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Management of Patients with Idiopathic Granulomatous Mastitis: Presentation of 13 Cases

İdiyopatik Granülomatöz Mastitli Hastaya Yaklaşım: 13 Vakanın Sunumu

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ABSTRACT

Objective: Idiopathic granulomatous mastitis is a rare benign chronic disease of the breast. In this study, we aimed to present our treatment experience in cases diagnosed with idiopathic granulomatous mastitis.

Materials and Methods: 13 treated cases of idiopathic granulomatous mastitis, diagnosed as a result of histopathological examination, were investigated retrospectively from January 2009 to December 2012.

Results: 13 patients were included in the study. Ultrasound was performed on all patients, mammography was performed in three patient and magnetic resonance imaging was performed in two patient. For the histopathological evaluation; Tru-cut biopsy was performed in 6 patients, fine-needle aspiration biopsy was performed in 2 patients, incisional biopsy was performed in one patient and, after abscess drainage, wall biopsy was performed in 4 patients presenting with a breast abscess. Recurrence occurred in 2 patients after six months of prednisolone treatment (15.3%). Simple mastectomy was performed in these patients. During one session Latissimus dorsi flap reconstruction was performed in one patient and silicone prosthesis reconstruction in the other one. There was no recurrence observed in the two-year follow-up. Simple mastectomy was performed in 1 patient with a common fistula formation of breast.

Conclusion: We considered that a conservative approach to idiopathic granulomatous mastitis is an appropriate treatment option. We felt that the most important factor in the response to treatment and prognosis of the disease is the severity of the disease at the time of treatment.

Key words: Mastitis, granulomatous disease, chronic, breast

ÖZET

Amaç: İdiyopatik Granülomatöz Mastit memenin nadir görülen, iyi huylu kronik bir hastalığıdır. Yapmış olduğumuz bu çalışmada idiyopatik granülomatöz mastit tanılı olgulardaki tedavi deneyimimizi sunmayı amaçladık.

Yöntem ve Gereçler: Ocak 2009 ve Aralık 2012 yılları arasında histopatolojik değerlendirme sonucunda idiyopatik granulomatöz mastit tanısı alıp tedavi edilen 13 olgu retrospektif olarak araştırıldı.

Bulgular: Çalışmaya 13 hasta dahil edildi. Ultrasonografi tüm hastalara, mamografi çekimi üç hastaya, manyetik rezonans (MR) görüntüleme iki hastaya yapıldı. Histopatolojik değerlendirme için 6 hastaya tru-cut biyopsi, 2 hastaya ince iğne aspirasyon biyopsisi, 1 hastaya insizyonel biyopsi ve apse kliniği ile başvuran 4 hastaya drenaj sonrası apse duvarından biyopsi yapıldı. Prednizolon tedavisi uygulanan 2 hastada (%15,3) altıncı ayda nüks gelişti. Bu hastalara basit mastektomi yapıldı. Aynı seansta bir hastaya latissimus dorsi flep rekonstruksiyonu yapılırken diğer hastaya silikon protezle rekonstruksiyon yapıldı. Her iki hastanın da iki senelik takiplerinde nüks izlenmedi. Memesinde yaygın fistül formasyonu bulunan 1 hastaya ise basit mastektomi yapıldı.

Sonuç: İdiyopatik granülomatöz mastitte konservatif yaklaşımın uygun bir tedavi seçeneği olduğunu düşünmekteyiz. Hastalığın tedaviye yanıtını ve prognozunu belirleyen en önemli etkenin hastalığın tedavi anındaki aktivasyon şiddeti olduğunu düşünüyoruz.

