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CASE REPORT

Integrative Medicine Treatment Strategy for Tuberculosis of the Breast Combined with Granulomatous Mastitis: A Case Report

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Background: Breast tuberculosis (BTB) is a clinically rare breast disease, and cases of BTB combined with granulomatous mastitis are even rarer. This type of disease is straightforward to misdiagnose or overlook during clinical diagnosis, thereby delaying treatment.
Methods: This case report describes a rare case of granulomatous mastitis complicated by breast tuberculosis in an elderly female patient admitted to the Breast Surgery Department of Beijing Traditional Chinese Medicine Hospital affiliated with Capital Medical University. Through a retrospective analysis of the integrated traditional Chinese and Western medicine treatment process, this study compares the patient's condition after three follow-up visits following the implementation of a traditional Chinese medicine (TCM) treatment regimen, as well as the six-month post-operative follow-up outcomes. Additionally, by referencing relevant prior literature, this study analyzes and summarizes the current status of diagnostic and therapeutic research on BTB.
Results: In this case, granulomatous mastitis was the first symptom in the early stage, and traditional Chinese medicine soup was taken internally as well as poultices applied externally, with a relatively obvious clinical effect. The diagnosis was confirmed by ultrasound, CT, tissue biopsy, Mycobacterium tuberculosis acid-fast stained smear, and other tests. The patient was treated surgically, and the diagnosis was finally confirmed by molecular testing and anti-tuberculosis treatment in a specialized hospital. The patient's condition was stable on follow-up, and the prognosis was good.
Conclusion: Early diagnosis and differentiation of breast tuberculosis is difficult, and it is very easy to misdiagnose and delay the disease. In the early stage of the disease, traditional Chinese medicine can be used in combination, and in the stable stage of the disease, a reasonable choice of surgical treatment can shorten the course of the disease. This also reveals the important value of integrated Chinese and Western medicine treatment in the clinical treatment of this type of patient.
Keywords: breast tuberculosis, granulomatous mastitis, misdiagnosis, surgical treatment, traditional Chinese medicine

Introduction

Tuberculosis of the breast is an ancient and rare disease, also known as tuberculous mastitis (TM), with chronic specific infection of the mammary gland, most commonly occurring in females. It was first reported by Astley Cooper in 1829, who described it as an "enlargement of the lymph nodes of the chest" in young women.[1] It was not until the end of the 19th century that the disease was first described in detail by Richet[2] and Powers.[3] According to the literature, the disease occurs mostly in Asia (67.9%), followed by Africa (16.8%), with an incidence of up to 3% in endemic areas.[4] Also, the disease can be generalized to any age (12~89 years) with a mean age of onset of 29.

The pathogenesis of BTB consists of primary and secondary, with the primary being infection through injury to the skin or ducts, and the secondary being dissemination through the blood and lymph. Some scholars believe that breast tissue is resistant to the survival and reproduction of Mycobacterium tuberculosis; thus, the incidence of this disease is extremely low, and secondary lesions are more common in clinical practice. Meanwhile, pregnant and lactating women are more likely to be infected due to ductal dilatation.[5] BTB can be classified into nodular, diffuse, and sclerotic types according to the clinical manifestations, with different characteristics, which pose a great challenge for clinical diagnosis.

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According to the literature, the most common clinical manifestations of the disease are unilateral breast lumps (74.9%) and breast abscesses (14.9%), most often in the upper outer quadrant of the breast, which may be accompanied by non-cyclical pain.[6]

However, due to its low incidence rate, this disease is often misdiagnosed or overlooked in clinical practice, leading to delayed treatment. Traditional Chinese medicine can provide symptomatic treatment based on local manifestations in the early stages of the disease, significantly shortening the duration of the illness and demonstrating significant practical value. Here we report a rare case of breast tuberculosis in an elderly woman with granulomatous mastitis as the first manifestation and explore the current progress of diagnosis and treatment of BTB by retrospectively analyzing its diagnostic and therapeutic history and combining it with previous reports in the literature.

