Idiopathic granulomatous mastitis

Erkan Ozturk, MD, Murat Akin, MD, Mehmet F. Can, MD, Ismail Ozerhan, MD, Bulent Kurt, MD, Gokhan Yagci, MD, Turgut Tufan, MD.

ABSTRACT

الأهداف: مناقشة السمات السريرية والإشعاعية وطرق العلاج لدى 14 مريضة تم تشخيص حالتهن بالتهاب الثدي الورمي الحبيبي التلقائي (GM).

الطريقة: تم تقييم السمات السريرية والنتائج الإشعاعية وطرق العلاج لدى 14 مريضة تعاني من التهاب الثدي الورمي الحبيبي (GM) بقسم الجراحة العامة – جامعة جولهين العسكرية – المدرسة الطبية – أنقرة – تركيا، خلال الفترة ما بين أبريل 2000م وحتى يونيو 2006م، في دراسة إستعادية.

النتائج: بلغ متوسط عمر المريضات 34.5 (27–41) عاماً. كانت الشكاوى عند الدخول للمستشفى وجود كتلة في الثدي لدى 7 مريضات (50%)، خراج وكتلة لدى 6 مريضات (42.8%)، وناسور لدى مريضة واحدة (7.2%)، كان التهاب الثدي الورمي الحبيبي (GM) وحيد الجانب لدى جميع المريضات (في الجانب الأيمن لدى 5 مريضات، وفي الجانب الأيسر لدى 9 مريضات). خضع جميع المريضات للتقييم بالموجات فوق الصوتية (USG)، كما تم إجراء تخطيط الثدي باستخدام الرنين المغناطيسي (MRI) والتصوير باستخدام (MG) لـ 8 و 5 مريضات على التوالي. كان هناك اشتباه إصابة بسرطان غدي حرشفي لـ7 مريضات (50%) وفقاً للنتائج الإشعاعية. أجري الاستئصال الكبير وأخذ عينة، بالإضافة إلى تصريف الخراج وأخذ عينة، وأيضاً تصريف الخراج والعلاج الطبي (بريدنيزولون، ميثوتريكسيت) لإحدى عشرة مريضة، مريضتين، ومريضة واحدة على التوالي. نتيجة إلى تطور الخراج بعد تسعة أشهر، تم إجراء التصريف والاستئصال الكبير أيضاً لدى مريضة واحدة والتي تلقت المعالجة الطبية.

خاتمة: يعتبر مرض التهاب الثدي الورمي الحبيبي (GM) مرضاً يؤثر بشكل عام على النساء الشابات وقد يتم تشخيصه عن طريق الخطأ كورم غدي سرطاني في الثدي بواسطة التقييم السريري والإشعاعي. يعد المقياس الذهبي للتشخيص تقييماً مرضي نسيجي.

Objectives: To discuss the clinical and radiological features and treatment approaches in 14 patients diagnosed with idiopathic granulomatous mastitis (GM).

Methods: We retrospectively evaluated the clinical features, radiological findings, and treatment approaches in 14 patients with idiopathic GM in the General Surgery Department, Gulhane School of Medicine, Ankara, Turkey between April 2000 and June 2006.

Results: The mean age of the patients was 34.5 years (range 27-41 years). The complaints at admission were a mass in the breast in 7 (50%) patients, an abscess and a mass in 6 (42.8%), and a skin fistula in one (7.2%). Granulomatous mastitis was unilateral in all subjects (on the right in 5 patients and on the left in 9). All of the patients underwent ultrasonographic evaluation. Mammography was performed in 8 and magnetic resonance imaging in 5 patients. Seven patients (50%) were suspected to have breast carcinoma according to radiological findings. We performed large excision in 11, incisional biopsy plus abscess drainage in one, and incisional biopsy plus abscess drainage plus medical treatment (prednisolone, methotrexate) in 2 patients. Due to the development of abscess after 9 months, drainage and large excision were also performed in one patient who received medical treatment.

Conclusion: Idiopathic GM is a disease that generally affects young women of reproductive age and may be mistaken for breast carcinoma in clinical and radiological evaluations. The gold standard for the diagnosis is histopathologic evaluation.

