Granulomatous mammary disease: ten years’ experience with fine needle aspiration cytology

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SUMMARY

OBJECTIVE: To determine the aetiological types of granulomatous disease of the breast in women presenting with mammary complaints in the Sudan.

METHODS: Clinical history and physical examination, complete blood counts, Mantoux test, histopathology and fine needle aspiration cytology (FNAC).

RESULTS: Granulomatous mastitis was seen in 11/2500 (0.44%) patients with mammary disease over a 10-year period. All were of childbearing age (mean 26.0 ± 5.9 years). Common presentations were diffuse swelling, well-circumscribed masses, nipple retraction, multiple sinuses and superficial skin ulcers. Lymphadenopathy was seen in more than 60% of the patients. Diagnosis was based on cytomorphological features in 10/11 cases and histopathology in one. Nine were diagnosed with tuberculous mastitis and two with idiopathic granulomatous mastitis. Acid-fast bacilli (AFB) could not be demonstrated in any of the cytology smears. Tuberculous mastitis responded to empirical anti-tuberculosis treatment, with a minimum follow-up of 2 years in seven women.

CONCLUSION: Tuberculous mastitis is a rare entity in women with mammary disease in the Sudan. Alternative diagnoses such as idiopathic granulomatous mastitis should be made only after failure of an adequate trial of anti-tuberculosis treatment. FNAC is a useful diagnostic tool even if AFB cannot be demonstrated.

KEY WORDS: tuberculous; granulomatous mastitis; FNAC

CHRONIC granulomatous mastitis is a rare breast disorder that can be caused by Mycobacterium tuberculosis, hypersensitivity to contraceptive pills or part of an autoimmune disorder. There are three forms of chronic mastitis: tuberculous, non-specific granulomatous and oleogranulomatous mastitis.† Tuberculous mastitis is a rare condition that typically presents with unilateral breast mass, abscess, superficial ulcers, multiple sinuses, nipple retraction, lymphadenopathy and destruction of mammary tissues. Tuberculous mastitis is most commonly an isolated disease, usually with no accompanying pulmonary disease, but with some lymph node enlargement. Although rare, it should be suspected in any woman with persistent abscess and sinuses. In its three clinical presentations (nodular, diffuse, and sclerosing), tuberculous mastitis can mimic benign conditions such as actinocycosis, recurrent subareolar abscess, later stages of bacterial infection and sarcoidosis and carcinoma of the breast.‡§ Tuberculous mastitis is a disease of younger women aged 20–40 years. Spread of mycobacteria to the breast is usually haematogenous, but lymphatic or direct spread can also occur.†§ Diagnosis is difficult, usually by demonstration of acid-fast bacilli (AFB) in biopsies and/or aspirate or culture and guinea-pig inoculation. The best results are obtained from excision biopsy and histopathology (60%). Fine needle aspiration cytology (FNAC) is useful in the diagnosis and classification of inflammatory breast conditions when the index of suspicion is low. It is a quick, non-invasive and inexpensive technique with variable accuracy.†§ FNAC cytology usually shows a picture of suppurating granulomatous mastitis; the diagnosis of tuberculosis can be established by demonstrating AFB in the aspirate.†© Overall, AFB positivity can reach up to 22.7% of microscopically examined cytology smears, and is greater in the presence of necrosis when epithelioid cells are absent. The commonest cytomorphological picture is that of epithelioid granulomas, necrosis and inflammatory cell infiltrate with Langhan’s giant cells.†© Tuberculous mastitis can be diagnosed with confidence in 72% of cases in the absence of AFB if epithelioid granulomas and necrosis

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Patients with mammary disease are referred to our cytology clinic at the Central Police Hospital, Khartoum, Sudan, for FNAC. Over the last 10 years (1991–2001), 2500 patients have been seen. The records and slides of women with a diagnosis of granulomatous mammary disease were re-evaluated for diagnosis and cytomorphological patterns.

Methods

If not already done, haemoglobin concentration, total white cell counts and erythrocyte sedimentation rate (ESR) were measured routinely for patients referred for FNAC. A Mantoux test and chest X-ray were usually done for those with suspected tuberculosis.

Following informed consent, FNAC was performed for all patients. Slides were stained with Geimsa stain and examined by trained pathologists. Surgical biopsies were usually done for those with repeatedly inadequate aspirates.

Patients diagnosed with tuberculous mastitis are given a 6-month course of rifampicin, thioacetazone and isoniazid, and are closely monitored for disappearance of nocturnal fever, reduction and/or disappearance of swelling, healing of sinuses and ulcers, and reduction in the ESR.