Anahtar sözcükler: Mastit, granülomatöz hastalık, kronik, meme

Introduction

Idiopathic Granulomatosis Mastitis is a benign, chronic, rarely seen breast disease (1). Although it is not certain, it is thought to be related with autoimmunity, infection, oral contraceptive usage and lactation (2, 3). While most of the patients consist of women in their reproductive age (4, 5), it is reported in the literature that there are cases diagnosed with granulomatosis between the ages 11 to 70 (6). Although it is generally seen in a single breast, it can be seen in both breasts in 25% of cases (1, 7). Clinically and radiologically, it is similar to granulomatosis diseases and carcinoma of the breast. There is no certain procedure for treatment in the literature. There are publications that suggest surgical treatments as well as those that suggest treatments with prednisolone, methotrexate, colchicine and hydroxyquinoline (8, 9). We can consider such a variety of treatment options as a result of the active severity of the illness during treatment. In our study, the relapse rate was found to be 15% with a conservative approach. In this study, we aim to present our treatment experience of the cases with idiopathic granulomatosis mastitis diagnosis.

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Materials and Methods

Based on the results of histopathological research between January 2009 and December 2012, 13 cases diagnosed with idiopathic granulomatosis mastitisand treated were analyzed retrospectively. There was no ethics commitee approval, however, written informed consent was obtained from patients who participated in this study. With the aid of hospital records, demographic features (age, gender, history, family history, marital status, the number of live births, lactation period, smoking habits, use of oral contraceptives), the reason for applying to the hospital, physical examination findings, imaging techniques (ultrasonography, mammography, magnetic resonance imaging), biopsy method (fine-needle aspiration biopsy, tru-cut biopsy, incisional biopsy) and treatment procedures (antibiotic, anti-inflammatory, abscess drainage, steroids, surgery) of the patients were recorded.

In order to perform a histopathological research on grafts and aspiration materials, Hematoxylene+Eosin (H+E) staining for detection of microorganisms, gram staining to detect tuberculosis agent, alkali-acid resistant bacteria (AARB) and Löwenstein-Jensen culture, polymerase chain reaction of the tissue (PCR), Erlich Ziehl-Neelsen (EZN) staining, and to investigate fungus infections, Periodic acid-Schiff (PAS) staining were implemented.

For the patients who were admitted with an abscess, drainage and sampling of the abscess wall were performed. For these findings and the findings that were in favor of inflammation, such as hyperemia and local temperature rise, empiric antibiotherapy was started then, based on culture results antibiotherapy was adjusted. Nonsteroid drugs were administered as anti-inflammatory treatment, for 14 days and histopathological analysis results were awaited.

In cases who were administered steroids, oral prednisolone was given in a 60mg/day dose, then this was reduced by 10 mg/month and ceased at the end of 6 months. As surgical treatment, cases with local excision, mastectomy, and reconstruction were recorded.

Statistical analysis

Data concerning demographic and clinical characteristics were analyzed by using descriptive methods (means, minimum-maximum). The statistical software used was SPSS for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA).

Results

13 patients were included in the study. The average age of the patients was 33, and 10 of the patients 76%) were in their reproductive age. Although no patients had a history of breast cancer, one of the patients had a history of breast cancer in a second degree relative and one patient had autoimmune connective tissue disease. The demographic features of the patients are shown in Table 1. The most common cause of admission was an aching palpable mass (8 patients). In the ultrasonographic evaluation of these patients, the average size of the mass was found to be 3.1 (1.8-5) cm. The other physical examination findings at the time of admission are shown in Table 2. (Figure 1)

Table 1. Demographic features of the patients

Demographic Feature	Number of Patients/ Percentage
Live Birth History	6 (46%)
Lactating History	6 (46%)
Oral Contraceptive Usage	4 (30%)
Smoking Habits	4 (30%)
Breast Cancer History	0
Autoimmune Disease History	1 (7%)
Breast Cancer History in the Family	1 (7%)

Ultrasonography was performed on all patients and three patients were found to have doubtful imaging in terms of malignity (one of them was 28 years old the other two were 33 years old), four patients were found to have an abscess cavity and six patients were determined to have imaging consistent with mastitis.

Mammography was performed on three patients over the age of 38 and reported as BIRADS (Breast Imaging Reporting and Data System) category 4. Magnetic Resonance (MR) imaging and ultrasonography were performed on two patients with doubtful imaging in terms of malignity.

