IDIOPATHIC GRANULOMATOUS MASTITIS: A RARE BENIGN INFLAMMATORY DISEASE MASQUERADING AS BREAST CARCINOMA

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Introduction

Idiopathic granulomatous mastitis (IGM) is an uncommon, benign, chronic inflammatory breast disease that was first described by Kessler and Wolloch in 1972 (1). The exact etiology of IGM remains uncertain, associations with tuberculosis, sarcoidosis, fungal infections, autoimmune disorders, oral contraceptive use, pregnancy, hyperprolactinaemia, foreign body reaction and alpha-1 antitrypsin deficiency have been recommended (2). Most patients are young parous women but males may also be affected.

ABSTRACT

Aims: Idiopathic granulomatous mastitis is an uncommon, benign, chronic inflammatory breast disease. In this study, we report our experience with idiopathic granulomatous mastitis of the breast and include a summary of the current literature to provide a reference for the management of this rare clinical entity.

Materials and methods: A retrospective study included 24 women who met the required histological criteria of idiopathic granulomatous mastitis and who were treated at Izmir Bozyaka Education and Research Hospital, Department of Surgery between January 2000 - 2014. Clinical data of the presentation, results of the diagnostic workup, histopathology, treatment and outcome were analyzed by review of medical records.

Results: The mean age at diagnosis was 36 years (range 21–51 years). The most common presenting symptoms were a palpable mass in the breast (18/24, 75%) and pain, erythema, and fistula formation (6/24, 25%). An ultrasonography was performed in all 24 cases and mammographic examination of the breast was performed in 10 (41%) patients. The major radiographic finding is an ill-defined mass, occurring in eight patients. In 10 cases the preoperative diagnosis was suspicion of breast malignancy. All patients underwent a wide local excision, and were diagnosed with idiopathic granulomatous mastitis by pathologists.

Conclusions: Idiopathic granulomatous mastitis is a rare and challenging condition. Therefore, a proper treatment method should be chosen on a case-by-case basis. Idiopathic granulomatous mastitis is a diagnosis of exclusion with histology of breast cancer. Surgical intervention in the form of wide local excision is necessary and there is a place for adjuvant treatment as steroid treatment in selected and recurrent cases.

Key words: Idiopathic, granulomatous, mastitis, breast, cancer.

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Age at diagnosis is generally between 20 and 50 years; however, patients at 11 and 83 years were reported (3). IGM is a chronic benign disease, constituting 24% of all breast inflammatory disease (4). Although it is a benign condition, it can present with local manifestations that mimic carcinoma. The treatment of IGM is challenging as there is a lack of consensus in the literature and management options vary widely (5).

In this study, we report our experience with IGM of the breast and include a summary of the current literature to provide a reference for the management of this rare clinical entity.
Materials and methods

A retrospective study included 24 women who met the required histological criteria of IGM and who were treated in Izmir Bozyaka Education and Research Hospital, Department of Surgery between January 2000 - 2014. The patients were referred both from the outpatient department of the hospital and from peripheral government health clinics with outpatient services. All the women underwent a clinical examination to identify palpable breast masses, skin thickenings, or axillary lymphadenopathies. In addition a breast ultrasonography was routinely performed.

Mammography was the initial imaging evaluation in women older than 40 years and was not performed in women younger than 40 years. Two standard views (mediolateral oblique and craniocaudal) of each breast were acquired. The most challenging cases and patients younger than 40 years were evaluated by breast magnetic resonance imaging (MRI). Clinical data, diagnostic workup results, histopathological findings (all histopathological preaprate were examined with hematoxylin-eosin (H&E) and special stains such as gram, Ziehl-Neelsen, and periodic acid-Schiff), treatments and outcomes were analyzed by review of medical records. We only include the patients with histologic criteria of IGM and other possible cause of granulomatous mastitis as tuberculosis, sarcoidosis etc and perpural mastitis, bacterial or fungal breast abscesses are excluded.

Results

All patients were women. The mean age at diagnosis was 36 years (range 21-51 years). Twenty three patients were multi-parous and one patient was pregnant at the time of diagnosis. None of the patients had a history of oral contraceptive use and a concomitant systemic disease. Five of 24 patients had undergone incision and drainage before admission to our Department due to diagnosis of breast abscess. Symptoms duration ranged from 2 to 12 months. The right breast was affected in 10 patients (41%) and the left breast in 14 patients (59%). Synchronous involvement of the contralateral breast was not found. The most common presenting symptoms were a palpable mass in the breast (18/24, 75%) and pain, erythema, and fistula formation (6/24, 25%) (Figure 1).

Associated nipple discharge and ulceration were seen in 3 and 1 patients, respectively. The radiological features of the patients were determined through ultrasound, mammography and MRI. An ultrasonography was performed in all 24 cases, which showed dilated ducts with thick debris, or cystic lesions with debris, or severe inflammatory changes. We did not use any serological parameter as inflammatory markers, breast cancer markers or iron metabolism.

