The Journal of Breast Health
meme sağlığı dergisi

The Journal of Breast Health 2011 Vol: 7 • No: 4
Meme Sağlığı Dergisi 2011 Cilt: 7 • Sayı: 4

RESEARCH ARTICLE/ARAŞTIRMA YAZISI

IDIOPATHIC GRANULOMATOUS MASTITIS

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Sunulduğu Kongre: X. Ulusal Meme Hastalıkları Kongresi, 30 Eylül-4 Ekim 2009, Çeşme, İzmir.

İDİYOPATİK GRANULOMATÖZ MASTİT

ÖZET

Amaç: İdiyopatik granulomatöz mastit, kronik inflamasyonla seyreden, etyolojisi bilinmeyen, nadir görülen, benign bir meme hastalığıdır. Klinik ve radyolojik olarak hem meme kanserinden hem de meme enfeksiyonlarından ayırt etmek zor olabilir. Bu çalışmanın amacı, idiyopatik granulomatöz mastitin özelliklerini geniş bir hasta serisinde gözden geçirmek ve uzun bir takip süresinde tedavi yöntemlerinin etkinliğini değerlendirmektir.

Hastalar ve Yöntem: İdiyopatik granulomatöz mastit tanısıyla 2005 – 2009 yılları arasında tedavi edilen hastalar çalışmaya alındı. Hastaların klinik, radyolojik ve histopatolojik özellikleri retrospektif olarak dosyalarından elde edildi.

Bulgular: Ortanca yaşı 33 olan 51 hasta çalışmaya alındı. Hastaların tümünde doğum ve emzirme öyküsü mevcuttu ve 45 hasta (%88.2) premenopozaldi. Hastaların tümündeki ana klinik bulgu memede mevcut kitleydi ve enfeksiyonu düşündüren klinik bulgular 7 hastada (%13.7) kitleye eşlik etmekteydi. Hastaların tamamına cerrahi uygulandı. Geniş lokal eksizyon 50 hastada (%98) tercih edilen tedavi yöntemiyken modifiye radikal mastektomi bir hastada uygulandı. Ortanca takip süresi 38 aydı ve üç hastada (%5.9) nüks saptandı. Bu hastalardan birisi iki kez nüksetti ve total mastektomi ve rekonstrüksiyon uygulandı. Diğer iki hasta ise yeniden geniş lokal eksizyonla tedavi edildi.

Sonuç: Cerrahlar, radyologlar ve patologlar, idiyopatik granulomatöz mastiti daha yakından tanımalıdır ve doğru tanı için klinik, radyolojik ve histopatolojik olarak tekrarlayan değerlendirmeler gereklidir. Tercihan aynı hekimler tarafından yapılan uzun süreli takip bu zor hastalığın tedavisi için gereklidir.

Anahtar sözcükler: meme, granulomatöz mastit, cerrahi

ABSTRACT

Purpose: Idiopathic granulomatous mastitis is a rare, benign breast disease of unknown etiology characterized by chronic inflammation. Distinguishing it from either breast carcinoma or infections both clinically and radiologically can be difficult. The purpose of this study is to review the characteristics of idiopathic granulomatous mastitis in a large series of patients and to evaluate the effectiveness of the treatment methods during a long follow up period.

Patients and Methods: Patients treated with the diagnosis of idiopathic granulomatous mastitis between 2005 and 2009 were included in the study. Patients' clinical, radiological, and histopathological findings were retrospectively obtained from the files.

Results: Fifty-one female patients with a median age of 33 were included. All patients had a history of childbirth and breastfeeding. Forty-five patients (88.2%) were premenopausal. The main clinical feature was a mass in the breast in all patients and clinical findings suggesting an infection accompanied the mass in seven patients (13.7%). Surgery was the definitive procedure in all patients. Wide local excision was the treatment of choice in 50 patients (98%) whereas modified radical mastectomy was performed in one patient. Median follow-up time was 38 months and three patients (5.9%) presented with recurrence. One patient recurred twice and total mastectomy with reconstruction was performed. Two other patients were treated with further wide local excisions.