For histopathological analysis, 6 patients underwent tru-cut biopsy, 2 patients fine-needle aspiration biopsy, 1 patient incisional biopsy and 4 patients admitted with abscess clinic had abscess wall biopsy after drainage. One patient who had previously had a fine-needle biopsy had an incisional biopsy as the previous results were not clear enough to distinguish inflammatory breast carcinoma.

Four patients who were admitted with mastitis and had complaints of empiric antibiotic and anti-inflammatory treatment hyperemia, ulcerated lesion and fluxion and 4 patients who had an abscess drainage were administered 1000 mg/day amoxicillin clavulanic acid or 1 gr/day ampiciline sulbactam with naproxen or diclofenac. Methicillin responsive, coaulase negative staphylococci reproduction was observed

Table 2. Physical examination findings at admission

Physical Examination	Number of Patients
Aching Mass in the Breast	8 (61%)
Serosis Fluxion	4 (30%)
Ulcerated Lesion	5 (38%)
Hyperemia	4 (30%)
Abscess	4 (30%)
Fistula/Sinus Formation	1 (7%)

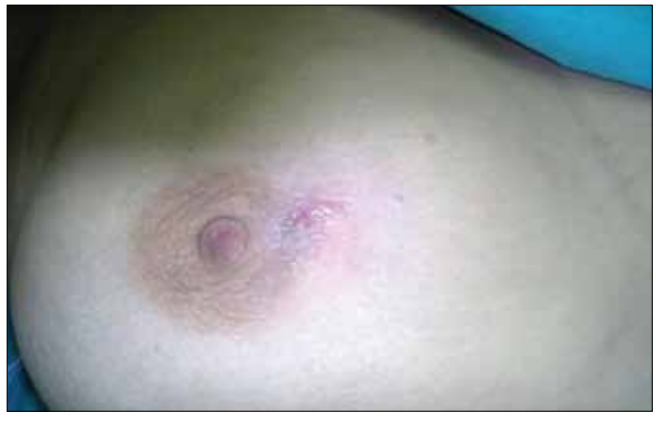

Figure 1. Right breast is erythematic on 4 according to clock dial

in the culture results of 3 patients and amoxicillin clavulanic acid treatment which it is responsive to was administered for 10 days. Due to lack of clinical healing, a tru-cut biopsy was performed.

Prednisolone treatment was administered to all patients except for the patient aged 57 with a diffuse fistula formation in her breast. Mastectomy was performed in this patient with fistula formation with the consent of the patient but after incisional biopsy; the patient did not consent to reconstruction due to social reasons.

In the histopathological analysis of the cases that had mastectomy, they had eosinophil leucocyte occupying breast lobular structures, polymorphonuclear leucocyte and granuloma structures which consisted of plasma cells and epitheloid multinuclear giant cells. The case who did not consent to reconstruction had small abscess cavities which were different from the others.

Two of the patients (15.3%) who were diagnosed with granulomatosis mastitis after a tru-cut biopsy had t relapse of the disease in the sixth month of their prednisolone treatment. These patients had multiple fistula tracts. In the breast imaging of both patients, there were BIRADS category 3 lesions. Mastectomy was performed on both patients at their own request. While one of the patients had latissimus dorsi flap reconstruction in the same session, the other patient had reconstruction with silicone prosthesis. In the 2 year follow-up period, neither of the patients had relapse of the disease. The treatments performed on the patients are summarized in Table 3.

No adverse effects were observed in cases administered prednisolone treatment.

Discussion and Conclusions

Granulomatosis mastitis is a rare chronic benign breast disease which can imitate breast cancer clinically and radiologically (3, 9, 10). It was defined in detail by Kessler and Wolloch (6) in 1972. It has two types, as idiopathic and specific. Specific granulomatosis mastitis can occur due to tuberculosis, sarcoidosis, fungal infections (such as actinomycosis, histoplasmosis, blastomycosis) and parasitic infections (such as filariasis, schistosomiasis). Although the etiology is not known for certain, idiopathic granulomatosis mastitis often occurs with autoimmunity- and oral contraceptive agent usage (metoclapramide, rantidine) (2, 3). In our study, the incidence of oral contraceptive usage was found to be 30% (4 patients) and autoimmune disease history 7% (1 patient).

