Original Research Article

Clinicopathological study of granulomatous lobular mastitis

Sapna Goel¹, Kanwar Singh Goel²*

¹Department of Pathology, ²Department of General Surgery, Faculty of Medicine and Health Sciences, (SGT Medical College) Under SGT University, Budhera, Gurugram, Haryana, India

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*Correspondence:
Dr. Kanwar Singh Goel,
E-mail: dr.kanwarsinghgoel@rediffmail.com

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ABSTRACT

Background: Granulomatous lobular mastitis is an uncommon disease. This condition may resemble malignancy and tuberculosis. It is characterised by granulomatous inflammation with multinucleated giant cells, epithelioid histiocytes. The inflammation is centred on lobules. The purpose of this study is to review the clinical and pathological aspects in 8 cases of granulomatous lobular mastitis and review of pertinent literature.

Methods: This is a prospective observational study. A total of 8 patients were studied. Investigations done. Patient were treated by erythromycin 250mg qid, tinidazole 500mg bid, for 7 days and steroids for two months. The lumps were excised, sinuses were excised and abscesses were drained, and oral steroids were given. Follow-up was done for 6 months.

Results: Most of the patients were multiparous and lactating, with age range from 18 to 36 years. Clinically the lesion was felt as malignant in 3 patients and benign in 5 patients. Most patients were using contraceptive pills. There was suppuration in 3 patients and sinuses were found in 2 patients. Histopathological examination revealed granulomatous inflammation centred on lobules.

Conclusions: The diagnosis of granulomatous lobular mastitis should be made very carefully to avoid any confusion with malignancy, tuberculosis, fungal infection, sarcoidosis, mammary duct ectasia, cystic changes in breast with over palpation and puerperal mastitis with over palpation. Though it is rare disease, but complete understanding by pathologist and surgeon is required for improving its identification.

Keywords: Abscess, Granulomatous, Histopathology, Lobular, Mastitis, Malignancy, Sinuses, Tuberculous

INTRODUCTION

Granulomatous Lobular Mastitis is also known as idiopathic granulomatous mastitis or post lactational granulomatous mastitis. Granulomatous lobular mastitis is an uncommon disease. It was first of all mentioned by Kessler et al, Rowe P, DeHertogh et al, Carmalt et al, Koelmeyer et al, and Brown et al, presented one or few cases.¹ Six Flether et al, presented large series.² Out of 10 cases of mastitis with granulomatous pathology, mostly as expected, will be of tuberculosis pathology, but one case approximately will be of granulomatous lobular mastitis. Further elaborations were made by Cohen C, in 1977.³ This condition may resemble malignancy and tuberculosis. It is characterized by granulomatous inflammation with multinucleated giant cells, epithelioid histiocytes and occasional features of presence of fat necrosis, abscesses, sinus tracts and eosinophils. Schaumann and asteroid bodies are absent or
found rarely. The inflammation is centred on lobules. But extensive inflammation may obliterate lobuocentric character. Ductal and periductal inflammation are usually minor. There is close association of this disease with pregnancy and lactation.9 The problem occurs usually 2 years after delivery, but occasionally after many years also. It has also been associated with oral contraceptive use. The purpose of this study is to review the clinical and pathological aspects in 8 cases of granulomatous lobular mastitis and review of pertinent literature. By this we want to increase awareness of this disease among surgeons and pathologist for improving its identification. It is because both of them have to be very careful while dealing with granulomatous mastitis so that its identification is improved.

METHODS

The study was performed in Surgery Department in SGT Medical College, SGT University, Budhara, Gurugram, Haryana, over a period of 2 years from September 2016 to August 2018. The study was prospective observational study. A total of 8 patients were studied. Informed consent was taken for examination and investigations, giving due respect to maintain the patient’s privacy and keep them comfortable.

Data collection

The patients were taken from outpatient department and emergency department of General surgery department. A detailed history and focused clinical examination were done. Investigations done in all patients included Hb, BT, CT, TLC, DLC, ESR, Mx test, blood sugar, blood urea, serum creatinine, HCV, HIV, HbsAg, CRP, X-ray chest PA view and ECG in relevant cases for fitness for anaesthesia purpose. Fine needle aspiration cytology was done in patients who presented with lumps. Patients were operated in emergency or routine OT, by excision of lump, or drainage of abscess, or excision of sinus as required in individual cases. Excised specimen, excised sinus or slough from abscess was sent for histopathology examination. Pus was sent for culture sensitivity. All slides were stained with hematoxylin and eosin, Ziehl-Neelsen and PAS stain.