Conclusion: Surgeons, radiologists, and pathologists should be familiar with idiopathic granulomatous mastitis and multiple assessments including clinical, radiological, and histopathological examinations are required for an accurate diagnosis. Long-term follow-up preferably by the same doctors is necessary for the management of such a difficult disease.

Key words: breast, granulomatous mastitis, surgery

Introduction

Idiopathic granulomatous mastitis (IGM) is a rare, benign breast disease of unknown etiology characterized by chronic inflammation. Kessler and Wolloch described IGM for the first time in 1972 (1). Until today, around 300 cases have been reported with only a few small series of patients (2). Almost all of the previously reported patient series included less than 25 patients (3-9). Similarly, patients with IGM were reported from national cancer centres (10). The main reason for the rarity of this disease could possibly be the difficulty in distinguishing IGM from either breast carcinoma or infections both clinically and radiologically. Reported pretreatment diagnosis of malignancy is 51% in IGM (2). Even after histopathological evaluation, IGM may be underdiagnosed due to its resemblance to carcinoma in some cases. In addition,

Gönderilme Tarihi: 11 Nisan 2011 • **Revizyon Tarihi:** 11 Mayıs 2011 • **Kabul Tarihi:** 10 Haziran 2011

Table 1. Demographic and clinical characteristics of the patients.

	N	%
Clinical findings		
Mass	51	100.0
Tenderness	27	52.9
Erythema	7	13.7
Sinus formation	1	1.9
Location		
Left breast	28	54.9
Right breast	23	45.1
Upper outer quadrant	24	47.0
Menopausal status		
Premenopausal	45	88.3
Perimenopausal	2	3.9
Postmenopausal	4	7.8

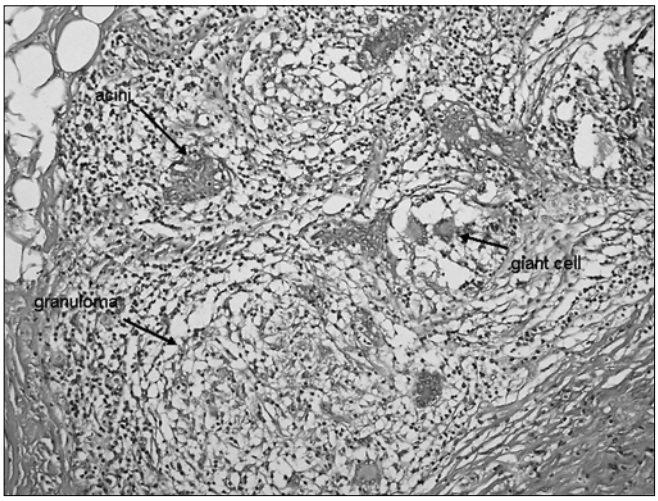

Figure 1. Granulomatous mastitis presenting in a lobule with histiocytic granulomas intermixed with a few inflammatory cells (HE, x400).

the optimal treatment of IGM is still controversial. Although surgical removal is accepted as the mainstay of treatment, antibiotics, steroids, and even chemotherapeutic agents were used to treat these patients. In this context, the purpose of this study is to review the characteristics of IGM in a large series of patients and to evaluate the effectiveness of the treatment methods during a longer follow up period.

Patients and Methods

Patients treated with the diagnosis of IGM between 2005 and 2009 were included in the study. Patients' clinical, radiological, and histopathological findings are retrospectively obtained from the files. Histopathological diagnosis of IGM was confirmed in all patients using special stains (gram, Ziehl-Neelsen, periodic acid-Schiff) in addition to hematoxylin-eosin. Treatment methods and related complications were evaluated. Patients were followed every 6 months with a thorough clinical examination. Bilateral breast ultrasonography and, if required, mammography were performed yearly. Recurrences detected during follow-up and their treatments were recorded as well.