Most of the patients were females in the breast feeding period (4). In our study, 76% of the patients (10 patients) were in reproductive period while 46% (6 patients) had a history of live births. It is Cases diagnosed with granulomatosis mastitis between the ages of 11 to 70 years have been reported in the literature (6). Although very rare, it can also be seen in male patients (7).

The most common cause of patient admissions is an unilateral aching mass in the breast (2, 3). Bilateral involvement is observed in 25% of the cases (1). In our study, the most common cause of admission was an aching mass in the breast observed in 61% of the patients (8 patients). The involvement was generally in the right breast (7 patients) whereas no bilateral involvement was observed. The other common findings apart for the mass in the breast were hyperemia, local temperature rise and sensitivity, areolar retraction, fistula and ulceration (11).

Even though ultrasonography and mammography are generally preferred in the radiological analysis of granulamatosis mastitis, the use of MR imaging is also increasing (12). Ultrasonographic findings are more significant but are very variable. An irregular hypoechoic mass, tubular hypoechoic expansion, parenchymal heterogeneity and multiple abscess collections are the most common ultrasonographic findings, but none of them are specific findings (13). In this study, the most common ultrasonographic image was a hypoechoic irregular mass seen in nine patients.

Since the granulomatosis mastitis patient population mostly consists of young females, the sensitivity of mammography is low. Although the mammographic findings are not also specific, most commonly, asymmetric density and contraction of skin are observed and also amorphous mass and axillary lymphadenopathy are often traced (13). In our study, the mammographic analysis was performed on three patients over the age of 38 and they were reported as BIRADS category 4.

In the imaging of granulomatosis mastitis, MR imaging is generally used as a subsidiary imaging technique (14). In our study, MR imaging was performed on two patients who had doubtful images in terms of malignity on ultrasonography. One of these patients was found to be consistent with granulomatosis mastitis after tru-cut biopsy, whereas the other patient had a fine-needle biopsy and since, as a result of histopathological analysis, it was not distinguished from inflammatory breast carcinoma, an incisional biopsy was performed and the diagnosis was granulomatosis mastitis. Although MR imaging was found to be high in sensitivity but low in specificity in other studies (12), in our study it was useful for diagnosis in two patients.

In the histopathological sampling of granulomatosis mastitis, fine-needle aspiration biopsy, tru-cut biopsy and incisional biopsy are performed. Fine-needle aspiration biopsy is easier to perform compared to tru-cut biopsy and incisional biopsy; however, its results are less accurate, and the accurate diagnosis rate is below 50%. In the literature, cases with mastectomy are reported because faulty positive results were reached in terms of malignity after fine-needle aspiration biopsy material was histopathologically analyzed (3, 7). Therefore, tru-cut and incisional biopsies are preferable and tru-cut biopsies are easier to perform than incisional biopsies (11). In our study, tru-cut biopsy was performed on 6 patients, fine-needle aspiration biopsy on 2 patients, incisional biopsy on 2 patients and abscess wall biopsy was performed on 4 patients after drainage. One of the patients who had an incisional biopsy had fine-needle aspiration biopsy; however, the results were not clear enough to distinguish from inflammatory breast carcinoma.

