

# Management of Patients with Granulomatous Mastitis: Analysis of 31 Cases

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## Keywords

Mastitis · Granulomatous mastitis, idiopathic · Treatment

## Summary

**Background:** Granulomatous mastitis is a benign recurrent disease. Accurate diagnosis is only by histopathology. **Patients and Methods:** 31 cases with histological diagnosis were retrospectively analyzed. **Results:** Mean follow-up was 42.4 months for recurrent and 27.8 months for non-recurrent cases. Etiology was tuberculosis in 1 case. 5 cases (16%) relapsed. 6 patients (19.3%) treated with abscess drainage healed completely, but 50% relapsed. Relapses were treated with excision or steroids. Steroid therapy was the initial treatment in 12 cases (38.7%), with 1 relapse (8.3%) which was treated in the same manner. 2 patients had incomplete response necessitating excision, and another 2 developed abscesses which were treated with steroids or excision after drainage. Surgical excision was preferred in 12 cases (38.7%) due to suspicion for carcinoma in 8 patients (25.8%) and/or low probability of poor cosmetic outcome. All healed without complication, and recurrence was observed in 1 case (8.3%) which was treated with re-excision. **Conclusion:** Both excision and steroid therapy had low and similar relapse rates, but excision was superior to steroid therapy in providing strict diagnosis with much faster healing and fewer complications. In refractory cases, and when deformity is inevitable, steroid therapy should be preferred.

## Schlüsselwörter

Mastitis · Granulomatöse Mastitis, idiopathische · Behandlung

## Zusammenfassung

**Hintergrund:** Granulomatöse Mastitis ist eine gutartige, zur Rezidivierung neigende Erkrankung. Eine genaue Diagnose kann nur nach histopathologischer Untersuchung gestellt werden. **Patientinnen und Methoden:** 31 histologisch diagnostizierte Fälle wurde retrospektiv analysiert. **Ergebnisse:** Das mittlere Follow-up betrug 42,4 Monate für rezidierte und 27,8 Monate für nicht-rezidierte Fälle. Die Erkrankung war in einem Fall durch Tuberkulose verursacht. Rezidive traten in 5 Fällen (16%) auf. 6 (19,3%) mit Abszess-Drainage behandelte Patientinnen zeigten eine komplette Heilung, 50% rezidierten jedoch. Rezidive wurden mit Extirpation bzw. Steroiden behandelt. Steroidtherapie wurde in 12 Fällen (38,7%) zur Erstbehandlung eingesetzt; davon rezidierte eine Patientin (8,3%), die in gleicher Weise weiterbehandelt wurde. 2 Patientinnen zeigten ein unvollständiges Ansprechen auf die Therapie und wurden chirurgisch behandelt. 2 weitere Patientinnen entwickelten Abszesse, die mit Steroiden bzw. Extirpation nach Drainage behandelt wurden. In 12 Fällen (38,7%) wurde die chirurgische Entfernung auf Grund eines vermuteten Mammakarzinoms (8, 25,8%) und/oder niedriger Wahrscheinlichkeit eines schlechten kosmetischen Ergebnisses bevorzugt. In allen Fällen verlief die Heilung ohne Komplikationen. Ein einzelnes Rezidiv (8,3%) wurde erneut entfernt. **Schlussfolgerung:** Sowohl Extirpation als auch Steroidtherapie zeigten niedrige und vergleichbare Rezidivraten. Die chirurgische Entfernung war der Steroidtherapie jedoch insofern überlegen, als dass sie eine definitive Diagnose einhergehend mit einer viel schnelleren Heilung und weniger Komplikationen bietet. Bei refraktären Fällen und unvermeidbarer Deformierung sollte die Steroidtherapie bevorzugt werden.

## Introduction

Granulomatous mastitis (GM) is a chronic inflammatory breast disease characterized by epithelioid cell granulomas with giant cells which are confined to breast lobules. Clinical and radiological features may sometimes mimic breast carcinoma [1, 2]. It is usually associated with recurrent attacks which are annoying to both the patient and the physician. The disease process may result in formation of fistulae, abscesses, nipple inversion, ulceration, and hardening of the skin [3]. Several agents, such as local irritants, trauma, undetected microorganisms, viruses, fungal and parasitic infections, and diabetes mellitus have all been considered in the etiology [4–6]. An autoimmune hypothesis is supported by most, with the observation of the response of the disease to steroid therapy, although serologic tests are usually negative [2, 4]. It is estimated that a localized immune response to luminal secretions extravasated from damaged ducts develops in the lobular connective tissue with migration of lymphocytes and macrophages [4, 7–9]. Rupture of ducts may result from trauma to the breasts, hyperprolactinemia, and long-term distension of ducts in prolonged breastfeeding leading to such a granulomatous reaction [10–12]. Therefore GM is frequently associated with parturition and lactation.