Ethical considerations

The Institutional Ethics Committee’s approval for Research on Human Subjects was taken. Throughout the study, strict ethical norms were maintained. Written informed consent was taken from patient in their local language (mother tongue).

The method of treatment was like this. First a course of antibiotics was given. The drugs given were Erythromycin 250mg qid, Tinidazole 500mg bid. Both the drugs were given for 7 days. The lumps were excised, sinuses were excised and abscesses were drained. In all the patients, pus was sent for culture and sensitivity test, and Ziehl-Neelsen staining done for acid fast bacilli and PAS stain for fungus was done. The complete lump and/or supplicative material/slough was sent for histopathology examination.

All slides were stained with hematoxylin and eosin. Oral steroids were given. The steroid given was tablet prednisolone 25mg per day for 2 months. prednisolone was tapered off in next 4 weeks. Although steroids are most effective, if IgG marker are positive. But the marker study was not done in our series and we relied on our clinical acumen. In our 2 patients there were recurrences of sinus formation and suppuration. In these 2 patients, we drained the sinuses/ abscesses. Recovery was complete. Follow-up was done for 6 months.

RESULTS

This prospective observational study was performed in Surgery Department in SGT Medical College, SGT University, Budhara, Gurugram, Haryana, over a period of 2 years from September 2016 to August 2018.

The results of clinical features are as follows: The age ranged from 18 to 36 years, with mean age of 28 years. Maximum patients were in the age ranging from 24 to 30 years. In present study there was no patient beyond 36 years of age (Table 1). In study done by Miliauskas et al, the age ranged up to 43 years, in study by Banerjee A et al, the age ranged up to 48 years.10,11

In present study four patients (50%), were para 3, two patients (25%), were para 2, one patient (12.5%) was para 4 and para 1 each (Table 1). In study done by Kfouri H et al, parity was 8 in maximum patients, and in some patients there were even para 9 and 10 also.12 None of the patients were pregnant at the time of symptoms. The symptoms occurred 3 months to 75 months after last delivery. Maximum cases (75%) were from 3 months to 18 months after last delivery (Table 1). In study done by DeHertogh et al, all patients had symptoms within 2 years after last delivery.3 The size of lesions ranged from 1 cm to 7 cm. 50% patients had lumps of size 1 to 3 cm. Rest 50% had size 4 to 7 cm (Table 1).

In study done by Kfouri H et al, the size of lesion was 4 to 10cm in all the cases.12 Patient presented with diseases in both the breasts. In our study in 4 patients (50%), left breast was involved and in 4 patients (50%), right breast was involved (Table 1). In study by Goings JJ et al, out of 19 patients in 9 patients (46.8%), right breast was involved.13 In 10 patients (53.2%), left breast was involved. Clinically evaluation of lump was done. It was found that clinical features suggested, lump as benign in 5 (62.5%) patients, and the clinical features mimicked malignant lesion in 3 (37.5%) patients (Table 1).
Table 1: Clinical data of patients with granulomatous lobular mastitis.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>18</td>
<td>24</td>
<td>26</td>
<td>27</td>
<td>29</td>
<td>30</td>
<td>34</td>
<td>36</td>
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<tr>
<td>Parity</td>
<td>2</td>
<td>24</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Months since last delivery</td>
<td>3</td>
<td>5</td>
<td>8</td>
<td>12</td>
<td>6</td>
<td>18</td>
<td>60</td>
<td>75</td>
</tr>
<tr>
<td>Size of lesion (cm)</td>
<td>4</td>
<td>5</td>
<td>1</td>
<td>3</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Side</td>
<td>L</td>
<td>R</td>
<td>L</td>
<td>R</td>
<td>L</td>
<td>R</td>
<td>L</td>
<td>R</td>
</tr>
<tr>
<td>Clinical diagnosis</td>
<td></td>
<td></td>
<td>Benign</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Benign</td>
</tr>
<tr>
<td>Breast feeding</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Contraceptive pills use</td>
<td>Former user</td>
<td>Never</td>
<td>Former user</td>
<td>Former user</td>
<td>Former user</td>
<td>Current user</td>
<td>Current user</td>
<td>Current user</td>
</tr>
</tbody>
</table>

Table 2: Clinical symptoms and signs with no. of patients.