Case Information

General Information

The patient was a 71-year-old Chinese woman (informed consent was obtained). She complained of "redness, swelling, and pain in her left breast for more than 1 year and ulceration for more than 1 month". One year ago, the patient had pain in her left breast with no obvious cause, and then a swelling was found underneath her left breast, which was treated several times at an outside hospital. The cytopathology of a tertiary western hospital in Beijing suggested that it was consistent with inflammation. She then consulted a hospital in Beijing and took oral Chinese medicine for 3 months, with no obvious effect, after which she found a new swelling above her left breast. Six months later, the patient underwent a puncture in a hospital in Beijing, and the pathology suggested: inflammatory changes in the breast tissue, extensive multiple acute and chronic inflammatory cell infiltration, and abscess formation. She was treated with antibiotics, which were not effective. Breast ultrasound showed: multiple hypoechoic nodules in the left breast, inflammatory changes were considered, and multiple lymph nodes in both axillae, the nature of which was to be determined. After another month, the patient was admitted to our hospital due to a spontaneous rupture of a breast lump one month earlier, which exuded thin pus. The patient was alert, fatigued, had a fair appetite, poor sleep, dry stools, no obvious abnormalities in urination, and no recent significant weight loss.

History: the patient has a history of lymph node tuberculosis 50 years ago, a history of hypertension for 2 years, and the highest blood pressure is 170/80 mmHg, now taking 25mg of potassium chloride orally to lower blood pressure. Type 2 diabetes mellitus for more than 1 month, now taking 50mg of acarbose orally. 2 daughters are born to the patient. She has been menopausal for 20 years. There is a history of breast cancer in both sisters.

Physical examination: The body temperature was 36.7 °C, pulse 72 beats/min, respiration 18 beats/min, blood pressure 122/74 mmHg. Both breasts were roughly symmetrical, with no nipple indentation or discharge, and there was a mass under and above the left breast, with a dark red color, hard to the touch, and about 4*3 cm in size, with a poorly defined border and irregular pattern, and a small amount of secretion from the sinus tract below, and no definite mass was palpable in the right breast (Figure 1A). Breast ultrasound and chest CT suggested a significant lesion in the left breast. There was no obvious abnormality in the thorax, the respiratory sounds of both lungs were clear, no dry or wet rales were heard, the heart rhythm was regular, there was no abnormality in the abdomen, and there was no edema in both lower limbs.

Treatment Methods

Based on the accessory examination results, the patient was initially diagnosed with mastitis. We treated this patient with internal treatment of Chinese medicine combined with external treatment. The main therapeutic principles and methods are to subdue swelling and dissipate nodules, and penetrate the pus. The following is a specific TCM medication regimen.

Radix Angelicae Sinensis 10g, Radix Phellodendron Bidentatae 10g, Pericarpium Citri Reticulatae 10g, Radix Astragali Praeparatae 30g, Ophiopogonis Macrocephalae 10g, Angelica Dahuricae 10g, Platycodon Grandiflorus 10g, Fried Jujube Kernel 15g, Poria cocos 15g, Bei Chai Hu 6g, Radix Dioscorea Sanghosa 15g, Trichosanthes Kirilowii 15g, Chicken Blood Vine 15g, Polygonum multiflorum stem 10g, Flammulina Fritillariae 15g, Scutellariae Radix 10g. Take 200 mL of it, warm twice in the morning and evening respectively.