The diagnosis of GM as 'idiopathic' is made by exclusion of other possible causes, such as infections (tuberculosis, brucellosis, filariasis, and actinomycosis), systemic disorders (sarcoidosis and Wegener's granulomatosis), foreign body reaction, and fat necrosis [2, 4, 6]. Sarcoidosis is diagnosed with the observation of noncaseating epithelioid granulomas diffusely scattered within the breast, and tuberculous mastitis with caseating granulomas and acid-fast bacilli. Actinomycosis can be excluded by the absence of sulfur granules in the discharge and by fungal cultures. To detect autoimmune causes, serologic tests (rheumatoid factor and antinuclear antibody) can be performed although found negative in most cases [7].

Ultrasonography (US) may be very helpful in the determination of abscesses, but both US and mammography (MG) might be misleading in some cases of GM. In several studies magnetic resonance imaging (MRI) is accepted as a complementary diagnostic tool [4, 13]. It is helpful in confirming the benign nature of breast lesions observed on US or MG but nonspecific in the determination of the character of an inflammatory process with limited diagnostic utility [4, 14]. Definitive diagnosis can only be made by histopathological examination of the diseased breast tissue. Appropriate management is unknown but surgical excision, or use of antibiotics, anti-inflammatory drugs, or corticosteroids have been proposed. In this study we aimed to present our 10-year experience with GM and outline the results of different considerations in the management of this potentially recurrent, non-malignant breast disease.

## Patients and Methods

A total of 31 cases with a histologically confirmed diagnosis of GM treated at our center between January 2000 and December 2009 were retrospectively evaluated for patient characteristics, symptoms, results of the diagnostic workup, treatment, and outcome. Pathological diagnosis of GM with the observation of granulomatous inflammatory reaction in the breast lobules was made by core biopsy or surgical biopsy. The mean follow-up period after the first attack was 42.4 months (range 18–81 months) for recurrent cases and 27.8 months (range 9–124 months) for GM cases with a single attack.

## Results

The records of 31 patients with a diagnosis of GM were retrospectively evaluated. 29 of the patients (93.5%) were of reproductive age, and 2 were postmenopausal. The mean age was 35 years (range 27–62 years). 3 patients were pregnant, and 2 were lactating. Previous oral contraceptive use was reported in 5 patients. 3 patients had breast cancer and 4 had other cancers in first-degree relatives.

The main complaints at presentation were a mass in 23 cases, breast pain in 15, and hyperemia in 8. Lesions were observed in the left breast in 18 cases (58%) and in the right breast in 12 cases (38.7%), while contralateral breast involvement in a relapse was detected in 1 case (3.2%). All patients had an US examination which was combined with MG in 15 cases and with MRI of the breasts in 10. US showed an irregular hypoechoic mass in 11 cases (35.4%), inflammatory changes consistent with mastitis in 18 (58%), and small abscesses in 3 (9.6%). No abnormal finding was detected on MG in 8 cases, but there was focal asymmetric density in 4, an ill-defined mass in 3, and dense parenchymal patterns in 2 cases. Pathological findings on MRI were focal homogeneous enhancing masses with irregular borders in 2 cases, inflammatory changes with parenchymal distortion in 2, and abscess formation in 1.

Clinical and/or radiological findings suggested malignancy in 8 patients (25.8%), and benign disease processes were considered in 23 (74.2%). Histopathological diagnosis was made by the examination of tissue obtained by core biopsy in 28 cases and by open biopsy taken from the abscess wall during drainage in 3. Microscopically all cases except 1 had noncaseating granulomas involving breast lobules with variable numbers of multinucleated giant cells, neutrophils, lymphocytes, plasma cells, and eosinophils. No specific microorganism was detected in the specimens, and no antibiotic was prescribed after the diagnosis of GM was made, but 6 patients had already been using some form of antibiotic at presentation with no evidence of regression of the breast lesion. GM was accepted as 'idiopathic', except for 1 case with tuberculosis which was diagnosed by polymerase chain reaction (PCR) examination of diseased tissue upon detection of caseating granulomas. Antituberculosis therapy was started. Steroid

**Table 1.** Treatment methods used at first presentation of all granulomatous mastitis cases and outcome

Initial treatment method	Other treatment methods required, n (type)	Complete healing with initial treatment, n (%)	Recurrence after complete healing, n (%)	Mean follow-up for recurrence-free cases, months
Antituberculosis therapy (n = 1)	0	1 (100)	0	25
Abscess drainage (n = 6)	0	6 (100)	3 (50)	37
Steroid therapy (n = 12)	1 (drainage, excision) 1 (drainage, steroid) 2 (excision)	8 (66.6)	1 (8.3)	30.1
Surgical excision (n = 12)	0	12 (100)	1 (8.3)	27.3