Results

Fifty-one female patients treated with the diagnosis of IGM were included in the study. Median age of the patients was 33 (range, 22-57). All patients had a history of childbirth and breastfeeding and one patient was pregnant with her second child at the time of diagnosis. Forty-five patients (88.2%) were premenopausal whereas the number of peri- and postmenopausal patients was two and four, respectively. The main clinical feature was a mass in the breast in all of the patients. Clinical findings suggesting a breast infection such as erythema accompanied the mass in seven patients (13.7%). The lesion was located in the left breast in 28 patients (54.9%) and in the upper outer quadrant in 24 patients (47.0%). Axillary lymph node involvement was not detected clinically and in radiological examinations. None of the patients had bilateral involvement of the breast with IGM. Demographic and clinical characteristics of the patients are shown in Table 1.

As a diagnostic imaging workup, bilateral breast ultrasonography was performed in all patients. In addition, bilateral mammography was performed in two and magnetic resonance imaging in one patient. Ultrasonographic examination revealed an irregular hypoechoic mass whereas mammographic examination showed an ill-defined mass as the main feature.

Excisional biopsy was the initial surgical intervention to obtain a histopathological diagnosis in 32 patients (62.7%). Incisional biopsy and fine needle aspiration biopsy were used in 13 (25.5%) and 6 (11.8%) patients, respectively. Macroscopically, the lesions appeared as firm, yellowish white masses. Microscopically, there was a non-caseating granulomatous inflammation especially in the breast lobules. Epithelioid histiocytes and Langhan's type multinucleate giant cells were the main cell types in the granulomas (Figure 1). Focal microabscesses were detected in cases clinically resembling an infectious process.

As an initial treatment, seven patients (13.7%) received oral antibiotics and abscess drainage was performed in only one patient. Pus culture obtained from this patient was negative for microorganisms. Surgery was used as the definitive procedure in all patients. Wide local excision was the treatment of choice in 50 patients (98%) whereas modified radical mastectomy was performed in one patient with the faulty diagnosis of breast carcinoma. None of the patients received steroids or any other drug treatment.

Median follow-up time was 38 months (range, 12-58). During follow-up, three patients (5.9%) presented with recurrence. All patients with recurrence had a mass in their breasts on the same

side of previous IGM. One of these patients recurred twice, 3 and 8 months after initial treatment and total mastectomy with implant reconstruction was performed to control the symptoms. The other two patients recurred only once, 7 and 15 months after initial treatment. These two patients were treated with further wide local excisions and did not show any signs of further recurrence.

Discussion

The current patient series represents the largest one (51 patients) reported from a single center until today, although the data were collected retrospectively. In addition, patients were followed for a long period of time (at least a year, median over three years) to delineate the clinical course of the disease after initial treatment. IGM represents 24% of all histopathologically defined inflammations in the breast (11). It is characterized by non-caseating granulomas restricted to breast lobules. The diagnosis of IGM is based on exclusion of other causes of chronic inflammation. In case of IGM, microorganisms will not be identified in pus cultures and during histopathological examination. Although its etiology is not well established, various reasons such as oral contraceptive use, autoimmune and infectious factors have been proposed. Today, widely accepted mechanism states that autoimmune response to secretions originating from damaged ducts may have a role in IGM. Accumulation of secretions in mammary ducts leads to ductal ectasia and, eventually, to the rupture of the involved ducts. Secretions spreading to the stromal tissue after ductal rupture result in a chronic inflammation (11). Multiple breast-feedings and prolonged lactation periods may be the reason for dilatation and rupture of the ducts and acini. In the current study, all of the patients (7 patients) clinically resembling an infectious process had a history of pregnancy and lactation within the last year supporting this hypothesis. In addition, Al-Khaffaf et al. compared demographic characteristics of IGM patients to patients with periductal mastitis and normal controls and reported that IGM patients are younger and have given birth recently supporting the above mentioned hypothesis (8).

Clinically, IGM may appear in various forms. Unilateral tender mass, infectious and inflammatory findings in breast skin such as ulceration and skin dimpling are the main clinical findings. In addition, axillary involvement has been reported as high as 15% (6). Patients in this study presented with a mass in the breast, and, some of them had additional findings suggesting an infectious process in the breast. Lesions were distributed evenly between the two breasts, but tend to be mainly located in the periphery of the breast.

