

Surgical treatment of granulomatous mastitis associated with autoimmune response

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Granulomatous mastitis (GM) is a rare breast disease with unknown etiology. Clinical management strategies for GM include surgery, antibiotics, and steroid treatments. As patients with GM often respond to steroids, GM is thought to be an autoimmune disease. Here we describe a case of trauma-induced GM that presented as autoimmune disease but was successfully treated by surgery without steroids. The patient showed no sign of recurrence for 11 months. This case provides useful information on both the underlying mechanisms and clinical management of GM.

Key words: Antibiotics, autoimmune disease, granulomatous mastitis, inflammation, recurrence, surgery, surgical treatment, steroid, trauma

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INTRODUCTION

Granulomatous mastitis (GM) is a breast disease of unknown origin. It usually affects women of childbearing age. Patients with GM often present with unilateral or bilateral breast masses of various sizes. Many factors have been implicated in the etiology of GM: Microbial infection, including corynebacterium, actinomycetes, and fungal infections;^[1,2] hyperprolactinemia and hormone imbalances; trauma and chemical stimulation;^[3] contraceptive use;^[4] and mammary duct blockade.^[5] When the disease cannot be attributed to any of the aforementioned factors, it is termed idiopathic granulomatous mastitis (IGM).^[6]

To date, there is no agreed gold standard treatment for GM. The clinical management often starts with tests to eliminate microbial infection and, when microbial infection can be ruled out, long-term oral steroid treatment or surgery is administered.^[7] Although many patients prefer breast-preserving treatment to surgery, systemic steroid treatments can have severe side effects and may not be suitable for patients with diabetes, glaucoma, heart disease, hypertension, or obesity. More importantly, as the recurrence rate of patients who undergo surgical resection is much lower than that of patients who undergo nonsurgical treatment, it has been suggested that surgery is more effective in preventing recurrence.^[8]

Most studies to date have focused on the diagnosis and treatment of IGM; however, little is reported on the management of GM cases with well-defined causes. Here, we describe a case of trauma-induced GM that was treated solely by surgery. We hope that the information presented herein will provide further insights into the underlying mechanisms of GM and help improve the clinical management of similar cases.

CASE REPORT

A 30-year-old woman presented with a 3-month history of a painful mass and a 1-month history of skin ulceration on her left breast. She had been pregnant once and delivered a son 18 months before the symptoms developed. Her left breast had been kicked by her son, after which a breast mass that measured approximately 4 × 4 cm in diameter developed. Initially, the patient developed pain in the left breast with progressive growth of the mass. Before being admitted to our hospital, she was initially treated with penicillin and cephalosporin intravenously, and she took oral and topical Chinese herbal medicines for 2 weeks previously. None of these treatments stopped the growth of the breast mass or alleviated her pain. Meanwhile, she developed other symptoms, including skin ulceration of the left breast, nodular erythema on both her shins, and swelling and pain in both knees and ankle area, which made walking without support difficult.

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Clinical findings

At the time of hospital admission, the patient was afebrile (temperature, 36.3°C) and in apparent good general condition. She complained of pain accompanied with tenderness in the left breast. Upon examination by a specialist, a hard mass measuring 10 × 13 cm with an ill-defined boundary was palpable in the left breast, which also had nipple retraction. Several skin ulcerations on her left breast were noted. The breast mass occupied almost the entire left breast and was connected to the ulcerated skin but not to the chest wall. The right breast appeared normal. The patient showed symptoms of an autoimmune disease: Moderate pitting edema in the lower limbs; swelling and tenderness in both knees and the ankle area; multiple erythematous nodules on both shins and around the ankle area; and tenderness in the erythematous area.

Consistent with diagnosis by palpation, Doppler ultrasound examination of the left breast revealed a diffuse thickening of the mammary gland [Figure 1], and mammography revealed a heterogeneously dense region with no sign of calcification in the left breast [Figure 2]. Magnetic resonance imaging (MRI) was also performed on both breasts and demonstrated evident asymmetry in the appearance of the breasts and ill-defined margin of the left mammary gland [Figure 3]. Consistent with the patient's lack of response to antibiotic treatment, there was no evidence of bacterial growth in the ulceration exudate in culture, and we did not detect any microbes in the smear test. Therefore, we excluded microbe infection as the cause of GM in this patient.