In making decisions about the treatment of granulomatosis mastitis, the clinical state of the patient, localization and size of the lesion and

Table 3. Applied treatments

8 patients: empiric treatment + prednisolone
4 patients: prednisolone → relapse in 2 patients → mastectomy + reconstruction
1 patient: mastectomy

the size of the breast should be taken into consideration (15, 16). There is no certain procedure of treatment in the literature. There are publications that suggest surgical treatments as well as the ones that suggest treatments with prednisolone, methotrexate, colchicines and hydroxyquinoline (8, 9, 11). We can consider such a variety of treatment options as a result of the active severity of the illness during treatment. The patients with inflammation findings should first be administered antibiotherapy. Thosethat present with abscess, are administered antibiotheraphy after drainage and pouch wall biopsy and the treatment is adjusted, based on culture results (17). At this point, by taking the factors of specific granulomatosis mastitis etiology into consideration, in order to eliminate tuberculosis, AARB and Löwenstein-Jensen culture, tuberculosis PCR and EZN staining should be implemented and to research fungus infection, PAS staining should be implemented on tissue samples and aspiration materials. In the literature, there are studies reporting that, along with wide local excision, with prednisolone treatment the rate of relapse of disease are low (3, 9, 18). In some studies it is reported that the relapse rate is up to 80% after local excision separately (18, 19). Oral prednisolone is often administered as a substitute to surgical treatment or in the cases when remission is not achieved (17). Although the dosage and duration of medication changes are based on clinical status, it is often administered as 60 mg/day and then reduced by 10 mg/month and finally terminated at the end of 6 months. In the literature, there are cases that report the usage of the medication until the healing is complete or up to 11 months (11, 17). The aim of steroid treatment is to prevent the relapse of disease as well as shrink the mass size, reduce skin findings and avoid wide resections. Thus, it is possible to avoid wide resections in cases of relapse of disease (11).

Some publications report that, after steroid treatment, the rate of relapse is 50% (11, 17), andthere are publications which compare the cases which had only surgical treatment to the ones which were administered only prednisolone and they prove that surgical treatment is more effective than prednisoloneadministration . In this study the response rate of the treatment was 79% in the cases that had partial mastectomy, 100% in cases that had total mastectomy and 42% in cases that were administered prednisolone. In the same study, the relapse rate of the disease was 58% in cases who were only administered prednisolone and 21% in cases who had surgical treatment (20). In our study, prednisolone treatment was administered to 12 patients and 2 cases who had a relapse were diagnosed by tru-cut biopsy.

In a similar study, 50 patients were treated by wide local excision and 1 patient had a modified radical mastectomy. Of the patients who had wide local excisions, three had relapses and 1 of these patients had a reconstruction along with modified radical mastectomy, 2 patients had re-excision (21). In our study 3 patients had mastectomy and 2 of these patients had a relapse in the 6th month during their prednisolone treatment and they had multiple fistula tracts, BIRADS category 3 lesions in their breast imaging. They had mastectomy and reconstruction at their own request. The other patient was 57 years old, had diffuse fistula formulation and, due to social reasons and at the patient's own request, mastectomy was performed after incisional biopsy.

In another study which analyzed immunomodulator treatment such as colchicine and hydroxyquinoline, when the patients were compared, the relapse rate of the disease was 78% in cases who only had surgical treatment and 46% in cases who had only steroid treatment. Four of the 6 patients who were administered colchicine treatment did not have a relapse (8).

In a similar study which analyzed systemic treatment, 13 patients were administered azotioprin along with prednisolone, and total response was achieved in 11 of them. 2 of the patients had a relapse, one of them had surgical drainage and the other patient was administered an increased dose of prednisolone (22).

Although there are various studies concerned with the choice of treatment in the literature, the consensus is the most conservative approach possible. In our study, with a conservative approach, we found the relapse rate of the disease to be 15%. We consider that a conservative approach is an appropriate treatment option for idiopathic granolomatosis mastitis.

In idiopathic granulomatosis mastitis which requires a multidisciplinary approach with surgery, radiology and pathology; treatment options and relapse rates vary greatly. Although we consider that the hypothesis of the activation severity of the illness during treatment as the most important factor, the fact that this is a retrospective study is a restricting factor. Multi centered studies with higher numbers of patients are needed.

Ethics Committee Approval: Due to the retrospective design of the study ethics committee approval was waired.

Conflict of Interest: No conflict of interest was declared by the authors.

Peer-review: Externally peer-reviewed.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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