Breast ultrasonography, mammography, and magnetic resonance imaging are the imaging modalities used for supporting clinical findings and excluding other diagnosis in IGM. However, imaging modalities are generally not useful enough to establish the correct diagnosis. Younger patient population and radiologic findings mimicking breast cancer decrease the diagnostic value of mammography. Many patients with IGM have either non-specific findings or even no abnormality on ultrasonography and mammography. Skin thickening and irregular hypoechoic lesions are the main ultrasonographic findings (12). On the other hand, an irregular ill defined mass, diffusely increased density or parenchymal distortion can be encountered on mammography (12). Magnetic resonance imaging can be utilized as a complementary diagnostic modality in IGM cases and it may have a role during the follow-up of patients treated conservatively. Dynamic contrast enhanced magnetic resonance imaging indirectly shows the vascular nature and malignant potential of the breast lesion. Benign time-signal intensity curves detected on magnetic resonance imaging can, at least, help to understand the benign nature of the lesion (3,13). Although magnetic resonance imaging can be regarded as an expensive diagnostic modality, preventing further unnecessary surgical interventions will reduce the overall cost.

Usually, the diagnosis of IGM is established after histopathologic evaluation. Tissue samples from the target lesion could be obtained by fine needle aspiration or core needle biopsy. Cytological evaluation requires an experienced pathologist to avoid misdiagnosis as breast cancer. The diagnostic cytological criteria for IGM remain poorly defined. The presence of granulomas, abscence of background necrosis, relatively higher proportion of epithelioid histiocytes, and presence of multinucleated giant cells support the diagnosis of IGM (14). However, fine needle aspirate may contain clusters of atypical cells with large nuclei, small nucleoli, and slight nuclear hyperchromasia (15). Modified radical mastectomy was performed in one patient in this series with the diagnosis of breast carcinoma. Similarly, previous studies reported on patients treated with mastectomy after a faulty diagnosis of carcinoma with fine needle aspiration biopsy (2,5,12,15,16). Thus, the diagnosis must be confirmed by tissue evaluation before performing mastectomy. In case of an accompanying abscess, tissue samples should be taken from the cavity walls during drainage. However, these methods are not adequate to reach a correct diagnosis in most cases and incisional or excisional biopsy is performed. Histopathologic evaluation reveals a non-caseating granulomatous inflammation accompanied by Langhan's type giant cells, epithelioid histiocytes, leucocytes, and macrophages as detected in our patients.

The treatment of choice for IGM is controversial. In a previous review, recurrence after initial surgical treatment was reported as 23.6% (34/144 patients) whereas recurrence after steroid treatment was 25.8% (8/31 patients) (2). However, surgery is a widely accepted primary treatment of IGM. Abscesses accompanying the breast mass suggesting IGM should be initially drained. Wide local excision of the breast lesion can be adequate. Oncoplastic surgical techniques can be added to obtain better cosmetic outcomes. Surgical treatment was the preffered method in our center. Although comparison of surgical and medical treatments was not the aim of the current study, low recurrence rate (5.9%) encountered after only surgical treatment may support the primary use of surgery.

Complications encountered during the treatment of IGM are recurrent infections, abscess and/or sinus formation, and delayed wound healing. In recurrent cases without any findings suggesting an infectious process, oral steroid therapy (prednisolone 2x30 mg/day) can be administered until a remission is obtained (11). Dose of the steroids is tapered off when a clinical response is observed. In case of recurrence, patients should be evaluated for tuberculous mastitis before initiating steroid treatment, especially in countries where tuberculosis is a widespread health problem. Recurrences after steroid treatment may be managed by administering methotrexate 10-15 mg/week in addition to low dose steroids for 12 to 24 months (17). When surgical and medical treatments are not adequate for local control of IGM, total mastectomy with reconstructive surgery can be a good option. In this series, total mastectomy with implant reconstruction was performed in one patient with frequent recurrences.

In conclusion, surgeons, radiologists, and pathologists should be more familiar with IGM due to its clinical significance. Differentiating IGM from breast infections and malignancy is the most critical part of the management. Multiple assessments including clinical, radiologic, and histopathologic examinations are required for an accurate diagnosis. Long-term follow-up preferably by the same doctors will be a logical solution for the management of such a difficult disease.

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