**RESULTS**

Patients diagnosed with chronic granulomatous mastitis constituted 0.44% (n = 11) of the 2500 patients presenting with breast complaints over the 10-year period. They came from different parts of the Sudan, and had a mean age of 26.0 ± 5.9 years. Malignancy was the provisional diagnosis for all patients. A breast mass was detected in all 11 patients: sinuses in three, ulcers in three and seven had lymphadenopathy. The duration of the lesion was known for seven patients (mean 7.6 ± 3.4 months; range 4–12). Lactation in the last 6 months was reported in three patients (27%).

Nine patients were diagnosed with tuberculous mastitis by FNAC (Patients 1, 2, 3, 4, 5, 6, 8, 9 and 11) (Table). The cytomorphological picture was dominated by a ground-glass background (necrotic material), paucity of cells, epithelioid granulomas, caseation and Langhan's giant cells. The cytomorphological pattern was that of necrotising and granulomatous/necrotising lesions in the smears. No AFB could be shown in any of the smears. All nine patients with tuberculous mastitis gave a history of nocturnal fever for variable durations during the course of the disease, and one of the nine gave a family history of pulmonary tuberculosis. The women had a mean Mantoux test induration of 18.3 ± 4.2 mm (range 12–25). The mean post-treatment ESR was significantly lower than that seen at diagnosis (30.5 ± 15 mm, range 10–50 vs. 92 ± 20 mm, P = 0.0). No abnormality could be detected on chest X-ray.

Patient 8 presented first, with a breast mass that was diagnosed by FNAC as tuberculous; she was temporarily lost to follow-up. She presented again with discharging breast sinus and bilateral cervical lymphadenopathy. The breast mass was surgically removed and no anti-tuberculosis treatment was given post-operatively. The breast mass and the cervical nodes were proven to be tuberculous on FNAC (Table).

The two patients diagnosed with idiopathic granulomatous mastitis (Patients 7 and 10) gave a vague history of dragging sensation in the affected breast, but no history of nocturnal fever. Patient 7 gave a few months’ history of a rapidly enlarging breast mass with ensuing skin ulceration; she had never conceived or used contraceptive pills. She had a huge left subareolar breast mass with a superficial skin ulcer that was diagnosed histologically; repeated FNAC showed paucity of cells with scanty non-caseating granulomas and few small lymphocytes, with no giant cells or caseation necrosis. No AFB could be demonstrated in the aspiration smear. Following diagnosis the two patients were referred back to their treating surgeons. Feedback on patient 10 indicated that she had been treated with surgical excision, with no recurrence at 12 months follow-up.

**DISCUSSION**

Tuberculous mastitis is a rare disease, but should be suspected in any woman with persistent abscess and...
sinuses even if AFB cannot be demonstrated in the aspiration smears or histological sections. Although nine patients with tuberculous mastitis had typical clinical presentations, none was suspected of having the disease. This clearly indicates that the index of suspicion for this disease is low in Sudan as it is in other countries. FNAC is the main diagnostic tool for breast lesions in our clinic for the initial differentiation between malignant and non-malignant conditions. We advocate surgical biopsy in the absence of typical cytomorphological features of tuberculous mastitis. Although no cytomorphological pattern is diagnostic, we believe that a cytomorphological picture of ground-glass (necrotic) material with epithelioid granulomas, Langhan’s giant cells and overt caseation is typical. Plasma cells and foamy macrophages were very scanty or absent in our smears; this is in agreement with other reports. Ground-glass background (necrotic material) is a common feature that was detected in most of our patients, especially the necrotising type. We suggest that such a cytomorphological picture should form a strong basis for starting anti-tuberculosis treatment, especially in countries where tuberculosis is prevalent.

Unfortunately, no bacteriological cultures were performed for these patients. Positive bacteriological results would have made stronger grounds for the diagnosis of tuberculous mastitis. Furthermore, the diagnosis is strongly supported by the excellent response to anti-tuberculosis treatment in our nine patients. In addition, in our experience, an ESR $\geq 100$ mm and a strongly positive Mantoux test (with blister formation at the injection site) usually indicates underlying mycobacterial infection. The ESR drops markedly after only a few days of anti-tuberculosis treatment.

We found that anti-tuberculosis drugs alone, with no conservative surgery, can give satisfactory results even in the presence of extensive disease, as seen in Patient 3 (Figures 1 and 2).

![Figure 1](image1.png)  
**Figure 1**  
Patient 3: tuberculous mastitis at diagnosis showing multiple sinuses, ulceration and nipple retraction.

