REVIEW ARTICLE

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Breast tuberculosis
Tuberculosis mamaria

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ABSTRACT
Mammary tuberculosis is an uncommon presentation of Mycobacterium tuberculosis infection, which constitutes a differential diagnosis of chronic breast lesions after ruling out malignant disease. In endemic areas, it primarily affects young women (between 20 and 40 years old) from rural areas, who are breastfeeding, with a history of pulmonary tuberculosis, or coinfected with HIV. Clinical and imaging findings are nonspecific, and the diagnosis is based on clinical suspicion and culture or inspection of the bacillus in breast tissue by biopsy. Pathognomonic features include granulomas composed of epithelioid cells with a central area of caseous necrosis and multinucleated Langhans giant cells in the periphery, located in the ductal lobular unit. Treatment has a high recovery rate and is primarily pharmacological, requiring surgical intervention only in selected cases. The present review aims to describe the clinicopathological characteristics, epidemiology and approach to breast tuberculosis, to expedite diagnosis and timely treatment.
Keywords: Mycobacterium tuberculosis, breast diseases, tuberculosis, diagnosis, treatment, mastitis.

RESUMEN
La tuberculosis mamaria es una presentación infrecuente de la infección por Mycobacterium tuberculosis, la cual constituye un diagnóstico diferencial de lesiones crónicas mamarias posterior al descarte de proceso neoplásico. En áreas endémicas afecta principalmente a mujeres jóvenes (entre los 20 y 40 años) provenientes de áreas rurales, que estén dando de lactar, con el antecedente de tuberculosis pulmonar o coinfectadas con el VIH. La prestación clínica e imagenológica, es inespecífica, y el diagnóstico se establece en base a una sospecha clínica y al cultivo o inspección del bacilo en el tejido mamario mediante biopsia, siendo patognomónico la visualización de granulomas conformados por células epitelioides con área central de necrosis caseosa, y células gigantes multinucleadas de Langhans en la periferia ubicados en la unidad ducto lobular. El tratamiento, tiene una alta tasa de recuperación, y es principalmente farmacologico, requieriendose solo en casos seleccionados el abordaje quirúrgico. La presente revisión, tiene como objetivo, describir las características clínico-patológicas, epidemiología y abordaje de la tuberculosis mamaria, con el fin de agilizar el diagnóstico y tratamiento oportuno.
Palabras clave: Mycobacterium tuberculosis, enfermedades de la mama, tuberculosis, diagnóstico, tratamiento, mastitis.

Introduction

Infection with Mycobacterium tuberculosis represents a significant disease burden in developing countries, such as Peru, which, according to the World Health Organization (WHO), has an incidence of 106 cases per 100,000 inhabitants[1]. Among the extrapulmonary forms of tuberculosis, the mammary form is rare, even in endemic areas, where it is associated with women of childbearing age who are breastfeeding or co-infected with the human immunodeficiency virus (HIV)[2]. In endemic areas, the incidence of breast tuberculosis ranges from 0.1% to 4% of extrapulmonary tuberculosis cases[3]. Given the nonspecific clinical presentation and the potential absence of an initial pulmonary focus, these cases are difficult to diagnose and require thorough investigations and the exclusion of differential diagnoses such as granulomatous mastopathy, abscesses, or breast cancer[1].

Given that this condition has been insufficiently studied in terms of its clinical management, and that it represents a differential diagnosis that should be considered in cases of undetermined mastitis—particularly in endemic regions with a high burden of tuberculosis—this review aims to describe the clinicopathological features, epidemiology, and management of breast tuberculosis, with the purpose of optimizing timely diagnosis and treatment.