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From the Departments of General Surgery (Ozturk, Akin, Can, Ozerhan, Yagci, Tufan), and Pathology (Kurt), Gulhane Military University Medical School, and the Department of General Surgery (Akin), Gazi University Medical School, Ankara, Turkey.

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Address correspondence and reprint request to: Dr. Murat Akin, Ayten Sok. 12/14 Mebusevler, Tandogan, Ankara 06580, Turkey. Tel. +90 (312) 2025716. Fax. +90 (312) 2150494. E-mail: makin@gazi.edu.tr

Granulomatous mastitis (GM) is a rare, chronic inflammatory breast disease of unknown etiology. Granulomatous mastitis is also named as granulomatous lobular mastitis or granulomatous lobulitis. This was first defined in 1970 as a benign and granulomatous lesion that simulated breast carcinoma. The specific diagnosis was first reported in 1972; they identified the histopathologic details of a series of 5 patients as multiple granuloma and abscess formations.[1-3] Most of the patients were reproductive women who presented a unilateral mass, delivered short time prior to their inclusion and had used oral contraceptives.[4] Tuberculosis, sarcoidosis, and some mycotic or parasitic diseases are all considered in GM's etiology, but the disease is generally idiopathic. Histopathologic diagnosis is achievable by the presence of an inflammatory reaction that impairs breast lobules and of multiple granulomas without caseous necrosis.[5,6] Although it is a benign disease, the possibility of confusion with breast carcinoma on clinical and radiological examinations attributes a level of importance to it. Treatment options are controversial due to the difficulty in preoperative diagnosis. Generally, no additional treatment is administered when GM is diagnosed histopathologically following biopsy, which creates a risk of recurrences. In order to prevent them, further surgical interventions or medical treatment modalities with immunosuppressive agents or corticosteroids are recommended.[7] In this study, we aimed to discuss the clinical features, radiological findings, and treatment approaches in 14 patients who were diagnosed with idiopathic GM in our clinics.

Methods. We retrospectively evaluated the clinical features, radiological findings, and treatment approaches in 14 patients who were histopathologically diagnosed with idiopathic GM in the General Surgery Department, Gulhane School of Medicine, Ankara, Turkey between April 2000 and June 2006. The institutional ethics committee approved the study before the beginning of data collection. Biopsy specimens (incisional or excisional) of all patients were obtained for histopathologic evaluation. Moreover, specific diseases that might lead to GM, such as tuberculosis, sarcoidosis, parasitic or mycotic illnesses, were evaluated as well. Cases with no any specific cause and included inflammatory reaction that impaired breast lobules, and granulomas without classification were diagnosed as idiopathic GM. Patients without histological diagnosis, those who had a concomitant diagnosis of breast cancer involved in another region of their breast, and those patients who were unwilling to participate were excluded. Statistical method was not used in this study because retrospective results were presented.

Results. The mean age of the patients was 34.5 years (range 27-41 years). The complaints at admission were a mass in the breast in 7 patients (50%), an abscess and a mass in 6 patients (42.8%), and a skin fistula in one patient (7.2%) (**Figure 1**). Granulomatous mastitis was unilateral in all patients (on the right in 5 patients and on the left in 9 patients). The mean diameter of the masses was 4.25 cm (2-7). Five of these masses were hard and had regular borders, 3 of them were soft and had regular borders, 5 were hard and had irregular borders and finally, one of them was soft and had irregular borders. There was a suspicion for malignancy in physical examinations of 3 cases with irregular borders and 2 cases with regular borders. An axillary mobile lymph node with regular borders and dimensions of 2x1 cm was present in only one (7.2%) patient. All patients underwent ultrasonographic (USG) evaluation. Mammography (MG) was performed in 8 of them and magnetic resonance imaging (MRI) in 5. Seven (50%) patients were suggested to have breast carcinoma according to radiological findings. Thickening of the breast skin, parenchyma edema, irregular heterogeneous hypoechoic masses with no evidence of posterior shading, and masses that were consistent with hypoechoic abscesses that included localized liquid densities were observed in USG evaluations (**Figure 2a**). The MG assessments revealed non-specific, asymmetrical density increase and skin thickening in 3 patients, evident masses in 3 and parenchyma distortion and asymmetrical density increase in 2 patients. There were lesions, suggested to be due to the inflammatory process, presenting unclear borders and slight heterogeneous contrasting in MRI evaluations. Magnetic resonance imaging findings suggested GM rather than carcinoma (**Figure 2b and**