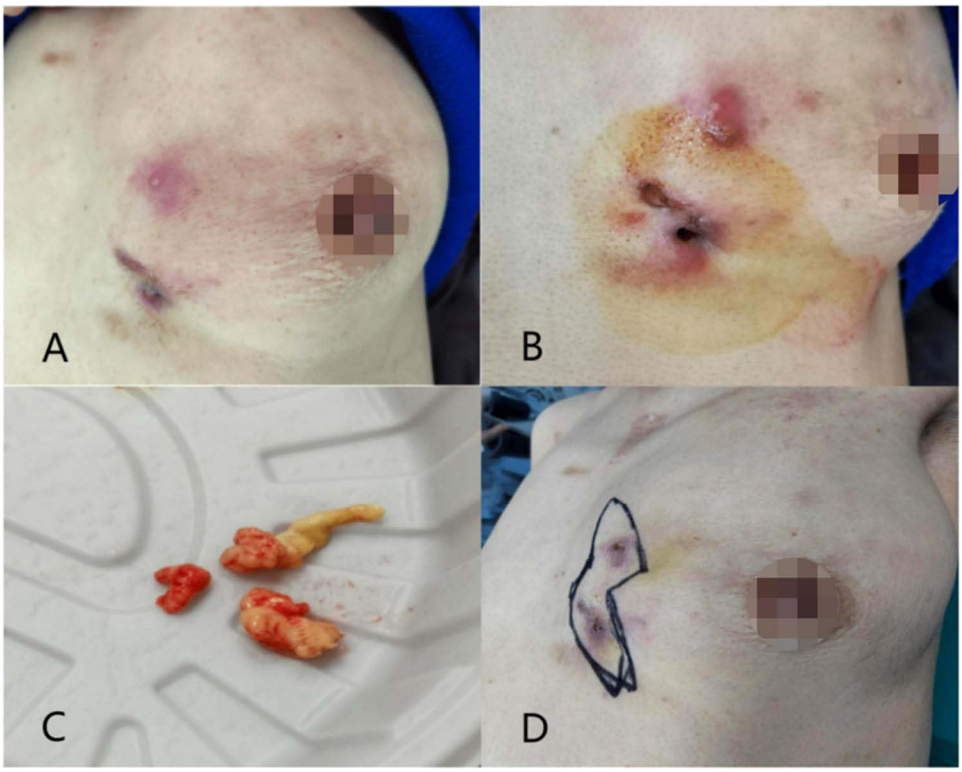

Figure 1 Comparison of clinical manifestations of patients treated. (**A**) Clinical manifestations at initial diagnosis; (**B**) Clinical manifestations after 1 week of treatment with localized mass reduction; (**C**) Yellow mucoid necrotic tissue on the surface of mass ulceration after 3 weeks of treatment; and (**D**) Further reduction of the mass and absence of significant exudation from the ulceration after 5 weeks of treatment.

In addition, purple anti-swelling ointment and hibiscus ointment (topical ointments manufactured in-house) are applied locally to the breast. The method of using the topical ointment is as follows: after cleaning and disinfecting the affected area, apply the ointment to a clean gauze pad and carefully apply it to the affected area. Apply twice daily, leaving it on for 3–4 hours each time. Their main functions are to clear heat and detoxify, and to disperse blood stasis and resolve nodules.

The follow-up results for patients after 1, 3, and 5 weeks of medication are shown in Table 1 and Figure 1B–D.

After 5 weeks of treatment, the patient underwent surgery treatment (Figure 2). At this point in time, the patient's imaging assessment of the mass in her left breast has improved significantly from her initial visit (Figure 3C vs Figure 3A and B). During the operation, some dark red fish-like necrotic material and a large amount of caseous necrotic material were seen, and two sinus tracts were split longitudinally along the direction of the pectoralis major muscle, which were seen to be connected in the deep side of the pectoralis major muscle, and the necrotic material in the deep side of the pectoralis major muscle was carefully removed by spatula scraping and the necrotic muscle tissue was resected. Postoperative histologic pathology suggested (Figure 4A and B): multifocal caseous necrosis and peripheral chronic granuloma formation were seen in the breast tissue, and antacid staining was suspiciously positive, which was considered to be a high possibility of tuberculosis.