Search methodology

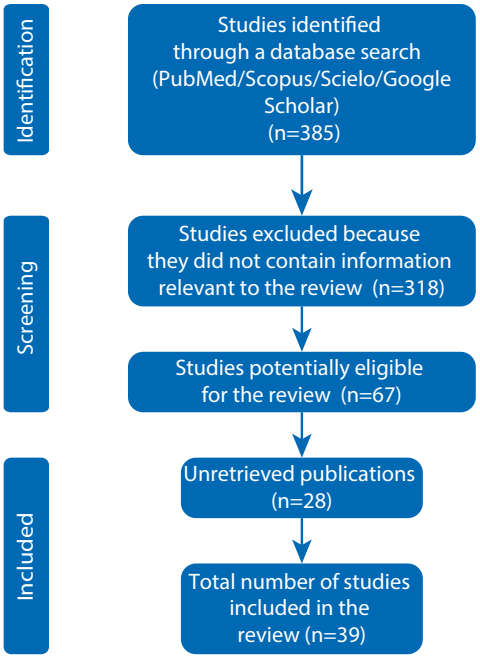
This narrative review was conducted in accordance with the PRISMA Statement guidelines [4]. The review was based on a search of PubMed, Scielo, Google Scholar, and Scopus conducted between October 21, 2024, and November 3, 2025. The following terms were used: "mastitis," "tuberculosis," "diagnosis," and "treatment," as they are directly related to the clinical nature and the diagnostic-therapeutic approach of the topic in question.

The qualitative criteria for selecting the studies were: a) original articles, short original articles, systematic reviews, case reports, reports, and technical guidelines; b) written in English, Spanish, or Portuguese.

Articles that provided relevant information on mammary tuberculosis, as well as epidemiological, clinical, diagnostic, and therapeutic data, were included. Regarding the approach, priority was given to studies conducted in countries with a high disease burden due to Mycobacterium tuberculosis.

Of the 385 articles initially selected, 318 were excluded for failing to meet the selection criteria. Subsequently, 67 potentially eligible studies were selected. Access to 28 articles was unavailable. Finally, 39 articles were included (Figure 1).

Figure 1: PRISMA flowchart



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Overview

Clinical Characteristics

Breast tuberculosis is a rare form of extrapulmonary tuberculosis with a reported average prevalence of 1.7% of cases[5], however, a Peruvian study found that in 2010 this condition accounted for 2%[2] of all extrapulmonary tuberculosis cases, while an observational study conducted at the Madre Niño San Bartolomé National Teaching Hospital found a rate of 2.9% in the Lima metropolitan area between 2002 and 2011[6].

The condition affects women aged 20 to 40[7] from rural areas (68.3%)[6], residents of or originating from regions with a high tuberculosis burden (sub-Saharan Africa, Southeast Asia, the Western Pacific, or Latin America)[8], who are breastfeeding (33% of cases according to an Indian retrospective study)[9], or co-infected with HIV[10], although it has also been reported in a 76-year-old patient without the aforementioned risk factors[1]. According to an observational study, only 10.3% of cases were associated with pulmonary symptoms, and the duration of illness ranged from 3 to 4 months in 70% of patients[6]. The history of prior tuberculosis infection was present in 19% of cases according to a systematic review of 1,478 patients[5]. Finally, according to a cohort study conducted in China, recurrence rates reached up to 29.5% after completing treatment, with a median time to recurrence of 5.7 years for non-multidrug-resistant tuberculosis and 7.2 years for multidrug-resistant tuberculosis[11].

The mode of infection can be categorized based on whether the patient is breastfeeding.

- Lactation: In breastfeeding patients, the route of entry is ascending through skin abrasions caused by the baby's sucking and increased dilation of the milk ducts due to the action of oxytocin[10]. In addition, increased vascularization and relative suppression of T-helper cells during pregnancy are contributing factors[12].

- Non-lactating: In patients without a history of breastfeeding, infection occurs primarily through lymphatic or hematogenous spread from an active or latent focus (Cooper's theory) [13]; this is why affected patients present with symptoms in the upper outer quadrant of the breast and involvement of the lymphatic chains in 40% of cases[14, 6].