<table>
<thead>
<tr>
<th>Clinical symptoms</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>4</td>
</tr>
<tr>
<td>Suppuration</td>
<td>3</td>
</tr>
<tr>
<td>Sinus</td>
<td>2</td>
</tr>
<tr>
<td>Pain</td>
<td>7</td>
</tr>
<tr>
<td>Inflammation</td>
<td>1</td>
</tr>
<tr>
<td>Lump</td>
<td>5</td>
</tr>
<tr>
<td>Axillary lymph nodes</td>
<td>Not Palpable</td>
</tr>
</tbody>
</table>

Table 3: Values of WBC count and ESR.

<table>
<thead>
<tr>
<th>Investigations</th>
<th>Within normal limits</th>
<th>Raised</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC count</td>
<td>6 patients</td>
<td>2 patients</td>
</tr>
<tr>
<td>ESR</td>
<td>7 patients</td>
<td>1 patient</td>
</tr>
</tbody>
</table>

In study by Going JJ et al., out of 19 patients, 6 (31.6%) patients presented clinical features of malignancy. 13 (68.4%) patients presented clinically as benign lump. In present study maximum patients i.e. 5 patients (62.5%), were lactating at the time of problem, and the breast feeding was done. In 3 (37.5%) patients there was no breast feeding. Findings of present study favours the etiopathogenesis, because the disease occurs most commonly in lactating women (Table 1).

In present study 1 patient never used contraceptive pills. In 4 (50%) patients, there was history of use of contraceptive pills. 3 (37.5%) patients, were currently using contraceptive pills (Table 1).

Use of contraceptive pills in past or present is an etiopathogenetic factor in this disease. There was history of fever in 4 patients. There was suppuration in 3 patients (Figure 1 and 3). Sinuses were found in 2 patients (Figure 2), pain locally was present in 7 patients and signs of inflammation was present in 1 patient (Figure 4).
cultures for acid fast bacilli and possible demonstration of acid fast bacilli, clinches the diagnosis. In fungal infections, the granulomatous inflammation is necrotising type and fungal hyphae may be present, PAS stain may be positive and the patient is generally immunocompromised.\textsuperscript{14}

In sarcoidosis, the sarcoid granulomas will be non-caseating type, it is naked and the disease is wide spread. In mammary duct ectasia or in cystic changes in breast or in puerperal mastitis, if there is over palpation of breasts the lesion may be centred on ducts, many giant cells are usually seen, but there is no formed granuloma. In puerperal mastitis there will be history of recent delivery. In malignancy we will find pleomorphic cells, anisonucleosis, prominent nucleoli, poorly formed glandular structure and anaplastic tumour cells forming solid nests or cords. But occasionally granulomas are also found. Clinical features of granulomatous lobular mastitis as reviewed from 8 cases, during a study period of 2 years from September 2016 to August 2018 at Surgery department of SGT medical college, SGT University, Budhera, Gurugram, Haryana, India were as below. The mean age in our study was 28 years. Most of the patients were more than para 1. It corresponds with the literature that this is a disease of young parous women <40 years of age. Most of the patients developed symptoms, within 1½ years after delivery. Studied 5 patients were lactating at the time of problem, and breast feeding was done. Most of the patients were using or had used contraceptive pills. It has been reported that granulomatous lobular mastitis is associated with lactation and use of oral contraceptive pills.\textsuperscript{15} In studied 5 patients, lump was palpable, it was hard irregular most common site being upper and outer quadrant of breast. It is mentioned in literature that granulomatous lobular mastitis may be mistaken for carcinoma and lead to unnecessary mastectomy. There was history of fever in 4 patients, pain was present in 7 patients. There was suppuration in 3 patients and sinuses were found in 2 patients.

Axillary lymph nodes were not palpable in any case. WBC count was within normal limits in 6 patients and raised in 2 patients. ESR was normal in 7 patients and raised in 1 patient (Table 3).

All studied patients were non-reactive to HIV. None of the patient was diabetic. Other breast was normal in all the patients. PAS stain for fungus was negative in all the cases. Ziehl-Neelsen staining for acid fast bacilli was negative in all the cases. Histopathological examination revealed granulomatous inflammation centred on lobules. There were multinucleated giant cells and epithelioid histiocytes were present in granulomas. Presence of fat necrosis or abscess formation or sinus tract was also there. Minor ductal and periductal inflammation was usually present. There were predominant T-cells present in infiltrate.