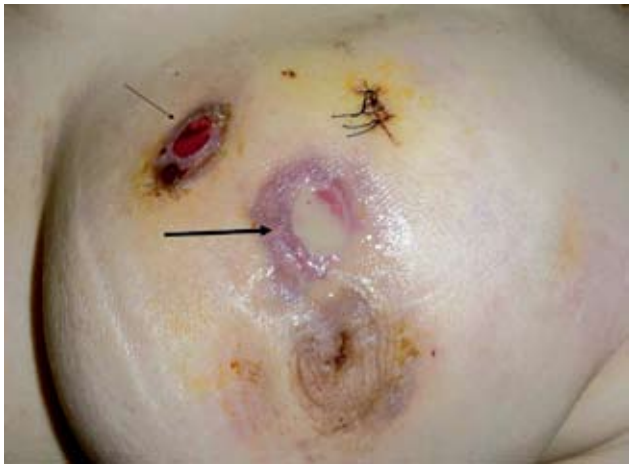

Figure 1 - View of the left breast in granulomatous mastitis patient with fistula (thin arrow) and abscess formation (thick arrow).

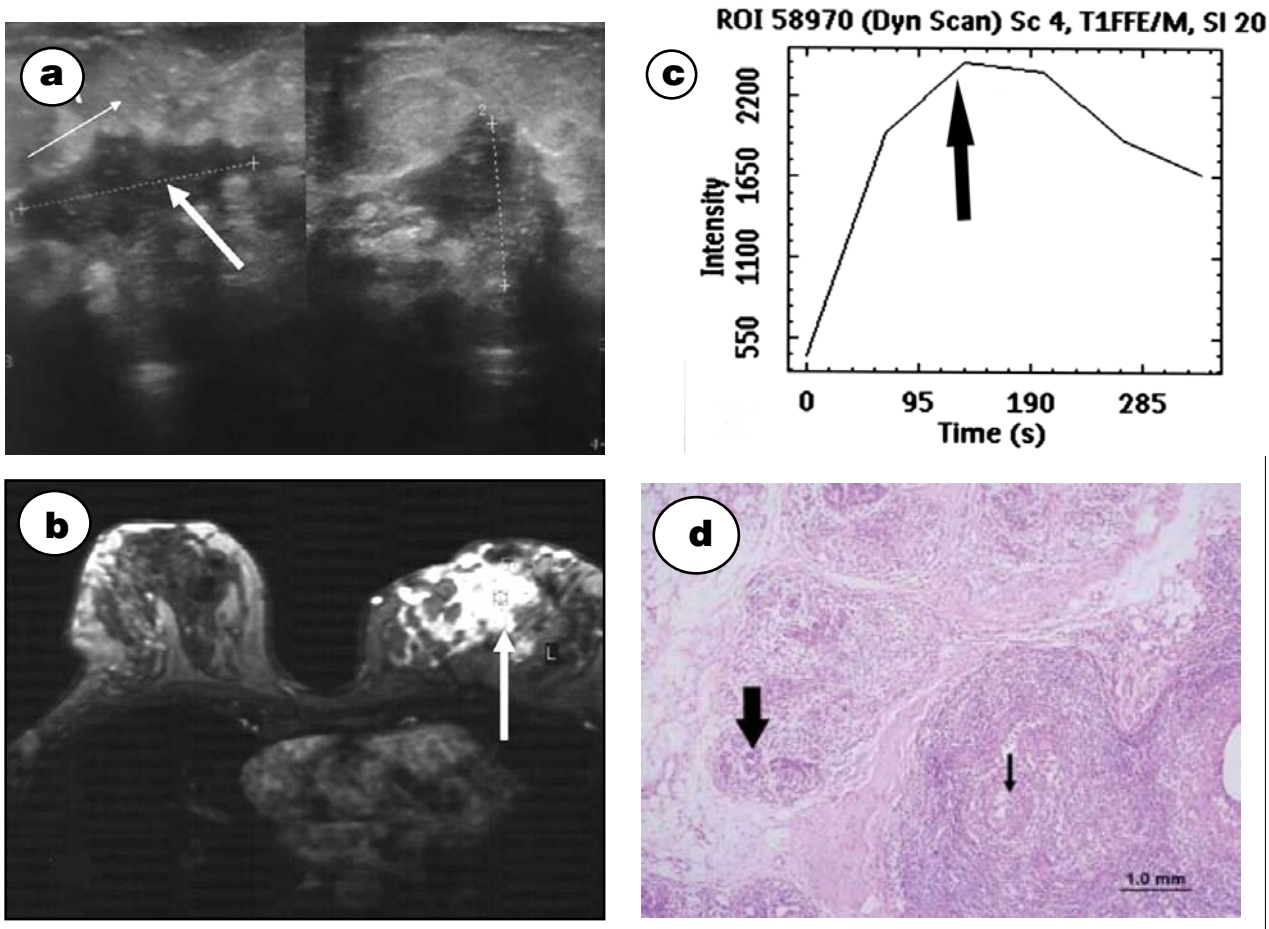

Figure 1 - Ultrasonography of the lesion shows **a**) thickening of the breast skin (thin arrow), parenchyma edema, and irregular heterogeneous hypoechoic masses (thick arrow). **b**) Intensive homogeneous enhancement of the lesion (thick arrow) and the presence of the adipose tissue infiltrations and multiple sinus tracts to the skin. **c**) time-intensity curve shows early peak enhancement and washout (thin arrow). **d**) Hispathology shows breast lobules (thick arrow), and a granuloma (thin arrow) (Hematoxylin and Eosin x100).

2c). Large excision was performed in 11 patients, incisional biopsy and abscess drainage were performed in one patient, incisional biopsy, abscess drainage and medical treatment (prednisolone, methotrexate) were performed in 2 of them. After treatment, the subjects were followed for a mean period of 39 months (range 18-78 months). Physical examination and USG were performed every 3 months during the first year and every 6 months afterwards. Due to the development of an abscess after 9 months, abscess drainage and large excision were performed in one (7.2%) patient who received medical treatment. No other recurrence was seen in this patient or in other patients under follow up. In the pathologic evaluation, we observed granulomas that included giant cells without caseous necrosis and inflammatory reactions that were rich in polymorphonuclear leukocytes, lymphocytes, plasmocytes, and histiocytes (**Figure 2d**).

Discussion. Granulomatous mastitis diagnosis is only possible through histopathologic evaluation. The 2 types of GM are defined as idiopathic and specific. Specific GM may be seen in sarcoidosis, tuberculosis, mycotic infections (actinomycosis, histoplasmosis, blastomycosis, sporotrichosis) and parasitic diseases (schistosomiasis, filariasis). This type of GM is generally existent in Asian and African countries.[1,4] The idiopathic type of GM is more common and typically present in reproductive ages, between the second and fourth decades, usually 2 months to 15 years after delivery. Twenty percent of the patients were in the lactation period, and 5-10% were pregnant. History of oral contraceptives use was stated by one third of the subjects.[5,7] The deficiency of alpha-1 antitrypsin is considered in the disease's etiology. Moreover, it was reported that idiopathic GM might develop during the course of some auto-immune diseases such as erythema nodosum, polyarteritis nodosa, Wegener's