According to the literature reviewed, there are four clinical presentations: chronic obliterative tuberculous mastitis, sclerosing tuberculosis, acute miliary tuberculosis, and tuberculous mastitis[14]; however, a 2005 review conducted in India simplifies this to three forms: caseous nodular tuberculous mastitis, tuberculous breast abscess, and disseminated tuberculous mastitis[15].

The most common form of presentation is the nodular form; a descriptive, retrospective study of 69 patients with this diagnosis who were enrolled in the Tuberculosis Control Program reported that 89.89% had a single nodule[16] located predominantly in the right breast[17], and may also be accompanied by pain, inflammatory signs, and mastalgia (31%) in the affected area, as well as purulent drainage and fistulas (20.7%) [6, 14]. In some cases, due to fibrosis (present in half of the cases) of the breast tissue and Cooper's ligaments secondary to the granulomatous reaction, there may be nipple retraction (present in less than 60% of cases and associated with advanced cases)[16], leading the initial diagnostic approach to favor breast cancer over an infectious etiology[7, 6]. Regarding systemic symptoms (night sweats, weight loss, and fever), these are present in only one-fifth of patients[14], which contributes to diagnostic delay; according to a retrospective review of 20 cases at Getúlio Vargas Hospital in Brazil, the average delay was 7.7 months (range 3–12 months)[17]. Atypical cases may even occur, as evidenced by a Qatari case report in which the presentation was accompanied by reactive arthritis and erythema nodosum[8].

Diagnosis

The gold standard for diagnosing breast tuberculosis is the Löwenstein-Jensen culture or the detection of bacilli via Ziehl-Nielsen staining in breast tissue obtained through a histopathological biopsy; however, these methods yield positive results in only 25% and 12% of cases, respectively[18].

The initial invasive method is fine-needle aspiration biopsy, which allows for the diagnosis of tuberculous mastopathy in 75% of cases, while excisional biopsy allows for a better evaluation of the differential diagnoses, which include[19]:

a. **Idiopathic granulomatous mastitis (IGM):** a benign disease of unknown cause that affects women of childbearing age, with a pathological anatomy characterized by lobular granulomas containing epithelioid histiocytes without caseous necrosis[16, 20, 21, 22]. The primary differential diagnosis is tuberculous mastitis; this was reported in a three-year follow-up cohort study conducted at ESIC Hospital in Turkey, in which 4 out of 10 patients initially diagnosed with IGM were later confirmed to have tuberculous mastopathy[23]. Another study with similar characteristics involving 152 patients initially diagnosed with MGI found that 11% (16 patients) responded to antituberculosis therapy[24].

b. **Rheumatological conditions (sarcoidosis and granulomatosis with polyangiitis):** autoimmune diseases characterized by noncaseating granulomas that primarily affect women of childbearing age. Systemic involvement must be addressed, and an immunological profile must be established to confirm the diagnosis. Good response to immunomodulatory therapy[25].

c. **Neoplastic breast process:** especially in patients with inflammatory symptoms, nipple retraction, or localization in the upper outer quadrant, it can be confused with Paget's disease and inflammatory breast cancer[26].

d. **Breast abscesses:** caused by S. aureus in 87.5–97.6% of cases (the most common causative agent, primarily affecting breastfeeding women), anaerobes (in non-breastfeeding women), Staphylococcus epidermidis, Vidrians, Corynebacterium[27], and more rarely by F. tularensis and B. henselae[28].

The pathognomonic biopsy of breast tuberculosis contains granulomas composed of epithelioid cells with a central area of caseous necrosis and multinucleated Langhans giant cells at the

periphery. According to a retrospective case series study conducted at the Cayetano Heredia National Hospital, these granulomas are in the lobular duct unit in 40.58% of cases, with suppurative granulomas being the most common, accounting for 85.51% of cases[16].

According to Veyssière, due to the difficulty of obtaining a culture and identifying the bacillus in breast tissue biopsies, he considers that the presence of caseating necrosis in the biopsy of a patient with clinical features suggestive of breast tuberculosis is just as confirmatory as isolating Koch's bacillus, a finding also supported by case series studies[29, 30].