Definitive Diagnosis

Immediately following, the pathology consultation at the Chest Hospital suggested chronic granulomatous inflammation of breast tissue with large areas of necrosis. The molecular pathology test result of Mycobacterium avium subspecies: TB-DNA (+), combined with the molecular pathology test result, suggested tuberculosis. The patient was started on anti-tuberculosis treatment after clarifying the final diagnosis. The anti-tuberculosis treatment regimen is as follows: Isoniazid (0.3 g), Rifampicin (0.45 g), Ethambutol (0.75 g), Pyrazinamide (1.5 g), oral medication, once daily. The patient's

Table 1 Specifics of the Patient's Three Follow-up Visits

Treatment Time (Weeks)	Specialist Examinations			Accessory Examination
	Skin	Lump	Exudate	
1	Skin color dark redness is less extensive than before	The mass is softer and smaller than before, with an extent of about 3*3cm (Figure 1B)	A small amount of oozing from the ulcer, a thin, thick water	1. Ultrasound (Figure 3A): Two inhomogeneous medium-high echogenic masses were seen in the lower quadrant of the left breast, with the approximate ranges of 4.8*1.2cm; 3.2*1.8cm, respectively, with reduced echogenicity on the margins, and the two hypoechoic masses communicated with each other in the deeper part of the gland, presenting as a hypoechoic area. 2. Chest CT (Figure 3D): Soft tissue swelling and subcutaneous nodules on the left anterior chest wall with limited thickened adhesions of the rib pleurae bilaterally. 3. Bacterial culture: no antacids found.
3	The range of dark redness in the skin color is further reduced	The mass is softer and smaller than before, with an extent of about 3*2cm	No obvious exudation from the ulcers, pus thick, fibrous-like (Figure 1C)	1. Necrotic tissue at the ulceration is sent for pathology (Figure 4A): caseous necrotic tissue and granulomatous inflammation around it. Infectious diseases such as tuberculosis need to be excluded. 2. Special staining results: weigerts (+), gram stain (suspicious G-). tb (-), pas (-), weak antacid stain (-), silver hexamine stain (-).
5	The dark red color of the skin extends only to the inner two areas	Further reduction of the mass to an extent of about 2*2cm (Figure 1D)	Upper and lower ulcers without obvious oozing, both with more white fibrous material inside	Ultrasound (Figure 3C): An inhomogeneous hypoechoic area was seen in the lower quadrant of the left inner breast, measuring approximately 4.9*1.8 cm.

condition improved significantly and stabilized, and the left mastectomy area healed well (Figure 5), and ultrasound showed no obvious lesions in our hospital six months later (Figure 3D).

Discussion

The diversity of clinical manifestations of BTB leads to high clinical diagnostic delay and misdiagnosis rates, and clinicians have to differentiate BTB from many diseases in a short time. There is no diagnostic test with high specificity for BTB, which causes great difficulties in clinical work.[6] The first disease to be considered in the clinical differential diagnosis of this case is inflammatory breast disease, ie granulomatous mastitis (GM);[7] secondly, BTB should also be differentiated from breast cancer, Wegener's granulomatosis,[8] various benign diseases such as fibroadenoma, nodular disease;[9] and other infectious diseases such as brucellosis, actinomycosis, fungal infections and fat necrosis. Infections and fat necrosis, etc., are distinguished. Early clinical manifestations of BTB and GM can be highly similar; both can be manifested as a localized breast lump with redness, swelling, and pain, and later the lump becomes pus and ulcerates, which can form a sinus tract, so there is a certain difficulty in differential diagnosis between the two. In this case, the early clinical manifestation of the patient is a localized breast lump, hard, and the border is not clear. With the progression of the disease, the lump gradually increases, the epidermis becomes red and swollen with pain, and the lump eventually ulcerates, oozing thin pus. At the same time, the pathology of two punctures in the outside hospital suggested inflammatory changes, and combined with her previous history of lymphatic tuberculosis, it should be

Figure 2 Intraoperative excision diagram (the size of the left internal sub-mammary tissue is about 9*6cm, and two ulcers on the surface are visible, as well as a large amount of dark red fish-like and cheese-like necrotic material).