DISCUSSION

Granulomatous inflammation may occur in tuberculosis, fungal infection, sarcoidosis, mammary duct ectasia, puerperal mastitis, granulomatous lobular mastitis and occasionally in malignancy.\textsuperscript{3} Granulomatous lobular mastitis is diagnosed by exclusion of other diseases. In tuberculosis there is epithelioid cell granuloma, but it is not centrilobular.\textsuperscript{2,3} Presence of caseous necrosis, positive

In sarcoidosis, the sarcoid granulomas will be non-caseating type, it is naked and the disease is wide spread. In mammary duct ectasia or in cystic changes in breast or in puerperal mastitis, if there is over palpation of breasts the lesion may be centred on ducts, many giant cells are usually seen, but there is no formed granuloma. In puerperal mastitis there will be history of recent delivery. In malignancy we will find pleomorphic cells, anisonucleosis, prominent nucleoli, poorly formed glandular structure and anaplastic tumour cells forming solid nests or cords. But occasionally granulomas are also found. Clinical features of granulomatous lobular mastitis as reviewed from 8 cases, during a study period of 2 years from September 2016 to August 2018 at Surgery department of SGT medical college, SGT University, Budhera, Gurugram, Haryana, India were as below. The mean age in our study was 28 years. Most of the patients were more than para 1. It corresponds with the literature that this is a disease of young parous women <40 years of age. Most of the patients developed symptoms, within 1½ years after delivery. Studied 5 patients were lactating at the time of problem, and breast feeding was done. Most of the patients were using or had used contraceptive pills. It has been reported that granulomatous lobular mastitis is associated with lactation and use of oral contraceptive pills.\textsuperscript{15} In studied 5 patients, lump was palpable, it was hard irregular most common site being upper and outer quadrant of breast. It is mentioned in literature that granulomatous lobular mastitis may be mistaken for carcinoma and lead to unnecessary mastectomy. There was history of fever in 4 patients, pain was present in 7 patients. There was suppuration in 3 patients and sinuses were found in 2 patients.

Axillary lymph nodes were not palpable in any case. WBC count was within normal limits in 6 patients and raised in 2 patients. ESR was normal in 7 patients and raised in 1 patient. All our patients were non-reactive to HIV. None of the patient was diabetic. Other breast was normal in all the patients. PAS stain for fungus was negative in all the cases. Ziehl-Neelsen staining for acid fast bacilli was negative in all the cases.

So far as etiology has been concerned, it is an uncommon disease, primarily affecting young women, most often during pregnancy and/or lactation. It has been suggested that there is an immune response locally to extravasated secretions from lobules, as many patients had pregnancy and were lactating. There may also be a local immune response to local trauma, local chemical irritant or viral infection, which might have induced lymphocytes and macrophage migration. If there is injury to ductal epithelium, it may cause T-cell mediated inflammation
and formation of centrilobular granuloma. Authors
diagnosed the patients by excluding all possible causes of
granulomatous inflammation like, tuberculosis, fungal
infection, sarcoidosis, mammary duct ectasia, cystic
changes in breast with over palpation, puerperal mastitis
with over palpation and malignancy. Authors did fine
needle aspiration cytology and histopathology
examination of slough or excised specimen meticulously.
Authors treated the patient like this, first a course of
antibiotics was given. The drugs given were
Erythromycin 250mg qid, Tinidazole 500mg bid. Both
the drugs were given for 7 days. The lumps were excised,
sinuses were excised and abscesses were drained. In all
the patients, pus was sent for culture and sensitivity test,
and Ziehl-Neelsen staining was done for acid fast bacilli
and PAS stain for fungus was done. The complete lump
and/or suppurative material/slough was sent for
histopathology examination. All slides were stained with
hematoxylin and eosin. Oral steroids were given. The
steroid given was tablet prednisolone 25mg per day for 2
months. Prednisolone was tapered off in next 4 weeks.
In many studies steroids have been given.16-18 Although
steroids are most effective, if IgG marker are positive.
But the marker study was not done in our series and we
relied on our clinical acumen. In studied 2 patients there
were recurrences of sinus formation and suppuration.
In these 2 patients, authors drained the sinuses/ abscesses.
Recovery was complete. Follow-up was done for 6
months. Authors lost 2 patients for follow up, remaining
6 patients were alright for 6 months. It was because of
our meticulous working for diagnosis, that no patient was
unnecessarily treated for tuberculosis or malignancy or
other causes of granulomatous mastitis.

CONCLUSION

The diagnosis of granulomatous lobular mastitis should
be made very carefully to avoid any confusion with
malignancy, tuberculosis, fungal infection, sarcoidosis,
mammary duct ectasia, cystic changes in breast with over
palpation and puerperal mastitis with over palpation.
Though it is rare disease, but complete understanding by
pathologist and surgeon is required for improving its
identification.

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Ethical approval: The study was approved by the
Institutional Ethics Committee

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