**Table 2.** Treatment of the attacks of granulomatous mastitis in recurrent cases (n = 5)

Case	1st attack		2nd attack		3rd attack	
	treatment	disease-free interval, months	treatment	disease-free interval, months	treatment	follow-up after healing, months
1	drainage	6	steroid/excision	6	–	6
2	drainage	10	steroid	72	–	72
3	drainage	4	excision	31	–	31
4	steroid	4	steroid	17	–	17
5	excision (L)	18	drainage/excision (R)	5	excision (L)	34

L = Left breast; R = right breast.

therapy involved oral prednisone, 16 mg twice a day. It was stopped in the presence of infection or abscess and reduced in dose when complications developed. Surgical excision was the first choice of treatment in 12 cases either because there was a suspicion for carcinoma or because excision of the lesion would not lead to a poor cosmetic outcome. Abscess drainage with biopsy was performed in 1 pregnant patient who had a relapse 2 months after delivery (case 2). The other 2 pregnant patients were either given low-dose steroid therapy or managed with excision, with no relapse at follow-up. Treatment methods used at first presentation and their outcomes are shown in table 1. Disease recurrence was noticed in 5 patients (16%) after complete healing, 3 with abscess drainage, 1 with steroid therapy, and 1 with surgical excision (table 2).

## Discussion

GM is a chronic benign disease, constituting 24% of all breast inflammatory disease [15]. It requires a prolonged course of treatment and follow-up as it is usually associated with recurrence. Although no ethnic predisposition was reported, Turkey is one of the countries where it is observed more frequently, as seen from the number of cases documented in the literature [16]. Most patients with GM are of reproductive age, although older women can also be affected [2, 4, 6]. Patients with GM most commonly present with a breast mass which may extend into the skin or the underlying muscle, usually associated with retraction of the nipple and axillary lymphadenopathy.

Unilateral involvement, regional lymphadenopathy, and an irregular hypoechoic mass on US may support the clinical

diagnosis of malignancy [4, 7, 17]. In our series, all 8 cases which had a hypoechoic irregular mass on US were managed with excision. 7 of them had pathological MG findings of asymmetric density or an ill-defined nodule. 5 also had an MRI which supported malignancy in 2 cases. However none of these patients revealed malignancy upon excision. Thus, the role of radiological imaging in distinguishing GM from carcinoma is limited [7]. Definitive diagnosis can only be made by histopathological examination of the breast lesion. However cytological features, observed especially in the material obtained by needle biopsy, may sometimes make it difficult to differentiate GM from other granulomatous diseases of the breast and from carcinoma [4, 7, 16]. In the past, false-positive needle biopsies resulted in unnecessary mastectomies [1, 9]. In our series we performed core biopsy or open surgical biopsy and obtained a correct diagnosis of GM in all cases. GM was idiopathic except for 1 case with tuberculosis. Ziehl-Nielsen staining and culture for acid-fast bacilli are recommended for the diagnosis of tuberculosis, but breast tuberculosis is usually paucibacillary, and only 2% of the stains were reported positive. Chest X-ray, tuberculin skin test, determination of erythrocyte sedimentation rate, and PCR may also help with the diagnosis [18, 19]. In our practice we do not commonly observe tuberculosis and perform diagnostic tests for tuberculosis only in selected cases. PCR was performed in our case after the observation of caseating granulomas, and complete resolution of the breast lesion was observed with the onset of standard antituberculosis therapy.

Treatment of GM is controversial, but use of antibiotics or corticosteroids and wide excision of the affected tissue have all been considered [1, 6, 7, 20]. It was reported that in situations where no therapy was given, almost 50% of patients had

a spontaneous and complete resolution with no recurrence, but the mean time to complete resolution in 1 study was 14.5 months [2, 3]. Therefore it is not acceptable to wait for spontaneous recovery without intervening with some form of therapy. Antibiotic use is debatable as most GM cases are either sterile or infected with undetected microorganisms. Mixed aerobic and anaerobic microorganisms may cultivate only after recurrence [4]. We do not prescribe antibiotics to patients with GM in our practice. However 6 patients presented to our clinic were already on antibiotherapy with no amelioration in the character of the lesion. The few unilocular abscesses which developed during the disease process were drained with no requirement for antibiotherapy; however most abscesses in GM are multilocular.

