A Case Series on GeneXpert Negative Tuberculous Mastitis and the Effect of Anti-tuberculous Treatment

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Introduction

Breast tuberculosis or tuberculous mastitis is essential to be diagnosed early and efficiently due to its rare occurrence and the dilemma it creates in its treatment and in its differentiation from neoplastic lesions.¹ This study aims to study the effect of anti-tuberculous treatment on GeneXpert CB-NAAT (cartridge-based nucleic acid amplification test) negative tuberculous mastitis.

Background: Breast tuberculosis is significant due to its rare occurrence and dilemma in prospective treatment and differentiation from neoplastic lesions. Tuberculosis of the breast usually affects women from Asia, most commonly, the Indian subcontinent and Africa. Tuberculous mastitis has a wide range of clinical presentation, radiological features, and even microbiological presentation.

Materials and Method: A prospective study was conducted over 6 months. 40 female patients with varied presentations correlating to tuberculous mastitis with a lump in the breast for a particular period of time were included in the study.

Results: The patients’ ages varied from 20 to 45 years. After routine investigations, the patients went in for incision and drainage or incisional biopsy or both and postoperatively their histopathological reports revealed granulomatous breast disease (tuberculous mastitis) with negative GeneXpert (CB-NAAT). Patients were started on an anti-tubercular treatment regimen and showed a progressive decrease in symptomatology.

Conclusion: Granulomatous breast abscess/ tuberulous breast abscess has a varied presentation and no fixed treatment regime. Anti-tuberculous drugs in such patients proved to be efficacious in symptomatic relief with prevention of recurrence/ fistula formation.

Keywords: Tuberculous Mastitis, Granulomatous Mastitis, Anti-tuberculous Treatment
The objective of this study is to assess in detail about:
- Diagnosis and identification of granulomatous/tuberculous abscess in breast lump/abscess presentations
- Drug regimen to follow up during post-surgical management
- Need for empirical anti-tuberculosis treatment despite being GeneXpert negative tuberculous mastitis
- Required anti-tuberculosis treatment
- To assess recurrence of abscess/fistula formation subsequent to surgical and anti-tuberculous drug treatment

Methodology
A case series study was conducted on 40 patients who had a lump in either breast; commonly presenting as a recurrent abscess with fistula in a few, and came to the outpatient department. Most of them were associated with pain; only 2% presented with painless abscesses with sinus.

No history of cough/nipple discharge/axillary swellings was reported. The study was a prospective study which was conducted in the Department of General Surgery at Chettinad Hospital and Research Institute over a period of 6 months from July 2021 to January 2022.

Inclusion Criteria
Patients within the reproductive age group (20-40 years) presenting with breast lump (commonly presenting as a recurrent abscess with or without fistula).

Exclusion Criteria
- Connective tissue disorder
- Pregnant women
- Diabetic women
- Patients with fibroadenoma/fibrocystic breast disease

Ethical Approval: The study was approved by the Institutional Ethics Committee.

After taking proper informed consent from the patients in a language they understood the best, routine investigations were done and assessed. They were made to understand the treatment protocol in detail in a language they understood best. As shown in Figure 1, the most common symptoms that the patients presented with were:
- Lump in the breast (100%) - associated with pain (98%)
- Breast abscess (60%)
- Fever (33%)
- Nipple discharge (33%)

All patients diagnosed with primary or recurrent breast abscess underwent incision and drainage, following which the abscess wall was sent for biopsy and GeneXpert CB-NAAAT and the pus was sent for culture and sensitivity testing (Figure 2).