Blood tests suggested that the patient had leukocytosis (white blood cells: $13.25 \times 10^9/L$; neutrophils: $10.60 \times 10^9/L$; lymphocytes: $1.89 \times 10^9/L$; eosinophils: $0.01 \times 10^9/L$; and

basophils: $0.02 \times 10^9/L$) without anemia or thrombocytopenia (hemoglobin: 114 g/L and platelet count $460 \times 10^9/L$). Her rheumatoid factor level (20.1 IU/mL) was slightly higher than normal (<20 IU/mL), and her C-reactive protein (5.11 mg/dL) was significantly higher than normal (<0.8 mg/dL). The levels of autoimmune antibodies, Such as antistreptolysin O, anticyclic citrulline peptide, immunoglobulin (Ig) G, IgA, and IgM, were all within the normal range and the levels of both perinuclear antineutrophil cytoplasmic antibody (pANCA) and cytoplasmic antineutrophil antibody (cANCA) were below the detection limit.

Treatment

Upon admission, the patient received levofloxacin and metronidazole intravenously for 1 week. The ulcerated area was cleaned and the abscess was drained. However, despite these treatments, her condition did not improve. Her body temperature fluctuated between 36.4°C and 37.8°C. Pathological examination on fine needle biopsy of the breast mass revealed the presence of a large number of neutrophils, lymphocytes, and plasma cells in the stroma of the left mammary gland. In addition, there was infiltration by multinucleated giant cells and the formation of small blood vessels [Figure 4]. This result further confirmed the clinical diagnosis of GM.

Oral steroids were offered as a treatment but rejected by the patient because of her concerns about adverse side effects. To debulk the mass, we performed abscess drainage, after which the patient developed increased joint pain and nodular erythema. Upon the patient's request, conservative surgical resection of the left breast was performed. The patient's condition improved significantly after the surgery. Her breast and joint pain resolved, joint swelling and nodular erythema disappeared, and she was discharged



Figure 1: Gray-scale Doppler ultrasound examination of the left breast. A diffuse thickening was detected in the mammary gland, and the thickest hyperechogenic region measured 2.2 cm in diameter. The echogenicity in the left breast was heterogeneous with an irregular anechoic structure in the 5 o'clock position, penetrating the fat pad and reaching beneath the skin

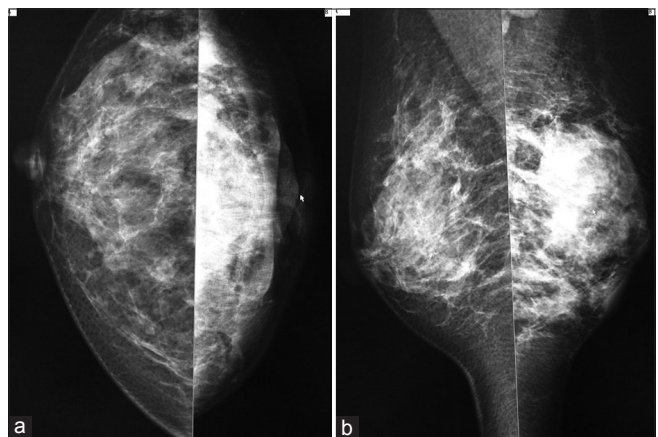


Figure 2: Mammogram of the right (a) and left (b) breasts, craniocaudal view. Mammogram of the right (a) and left (b) breasts, mediolateral oblique view. A heterogeneously dense region measuring 46 × 68 mm was observed in the left breast. The margin of the hyperdense region was ill defined with no sign of calcification. The nipple on the left breast was retracted, and the skin was thickened. Multiple axillary lymph nodes in the left armpit were swollen and enlarged

