]

Tabel 2: Distinguishing features of tuberculous mastitis and idiopathic granulomatous mastitis.[8]

	Granulomatous Mistitis	
Clinical	**Idiopathic granulomatus mistitis** • Appears after pregnancy • No constitutional symptoms • No relation to breast feeding • Possible relation with oral pills • Age 17-42 years • Parous patient • Hard mass, any site of breast but spare subareolar area • Bilateral is uncommon • Rare nipple discharge • Tenderness present • Rare axillary LN enlargement • Size of mass 1-8 cm • Clinically and Radiologically mimics carcinoma	**Tuberculous mistitis** • No relation to pregnancy • Constitutional symptoms present • No relation to breast feeding • No relation eith oral pills • Any age • Parous and Nonparous • Hard mass any site of breast • Bilateral is common • Accasional nipple discharge • Tenderness rare • Axillary LN can be enlarged • Size of mass 1-8 cm • Clinically and Radiologically mimics carcinoma

	Granulomatous Mistitis	
Histology	**Idiopathic** • Lobules of Breast are affected • Granulomas within the lobules • Granuloma composed of Histiocytes, Langharns giant cells, lymphocytes, plasma cells, and occasional eosinophills • Caseation necrosis absent • Fat necrosis • Fibrosis • Abscess common	**Tuberculosis** • Any component of Breast tissue is affected (lobiles, ducts and fat) • Granulomas anywhere • Granuloma composed of Histiocytes, Langhans giant cells, lymphocytes, rare plasma cells and eosinophills • Cascation necrosis present • Fat necrosis • Fibrosis • Abscess uncommon

Mantoux testing does not offer definitive diagnosis, but confirms exposure of the patient to tubercle bacilli. Mammography is not helpful, especially in young women, due to high density of the breast tissue. At USG mammosonogram, a hypoechogenic mass is found in 60% of patients. CT-scan and MRI are used to evaluate the extension of the lesion beyond the breast, principally towards the thoracic wall.[2,5]

The principal differential diagnosis of mastitis TB is that of breast carcinoma. Other diseases of the breast such as fatty necrosis, plasma cell mastitis, periareolar abscess, idiopathic granulomatous mastitis and infections like actinomycosis and blastomycosis are to be considered.[5]

The treatment of breast TB consists of anti-tubercular treatment and surgery by specific indications.[5] *Anti-TB treatment is the mainstay in the management of breast TB but is controversial. Most current guidelines recommend the same regimen for both pulmonary TB and extrapulmonary TB.*[9] *When mastitis TB achieved, anti-TB therapy is the mainstay of therapy with studies showing high success rates.*[4]

Anti-tubercular therapy with four drugs is the primary line of treatment. The six-month regimen comprises of a two-month intensive phase with four drugs used orally (ethambutol, pyrazinamide, rifampicin and isoniazid), followed by a continuation phase of four months with two drugs (isoniazid and rifampicin). The treatment is for 6 months and results in a good clinical response. Most series have reported a success rate of medical therapy to be approximately 95%.[5,10,11,12]

Surgical intervention in the form of an excisional biopsy is necessary mainly for diagnostic purposes and is required for excision of residual sinus tracts or lumps after poor response to anti-tuberculosis therapy. Simple mastectomy, most often without axillary lymph node dissection, is reserved for cases with extensive disease.[7] *In this case based on the National Guidelines for TB Control and Pedoman Nasional Pengendalian Tuberkulosis, mastitis TB was treated with FDC, intensive phase in 2 months using 4 FDC, 5 tabs/ day (rifampicin 750 mg, isoniazid 375 mg, pyrazinamide 2000 mg and ethambutol 1375 mg per day) and advanced phase in 4 months using 2 FDC 5 tabs, 3 times per week (rifampicin 750 mg, isoniazid 375 mg). Follow up in 2 months, patient recovered very well and advised to continue treatment.*[11,12]

CONCLUSION

TB mastitis is rare even in countries with TB endemic. Diagnosis of primary mastitis TB based on clinical, radiological, pathological and microbiological. Treatment of TB mastitis with OAT for 6 months consists of an intensive phase and an advanced phase.

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