If the pathological and microbiological tests are negative, it is recommended to use the IS6110 sequence (an insertion element located in the M. tuberculosis genome) via the PCR technique. Although its performance in breast tuberculosis has not yet been determined[14], in cases of extrapulmonary tuberculosis, it has a sensitivity of 50% and a specificity of 93.4%, respectively[31], like Gen Probe or AMPLICOR-MTB[32].

Imaging tests are often nonspecific and are typically used to rule out differential diagnoses; radiographically, three characteristic patterns are described (nodular, disseminated, and sclerosing), with the first two being confused with breast cancer, while the third is associated with extensive fibrosis[33]. Serial ultrasound is particularly useful for monitoring patients who have already started antituberculosis treatment[7].

In the case of the PPD test, routine use is not recommended due to its low sensitivity, especially in endemic areas where most of the population has been exposed to Koch's bacillus[34].

Although the time required to reach a definitive diagnosis varies and depends on the characteristics of the healthcare system, a retrospective study by Kaohsiung Medical Center (Taiwan) found an average of 54.4 days from symptom onset to definitive treatment[13], although diagnosis may take up to a year or more after symptom onset in developing countries[35].

Treatment

Treatment is primarily pharmacological, with success rates exceeding 90% [14]. The drug regimen may vary depending on the country, region, and resistance profile of the bacillus. Although there are no specific guidelines for mammary tuberculosis, we have included the 6-month treatment regimen for drug-sensitive extrapulmonary tuberculosis stipulated in the Technical Health Standard for the Prevention and Control of Tuberculosis NTS No. 221-MINSA/DGIESP-2024 [36] of the Ministry of Health, currently in force in Peru:

Initial phase (2 months):

- Isoniazid (H): 300 mg/day
- Pyridoxine (vitamin B6): 10 mg/day
- Rifampicin (R): 600 mg/day
- Pyrazinamide (Z): 1500 mg/day
- Ethambutol (E): 1200 mg/day

Maintenance phase (4 months):

- Isoniazid (H): 300 mg/day
- Pyridoxine (vitamin B6): 10 mg/day
- Rifampicin (R): 600 mg/day

In addition, a study conducted in Turkey administered a regimen of isoniazid (300 mg/day), rifampin (600 mg/day), morphazinamide (2.5 g/day), and ethambutol (1.5 g/day) for two months, followed by continued treatment with isoniazid and rifampicin for up to nine months, in a male patient diagnosed with breast and osteoarticular tuberculosis, after which there was complete remission of the condition[37]. Meanwhile, in the case of a woman with symptoms consistent with isolated breast tuberculosis 13 months after her last pregnancy, the regimen of isoniazid 300 mg, rifampicin 600 mg, pyrazinamide 1500 mg, and ethambutol 1000 mg daily for 2 months,

followed by rifampicin and isoniazid for an additional four months, resulting in remission of the lesions[10]. Finally, a third regimen administered to a nulliparous patient at General Hospital Zone No. 1 (Mexico), who had previously been immunosuppressed with methotrexate and prednisone, consisted of an intensive phase of rifampicin 150 mg, 75 mg of isoniazid, 400 mg of pyrazinamide, and 300 mg of ethambutol for 10 weeks, followed by 300 mg of rifampicin and 400 mg of isoniazid for 15 weeks[38].

Surgical intervention accounts for only 0.1% to 3% of cases and is reserved for cases of widespread disease, resistance to antituberculosis treatment, fistula formation, extensive painful ulcers, and abscess drainage[14, 7]. According to a systematic review of surgical cases, excision was performed in 39% of cases, drainage in 23%, and mastectomy in 5%[5].

Special consideration must be given to immunosuppressive therapy in the context of breast disease of undetermined etiology. Since most cases of breast tuberculosis are initially misdiagnosed as IGM, the use of glucocorticoids (1 mg/kg/day of prednisone three times a week) and/or methotrexate (10 mg weekly)[39], by causing immunosuppression, worsens the infectious condition[40].

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