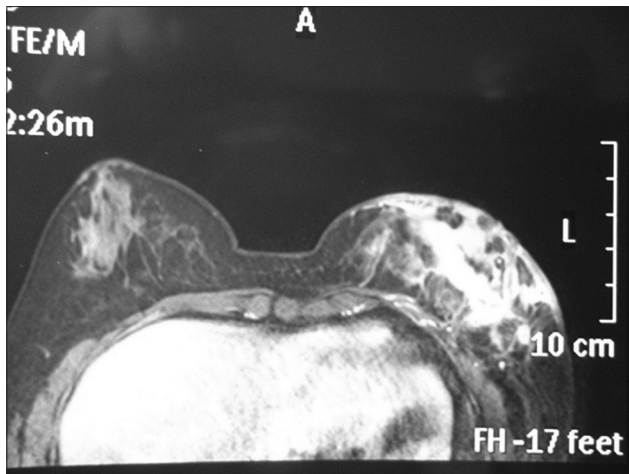


Figure 3: Contrast-enhanced magnetic resonance imaging of both breasts. L indicates left side. The right breast appeared to be normal. In the left breast, there was a segmental enhancement of signal intensity in the mammary gland. The margin of the left mammary gland was indistinctive. The connective tissue near the chest wall was thickened.

6 days after the surgery. To date, the patient has been followed-up for 11 months, and no recurrence has occurred.

DISCUSSION

In the case presented here, the patient's left breast was traumatized shortly before the development of GM. The temporal relationship between these two events and the lack of other known diseases at the time of diagnosis suggested that trauma was the trigger for GM in this case. Two months after the breast mass had occurred, the patient developed swelling and tenderness in her joints and nodular erythema on her shins, all of which are symptoms of autoimmune diseases. As she had no autoimmune disease prior to the development of GM, and her autoimmune symptoms disappeared soon after the removal of the breast mass, we suspected that the autoimmune responses were probably secondary symptoms of GM. As the patient did not receive treatment with anti-inflammatory agents during the initial disease phase, the autoimmune response induced further damage to the breast tissue, which in turn aggravated the inflammation. After clinical pathological examination revealed the presence of leukocytosis, we recommended that oral steroids be given to the patient. However, her brother had been treated with oral steroids and had developed several side effects; therefore, she rejected the treatment plan and insisted on surgery. Respecting the patient's choice and considering that surgery was a good option for her condition, we surgically removed the affected mammary tissue but preserved the nipple and the upper-quadrant areola. The removal of the diseased breast mass led to a complete resolution of her autoimmune symptoms, which further supported the notion that the autoimmune responses were secondary symptoms of GM in this patient. During the subsequent follow-up period of 11 months, she showed no

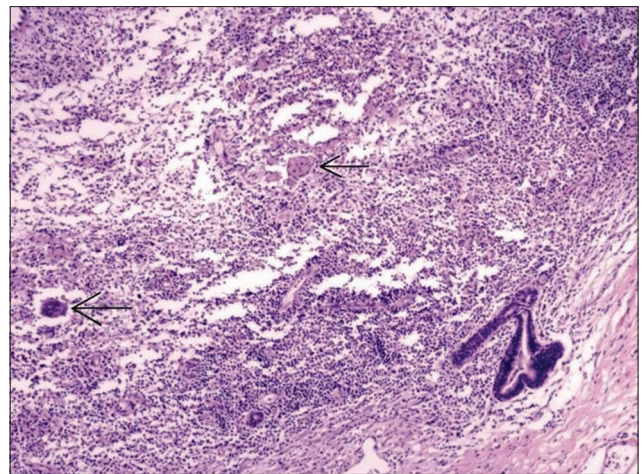


Figure 4: Hematoxylin and eosin staining of the surgical specimen ($\times 200$). Infiltration of neutrophils, lymphocytes, and multinuclear cells are present in the stroma. The arrows show multinucleated giant cells.

sign of recurrence. Further follow-up examinations will be conducted to assess whether recurrent GM will develop.

Although treatment with systemic steroids has been reported to be successful in some patients with GM,^[9,10] adverse side effects have been reported after long-term steroid treatment.^[11] Unlike most reports of GM with symptoms of inflammation, no steroid treatment was used in this case, and the patient has not relapsed to date. Therefore, surgery can be considered in GM cases that have systemic inflammation but are not treatable with steroids.

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AUTHOR'S CONTRIBUTION

HZ agreed for all aspects of the work. MY contributed in the conception of the work. XDG contributed in conducting the study. ZZL contributed in the approval of the final version of the manuscript. SXC contributed in revising the draft.

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