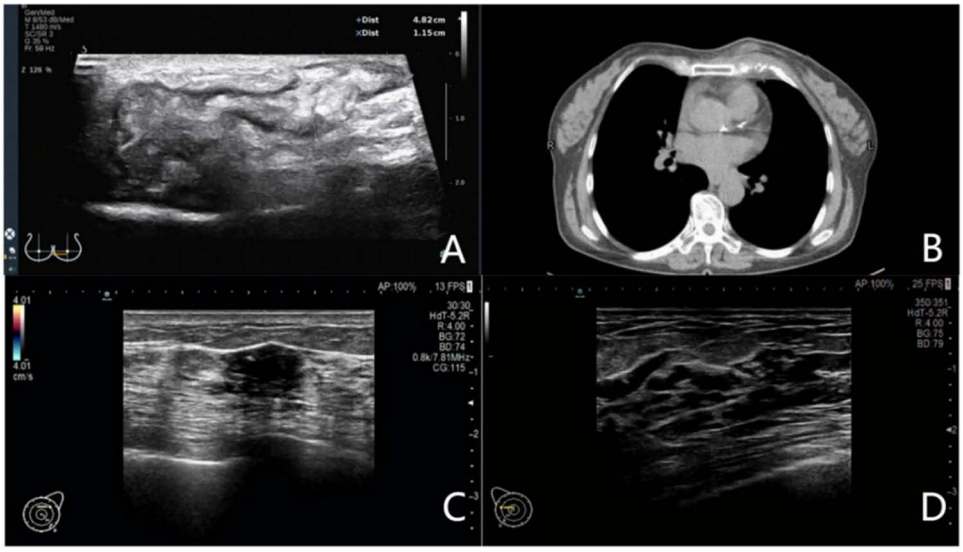

Figure 3 Comparison of imaging examinations. (**A**) Initial breast ultrasound manifestation, two inhomogeneous medium-high echogenic masses were visible in the lower quadrant of the left inner breast; (**B**) initial chest CT manifestation left anterior chest wall with soft tissue swelling and subcutaneous nodules, and limited thickening and adhesion of bilateral costal pleura; (**C**) Breast ultrasonographic manifestation after 5 weeks of treatment, an inhomogeneous hypoechoic area was visible in the lower quadrant of the left inner breast; (**D**) Breast ultrasonographic manifestation half a year after the operation, which was already without obvious lesions.

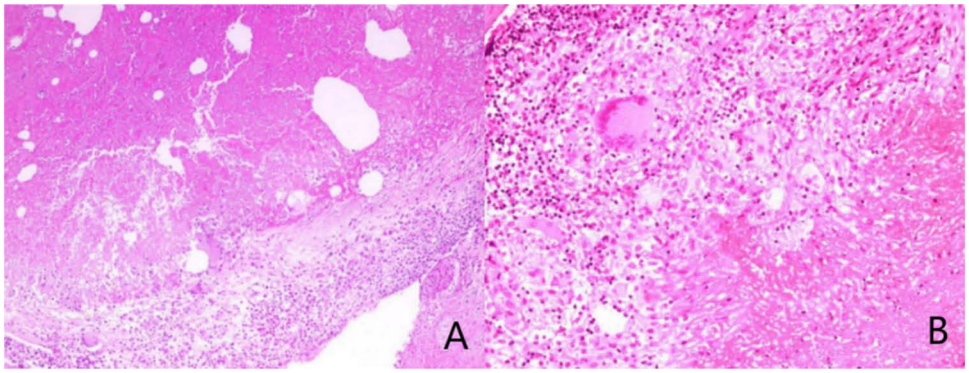

Figure 4 Pathological examination (**A**) Caseous necrotic tissue and surrounding granulomatous inflammation; (**B**) Massive caseous necrosis surrounded by epithelioid cells and multinucleated giant cells, seen to form a granuloma-like structure.