Figure 1. Symptom Predominance in the Study Population

| Symptoms | No of Patients |
|----------|----------------|
| LUMP IN BREAST | 30 |
| PAIN | 20 |
| SINNING FISTULA | 10 |
| NIPPLE DISCHARGE | 5 |
| BREAST ABSCESS | 4 |

Figure 2. Pictures Depicting Intraoperative and Post Operative Progress

Figure 3. Histopathological Examination of the Breast Lesions of the Participants

Histology of the breast lesions showed similar appearances: florid granulomatous inflammation with well-formed granulomas along with multinucleate giant cell formation and Langerhans cells (Figure 3).
Treatment and Follow-up
All patients were explained in detail about the study and informed written consent was obtained from the patients included in the study. All patients were started on anti-tuberculous treatment based on their weight and were on continuous follow-up every 2 weeks for 1 month followed by a monthly review.

Results
It was observed that despite being GeneXpert negative tuberculous mastitis, the lump size and symptoms reduced after a course of anti-tuberculous treatment.

Out of 40 patients, 37 underwent anti-tuberculous treatment for 6 months and effectively showed improvement after 2 months of regular anti-tuberculous treatment (Figure 4). No recurrence of abscess/ fistula was noted in the follow-up period. 1 out of 30 patients was non-compliant and ended up having similar complaints after 2 months of irregular anti-tuberculous treatment.

Discussion
Tuberculous mastitis is an uncommon disease noted in varying possibilities in developing nations. Tuberculous mastitis time and again arises or occurs as a lump in the upper outer or central quadrant of the mammary gland. Customarily, the presentation is unilateral and seldom bilateral. Breast tuberculosis can manifest as primary when breast lesion is the solitary incidence (considered to be sporadic) or secondary when there is an evincible focus of TB elsewhere. The infection can metastasize to breast tissue by:

- Blood (hematogenous spread)
- Lymphatic dissemination
- Contagious structures
- Direct transmission
- Ductal infection

Lymphatic dissemination is the preferred mode of spread. According to literature tuberculous mastitis has been tabulated into various genres as shown in Figure 6.

![Graphical Representation of the Derived Results from the Study Population](image1)

Figure 4. Graphical Representation of the Derived Results from the Study Population

2 out of 30 patients underwent anti-tuberculous treatment for 9 months.

The most predominant age group which was involved was 20 to 30 years as shown in Figure 5 (most commonly seen in 26 to 30 years of age).

![Age wise Distribution of Patients in the Study Population](image2)

Figure 5. Agewise Distribution of Patients in the Study Population

Tuberculous mastitis is distinguished definitively by specific histopathological features evocative of Langhans’ giant cell, epithelioid cell granulomas, and lymphohistiocytic cohesions. Imaging modalities like ultrasonography, mammography, or ultrasono-mammography cannot accurately diagnose and discern forms of granulomatous mastitis, and cannot categorically differentiate between tuberculous mastitis and malignancy. This is attributed to the mercurial pattern of how tuberculous mastitis presents. The radiological findings in the case of granulomatous breast disease are:

- Coarse stromal texture which can be associated with an ill-defined breast lump
- Skin thickening

These are not specific and do not help with the diagnosis. Medical ministrations subsisting of a four-drug regimen form the substratum of primordial medicaments. Aspiration and drainage of cold abscesses, with excision of presenting residual sinuses and masses, are the cardinal surgical management in such scenarios. In refractory or unresponsive
to medical treatment cases with the destruction of the breast, simple mastectomy is indicated. Breast tuberculosis is an exclusion diagnosis that should be considered in patients who have had a poor response to earlier antibiotic treatment for breast inflammation, particularly in patients from tuberculosis-endemic countries.

**Conclusion**

Tuberculous mastitis being a rare entity, there is no sole diagnostic value to GeneXpert. With an increased number of recurrent breast abscess cases noted, a new modality of treatment is required to counter multiple abscesses or fistula formation in younger women. Distortion in size/symmetry of breast with the requirement of mastectomy (advanced stage) if not treated or identified in early stages leads to increased morbidity in the younger age group. Empirical anti-tuberculous treatment initiated based on a histopathological report was found to be effective and relieved the patients of their symptoms and mainly prevented recurrence, thus proving that GeneXpert negative tuberculous mastitis responds to medication (ATT).

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**Conflict of Interest:** None

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