Surgical excision of the GM lesion, on the other hand, has been supported by many authors. It provides a definitive diagnosis, causes few side effects, and cures the patient more rapidly with observation of fewer recurrences [6, 7]. Authors who are opposed to excision in the management of GM report that wide excision in the presence of mastitis is associated with delayed wound healing with subsequent disease recurrence and poor cosmetic outcome [2, 7]. However excision is usually performed because of discrepancies between needle biopsy findings and clinical findings [17]. It was reported that more than 50% of GM cases were initially misdiagnosed as carcinoma [2, 21]. In such cases surgical excision can be both diagnostic and therapeutic, because further therapy is not needed after surgical excision if no delayed wound healing or infection results [4]. In our series malignancy was suspected in up to 26% of the cases with clinical and/or radiological findings, and we performed excision to obtain an accurate diagnosis. All cases recovered completely with no delayed healing. Different relapse rates after surgical excision, ranging from 5.5 to 50%, have been reported in the literature [1, 4, 7, 22, 23]. In our series we performed surgical excision as the first treatment modality in 12 cases, and no further therapy was required in any of the cases. 1 patient had another attack of GM in the contralateral breast at 18 months and a relapse in the ipsilateral breast at 25 months. Thus, in our series, the relapse rate after excision was 8.3%. Some authors propose re-excision upon recurrence, however discordance between the size of the lesion and that of the breast does not always allow re-excision [4, 7]. In our single relapse observed after healing with surgical excision, we also performed re-excision as the breast size was adequate. Relapses after abscess drainage or steroid therapy were also treated with surgical excision for fear of an underlying missed malignancy. No malignancy was detected but surgery provided rapid healing with no further relapses.

Steroid therapy, on the other hand, was reported to decrease the size of the lesion and provide complete healing when used long-term [4, 7, 20]. Although some reports suggest use of steroid therapy until complete resolution, prednisolone has several side effects, such as glucose intolerance,

Cushing's syndrome and avascular necrosis, and can exacerbate undetected underlying breast infection [2, 4, 7, 20, 21, 24]. Therefore long-term use of steroid therapy is not usually possible and is recommended only for use in recurrent and refractory cases with close observation and only when an infectious etiology has been excluded [4, 7, 20, 24]. Furthermore, steroid use prior to excision may permit a more conservative surgery [4, 21]. When abscess formation is observed, drainage of the abscess should be performed before the start of steroid therapy [15, 25].

In our series abscess drainage itself had the highest recurrence rate (50%). Thus it is not feasible to perform abscess drainage alone in the treatment of GM. As most abscesses in GM are multilocular, it may be better to perform wide excision instead of abscess drainage or to continue with steroid therapy following the drainage procedure. The recommended initial dose of prednisolone in advanced disease is 0.8 mg/kg/day in divided doses, provided the lesion is sterile [3]. It is usually continued in low doses for at least 6 weeks until a complete clinical response is observed [15]. Cessation of steroid therapy, on the other hand, is usually associated with high recurrences, reported by 1 study to be as high as 50% [25]. In our series steroid therapy was used as the first treatment modality in 12 cases of GM (38.7%). Inadequate response in 4 cases necessitated further treatment with other methods, and 1 patient out of the 12 had a relapse (8.3%). However the relapse responded well to steroid therapy. We did not observe many severe side effects as the dose of prednisolone used was lower than that reported in the literature, and close follow-up allowed dose modifications when necessary.

In the literature the recurrence rate of GM is reported to be 16–50% even if complete resolution is obtained [16]. In our series 5 out of 31 cases relapsed forming a recurrence rate of 16%. Most of the recurrences occurred following abscess drainage, and relapse rates of surgical excision and steroid therapy were low and similar (8.3%). However we think excision is superior to steroid therapy in that it provides a strict diagnosis as well as much faster healing and fewer complications. Wide excision and re-excision may sometimes cause deformity of the breast. However healing with steroid therapy is slow requiring close follow-up for complications, causing weight gain, and potentially leaving the patient with hardened skin and discoloration of the breast, all of which are annoying factors to the patient. It may be better to reserve steroid therapy for refractory and recurrent cases.

## Conclusion

GM is a potentially recurrent chronic benign disease. It is important to differentiate this breast lesion from carcinoma. Each case of GM should be evaluated separately, and the appropriate treatment modality should be chosen according

to patient and disease characteristics. However our results confirm several reports in the literature which recommend excision for the treatment of GM, as it has a lower recurrence rate and a much more rapid healing time. Steroid therapy also has a low recurrence rate but complications do not allow routine use.

## Disclosure Statement

There are no conflicts of interests. The authors did not receive any funding or sponsorship relating to the study.

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