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Figure 5 Localized picture of the patient on follow-up after six months (Good healing of the operated area and disappearance of localized lesions).

considered as lymphatic disseminated breast tuberculosis with granulomatous mastitis as the first symptom.[10] As a result, clinical attention should be paid to elderly patients with GM as the first symptom in the early stage. They should be asked in detail about their past medical history, fully grasp the clinical features, and promptly exclude the possibility of breast tuberculosis with auxiliary examinations for a more accurate early diagnosis. The differential diagnosis should also take into account the fact that BTB can coexist with a variety of diseases,[11] such as breast cancer, granulomatous mastitis, etc.,[12] and the clinical diagnosis should be cautious and comprehensive.

On the other hand, the low sensitivity of BTB detection is another important reason for its high misdiagnosis rate. Among them, the Mycobacterium tuberculosis test is the gold standard for its clinical diagnosis with high specificity, but at the same time, Mycobacterium tuberculosis culture has a high false-negative rate, so relying on the bacterial culture alone may result in a high misdiagnosis rate.

Imaging is also one of the important means of clinical detection and identification of BTB, including ultrasound, mammography, CT, MRI, etc.[13] Mycobacterium tuberculosis invasion of breast tissue causes a cellular immune response, resulting in granulomatous lesions and caseous necrosis of breast tissue, which may appear as hypoechoic solid nodules on ultrasound.[14] With the progression of the disease, the lesion tissue liquefies to form an abscess, and the CT enhancement scan can see that the local ring-shaped enhancement is obvious, which may be accompanied by calcification,[15] and the MRI can show an irregular, high signal dense shadow. Eventually, the lesion extends to the skin surface to form a sinus tract, leading to skin thickening and deepening of skin color, which can be observed in mammography. The pathological changes above BTB can recur with changes in the body's immunity, leading to a prolonged course of the disease, which does not heal over time.[16]

In addition, pathological examination is a very important method in the diagnosis of BTB. Granulomatous lesions with caseous necrosis are the characteristic pathological changes of BTB,[17] including tissue biopsy and fine needle aspiration cytology (FNAC). Tissue biopsy has high sensitivity but low specificity; FNAC has lower sensitivity and specificity than tissue biopsy, and clinical diagnosis should emphasize the combination of pathological examination. When there is a lack of pathological specimens as the basis for diagnosis, tuberculosis screening tests can be chosen to assist in the identification, including the T-cell spotting test (T-SPOT), purified protein derivative (PPD), and tuberculosis antibody (TB-Ab). Among them, the T-SPOT positive detection rate is the highest, and the PPD test is the most economical and practical. Tuberculosis infection-specific T-cell test (T-SPOT.TB) is more sensitive than PPD[18] and has been widely used in the diagnosis of a variety of extrapulmonary tuberculosis, which is important for the early diagnosis of BTB, but its cost is relatively high. In addition, polymerase chain reaction (PCR) has also been increasingly used in the clinical diagnosis of tuberculosis due to its high specificity and sensitivity.[19] According to literature statistics, among the above auxiliary tests, FNAC (31.6%) is the most commonly used in clinical practice, followed by tissue biopsy

(27.1%), antacid staining (25.8%), bacterial culture (12.9%), and PCR (2.5%). Among them, tissue biopsy had the highest positive rate, followed by FNAC.[20]

The early diagnosis of this patient should be highly emphasized on her previous history of lymphatic tuberculosis, and the possibility of secondary breast tuberculosis should be considered. It should also be noted that the patient was an elderly woman with a relatively long history of disease. Combined with the pathologic diagnosis of the outside hospital and her granulomatous mastitis-like first clinical manifestations, the possibility of breast tuberculosis should be excluded at an early stage to avoid delaying treatment.