![Figure 2](image2.png)  
**Figure 2**  
Patient 3 post-treatment, showing complete healing of sinuses and ulcers.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (years)</th>
<th>Presenting symptoms</th>
<th>Clinical appearance of lesion</th>
<th>Mantoux test size at diagnosis (mm)</th>
<th>ESR (mm/first hour) at diagnosis</th>
<th>Follow-up duration (months)</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>1</td>
<td>23</td>
<td>+ + + + + +</td>
<td>Nodular</td>
<td>20</td>
<td>110</td>
<td>6</td>
<td>Cured</td>
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<td>2</td>
<td>26</td>
<td>+ + + + + +</td>
<td>Nodular</td>
<td>25</td>
<td>100</td>
<td>6</td>
<td>Cured</td>
</tr>
<tr>
<td>3</td>
<td>21</td>
<td>+ + + + + +</td>
<td>Nodular, sclerosing</td>
<td>18</td>
<td>120</td>
<td>2</td>
<td>Cured</td>
</tr>
<tr>
<td>4</td>
<td>35</td>
<td>+ + + + + +</td>
<td>Nodular, sclerosing</td>
<td>18</td>
<td>100</td>
<td>2</td>
<td>Cured</td>
</tr>
<tr>
<td>5</td>
<td>23</td>
<td>+ + + + + +</td>
<td>Diffuse</td>
<td>12</td>
<td>70</td>
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<td>Cured</td>
</tr>
<tr>
<td>6</td>
<td>35</td>
<td>+ + + + + +</td>
<td>Diffuse</td>
<td>20</td>
<td>120</td>
<td>6</td>
<td>Cured</td>
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<tr>
<td>7</td>
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<td>+ + + + + +</td>
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<td>70</td>
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<tr>
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<td>30</td>
<td>+ + + + + +</td>
<td>Diffuse</td>
<td>18</td>
<td>100</td>
<td>6</td>
<td>Possibly cured</td>
</tr>
<tr>
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<td>+ + + + + +</td>
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<td>Not done</td>
<td>Not done</td>
<td>12</td>
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</tr>
<tr>
<td>11</td>
<td>40</td>
<td>+ + + + + +</td>
<td>Nodular, sclerosing</td>
<td>27</td>
<td>115</td>
<td>4</td>
<td>Improved</td>
</tr>
</tbody>
</table>

* Bilateral cervical lymphadenopathy developed 4 months after breast lump excision.
† Clinically cured after 6 months of treatment, under follow-up.
LN = lymph nodes; ESR = erythrocyte sedimentation rate.
The use of the non-committal term ‘granulomatous lesions of the breast’ may lead to delays in giving an adequate trial of anti-tuberculosis treatment and prolong a patient's suffering. Superficial skin ulcers and nipple inversion can be presenting features in tuberculous as well as idiopathic granulomatous mastitis, as seen in Patients 3, 4 and 7 (Figure 1).25

CONCLUSION
Although tuberculosis mastitis is rare in Sudan (0.44%), awareness among surgeons and pathologists of its presence is important. This study confirms the fact that a low index of suspicion continues to prevail in this country as in other tuberculosis endemic countries.

References

RESUMEN

OBJETIVO: Determinar los tipos etiológicos de la enfermedad granulomatosa del seno en mujeres que se presentan con molestias mamarias en Sudán.

MÉTODOS: Historia clínica y examen físico, recuentos sanguíneos, test de Mantoux, examen histopatológico y examen citológico de los productos de aspiración con aguja fina (FNAC).

RESULTADOS: Se diagnosticó una mastitis granulomatosa en 11 (0,44%) de 2500 mujeres con enfermedad mamaria en un periodo de 10 años. Todas estaban en edad de procreación (promedio 26,0 ± 5,9 años). Los signos más frecuentes eran un aumento de volumen difuso, masas bien circunscritas, retracción del mamelón, fístulas múltiples y úlceras cutáneas superficiales. En más del 60% de las pacientes se observaba una linfadenopatía. El diagnóstico se basó sólo en las características cito-morfológicas en 10/11 casos y en la histopatología en un caso. En nueve se diagnosticó una mastitis tuberculosa y en dos una mastitis granulomatosa idiopática. En ninguno de los frotis citológicos se pudo demostrar la existencia de bacilos ácido-alcohol-resistentes (BAAR). Las pacientes con mastitis tuberculosa respondieron a un tratamiento empírico, con un periodo mínimo de seguimiento de 2 años en siete de ellas.

CONCLUSIÓN: En Sudán, la enfermedad granulomatosa tuberculosa es una entidad rara en las mujeres con enfermedad del seno. Diagnósticos alternativos, tales como mastitis granulomatosa idiopática, sólo pueden ser planteados después de un fracaso de un ensayo adecuado de tratamiento antituberculoso. La FNAC es una herramienta diagnóstica útil, aun si no se puede demostrar la presencia de BAAR.