granulomatosis, giant cell arteritis and lymphocytic alveolitis.[1,5-9] Ehrlich Ziehl-Neelsen dye and purified protein derivative (PPD) test were negative in all of our patients and there was no radiological finding consistent with sarcoidosis or tuberculosis. The focuses of micro abscesses that were present in histopathologic evaluation were inconsistent with sarcoidosis. None of our patients had any rheumatologic illness and the period between the last delivery and the onset of the disease was 4-61 months. Four (28.5%) of our patients had a history of oral contraceptive use. These observations were in accordance with the literature. Idiopathic GM is generally confused with breast carcinoma in clinical and radiological examinations. The most common feature is a hard, unilateral (60-70%) mass with regular or irregular borders accompanied by skin inflammation signs. Like breast carcinoma, it may lead to retractions and ulcerations on the skin. Axillary lymph nodes are present in 15% of the patients and may be seen in all quadrants.[1,8,10] In our study, all of the cases were unilateral. There were masses in 13 subjects and one had an axillary lymph node. Radiological findings of idiopathic GM are not specific, and generally resemble carcinoma of the breast. Non-homogeneous, focal, generally irregular, hypoechoic lesions with posterior shading or multiple hypoechoic lesions with regular borders and tubular configurations can be observed in USG evaluations. Han et al[11] reported that the presence of tubular hypoechoic lesions and surrounding echogenicities was important for the diagnosis of idiopathic GM. Although MG findings may appear completely normal, suspicious lesions with various dimensions, focal asymmetrical density increases and structural distortion may be seen. Microcalcification, spicular extensions or modifications of the nipples were not reported.[6,11-13] No specific MRI finding was yet defined. Images differing from one or a few lesions that showed surrounding contrasting to heterogeneous and hypertensive lesions with indefinite borders were reported. Although differential diagnosis of breast carcinoma and inflammatory process is not possible, MRI evaluation is especially beneficial in the detection of active lesions and the spread of the disease.[6] More than 50% of the patients are diagnosed with carcinoma until histopathologic evaluation is completed. In this investigation, different imaging techniques were combined and 7 patients were then suspected to have carcinoma. However, after histopathologic evaluation and association with clinical findings, idiopathic GM was the final diagnosis.

Histopathologic diagnosis of GM is very important for treatment planning and for exclusion of breast carcinoma. Fine needle biopsy, tru-cut biopsy, open incisional or excisional biopsy may be performed. Histopathological observations show, within the breast lobules, non-classified granulomas with inflammatory infiltration, composed of epithelioid histiocytes, Langerhans-type giant cells, eosinophils, polymorphonuclear leukocytes and plasma cells. The presence of small foci of abscesses is significant in the differential diagnosis and in some cases there is fibroblastic activity around the lobules. The exact diagnosis is possible in the presence of characteristic histopathologic findings, and after excluding other diseases such as tuberculosis, sarcoidosis, Wegener's granulomatosis, mycotic and parasitic diseases. In previous immune phenotypic studies, a constant dominance of T-cells was evidenced.[6,14] The treatment for idiopathic GM is controversial. Although surgical resection and drainage receive general acceptance, there are also disagreements regarding the dimensions of the resection. While some reports favor a simple incision and drainage, a larger excision is recommended in others. Other important aspects are postoperative recurrences and development of skin fistulas. Fistula development is present in 20-30% of the patients.[14] As some autoimmune mechanisms are considered to be effective in the disease etiology, immunosuppressive treatment is advised in cases with recurrences following surgery. DeHertogh et al[15] first recommended corticosteroid treatment in 1980. Although various regimens are administered nowadays, the most common recommendation is as follows: prednisolone 2x30 mg/day for at least 3-6 weeks until remission, then decremental dose decreases until stopping. There are reports of recurrent cases following corticosteroid treatment, but other studies state that high-dose administration following fine needle biopsy would lead to favorable outcomes. Low-dose methotrexate administration (10-15 mg/week) for immunosuppression with the aim of decreasing corticosteroid dose was reported to treat recurrent cases successfully.[7,15-18] In our series, while we did not identify any recurrence in the patients' submitted to large excision, it was still detected at the ninth month in one of the patients who underwent incisional biopsy and medical treatment. After abscess drainage and large excision, recurrence was no longer observed in this subject.

As a conclusion, idiopathic GM is a disease affecting young and reproductive women, which mimics breast carcinoma in both clinical and radiological aspects. The golden standard for the diagnosis is histopathologic evaluation. Although large local excision appears to be the most suitable treatment approach in order to decrease the prevalence of recurrences, comparative studies with larger patient populations are necessary.

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