Anti-tuberculosis treatment is still recognized as the preferred treatment option for BTB; however, there is no specific regimen, and there is a lack of objective efficacy indicators for the evaluation of each regimen. The most common anti-tuberculosis treatment program is to apply isoniazid, rifampicin, pyrazinamide, and ethambutol for 2 months, followed by isoniazid and rifampicin for 4 months. Clinical should be based on the condition and the patient's condition, rationally formulate the treatment program and cycle, and the total clinical relapse rate is low.[21] BTB drug-resistant Mycobacterium tuberculosis should follow the dual management norms of drug-resistant tuberculosis and extrapulmonary tuberculosis, selecting five to six sensitive drugs, and the course of treatment should be prolonged depending on the condition.[22]

Literature reports that patients treated with simple anti-tuberculosis drugs have a high rate of local mass reduction, but long-term drug therapy makes it difficult to completely eliminate the lesions, which often migrate repeatedly. At the same time, long-term medication can aggravate liver damage; only based on drug therapy to control the condition, combined with surgical treatment to remove the lesions, can completely control this disease.

Surgical treatment of BTB is mostly used in disseminated cases or cases that are not sensitive to drug treatment. In the choice of the timing of surgery, those with localized abscesses and sinus tract formation in the lesion should first change the medication regularly, which can be combined with TCM treatment. Apply local or systemic anti-tuberculosis treatment early after the diagnosis is confirmed, and then perform surgical treatment after the pus is exhausted, the mass is significantly reduced, and the local infection is controlled.[23,24] Due to the variable site of BTB and various clinical manifestations, the flexibility of its surgical procedure is determined. In the choice of operation, local lesion excision, segmental mastectomy, or simple mastectomy should be reasonably selected according to the size and location of the local mass and the stage of disease progression. If patients with coexisting types of cancer are encountered, radical mastectomy should be performed promptly.[25]

In this case, the patient applied the TCM treatment protocol to control the local infection at an early stage. After the scope of the abscess was reduced and limited, and the inflammatory reaction was significantly reduced, timely surgical treatment was adopted to completely remove the necrotic tissue from the local lesion. It can significantly shorten the disease process, with remarkable efficacy and good prognosis. Thus, clinical experience confirms that combined surgical treatment of BTB is a thorough and highly effective treatment method.

However, this manuscript has certain limitations. First, clinical cases of breast tuberculosis combined with granulomatous mastitis are extremely rare, and our manuscript only involves one patient, which may result in a certain bias in the effectiveness of the treatment regimen, making it difficult to generalize clinically; second, there are very few relevant literature reports, leading to limited reference materials available to us; finally, due to some practical factors, the follow-up period for this patient was relatively short, which may have influenced our conclusions to some extent.

Conclusion

To summarize, breast tuberculosis greatly increases the difficulty of clinical diagnosis and differential diagnosis due to its diverse clinical manifestations and low specificity of detection means. This type of disease requires clinicians to fully grasp the clinical features of BTB, improve the sensitivity of differential diagnosis, and reasonably select auxiliary examination means to help clarify the diagnosis. In clinical diagnosis, special attention should also be paid to whether the patient has a previous combined medical history, and a comprehensive analysis of the patient's symptoms and signs can effectively improve the early diagnosis rate. In the early stage of BTB, the combined application of the TCM treatment program can effectively shorten the course of the disease. Meanwhile, after the inflammation subsides and the infection is controlled in the middle and late stages, surgery can be used for complete treatment with remarkable efficacy.

Ethical Approval

This study has been reviewed by the Ethics Committee of Beijing Hospital of Traditional Chinese Medicine, Capital Medical University (No: 2023BL02-120-02). The patient included in the study has signed informed consent, and the treatment methods and testing methods adopted in this study are known safe methods in clinical practice; the general information and clinical data are only used for study analysis, not for other purposes. Informed written consent was obtained from the patient for publication of this report and any accompanying images. We have obtained approval from Beijing Hospital of Traditional Chinese Medicine, Capital Medical University to publish this case report.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest.

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