Mammographic examination of the breast was performed in 10 (41%) patients. The major radiographic finding is an ill-defined mass, occurring in eight patients (Figure 2).

Three patients were subjected to an MRI, which showed a heterogeneous mass with an irregular border (Figure 3).
In 10 cases the preoperative diagnosis was suspicion of breast malignancy. In four patients, the surgery was planned for persistent breast abscess or nipple discharge. All patients underwent a wide local excision, and were diagnosed with IGM by pathologists. Microscopically all cases had non-caseating granulomas involving breast lobules with variable numbers of multinucleated giant cells, neutrophils, lymphocytes, plasma cells, and eosinophils (Figure 4A-4B).

Mean follow up duration of 3 cases operated due to recurrence was 28\textsuperscript{12-36} months and no pathologic finding is seen so far.

**Discussion**

This disease usually affects women of child-bearing age or those with a history of oral contraceptive use. Mechanisms that have been proposed as etiologic factors include chemical reaction associated with oral contraceptive pills, autoimmune phenomenon, infection with yet unidentified pathogens, and localized immune response to extravasated secretions from lobules. Conditions such as pregnancy, breast feeding, breast trauma, hyperprolactinemia with galactorrhea, and alpha-1-antitrypsin deficiency have been associated with an increased risk of IGM\textsuperscript{6}. However, serologic tests for antinuclear antibody and rheumatoid factor, which are evidence of an autoimmune phenomenon, are usually found to be negative. Some studies suggest a possible relationship between smoking and IGM. However, more clear evidence is needed\textsuperscript{7}. In our study, 23 patients were multi-parous and one patient was pregnant at the time of diagnosis. In contrast to literature, none of the patients had a history of oral contraceptive use and a concomitant systemic disease.

The most common presentation is that of unilateral breast mass (57\%) or breast pain (33\%). It has been reported that up to 25\% of cases can involve both breasts. IGM can be located in any quadrant of the breast except for the subareolar region. Nipple retraction, axillary lymphadenopathy, and abscess or fistula formation were all less common symptomatic presentations and may be seen\textsuperscript{8}. Due to granulomatous inflammation, IGM can cause nipple discharge or peau d’orange that can mimic a malignant tumor\textsuperscript{9}.

In our study, most common presenting symptoms were a palpable mass in the breast (18/24, 75\%) and pain, erythema, and fistula formation (6/24, 25\%). Associated nipple discharge and ulceration were seen in three and one patients, respectively.

There are no radiological findings that are specific of IGM, but in the appropriate clinical settings, the diagnosis can be suggested by the radiologist. Mammography usually shows an ill-defined mass with surrounding normal breast parenchyma or irregular asymmetric density, and skin thickening. However, ultrasonic examination commonly

Figure 4 A: Breast tissue containing ductuli were present on the right side, and a granuloma were seen on the left side of the image (Hematoxylin-Eosinx40).

Figure 4 B: Epitheloid histocytes stained acidophilic and lymphocytes (on the left) were seen in the wall of the granuloma. (Hematoxylin-Eosin X200).
demonstrates a non-mass lesion or hypoechoic lesion that is often tubular or is associated with a tubular portion or mixed hypo and hyperechogenicity lesion. A “Dynamic contrast-enhanced magnetic resonance mammography” focuses on the dynamic rather than morphological attributes of the lesions, indirectly reveals their vascular nature, and could potentially be used to discriminate between benign and malignant processes; nevertheless, the difference between carcinoma and inflammatory process remains difficult.

The diagnosis of IGM is one of exclusion where atypical infection and breast carcinoma are among the probable differentials. Histology in the form of core or open biopsy is the mainstay of diagnosis. Histopathological findings include non-caseating granulomas, necrosis, giant cell formation and neutrophils. Other systemic granulomatous conditions such as sarcoidosis, Wegener granulomatosis, or tuberculosis must be excluded, and a negative microbiology with standard and special stains has to be demonstrated. In our study, no microorganisms (bacteria, mycobacteria, fungi and parasites) were demonstrated by Gram, periodic acid-Schiff, Ziehl-Neelsen or Giemsa stains.

The therapeutic choice for IGM has not yet been established because of its rarity. Although several studies have reported varying approaches to the treatment of IGM, many of these treatment algorithms were formulated without a definitive initial diagnosis. The treatment methods known to date include observation, antibiotics, steroids, drainage, excision, and mastectomy. Wide surgical excision is the most commonly used optimal treatment of IGM. Since IGM is a challenging condition to diagnose for any physician, we think that surgery is the mainfoot for diagnosis and treatment of IGM. As in our study preoperative diagnosis for ten patients was the suspicion of breast malignancy, we have to use wide local excision to rule out of breast neoplastic disorders. Surgery is also helpful in management of persistent breast abscess or nipple discharge. Steroid therapy is also used as a first line treatment or secondary to surgical therapy. Steroids not only reduce the size of the lesion, but also enhance complete healing after surgery.

Nevertheless, steroid therapy has many serious side effect, such as Cushing syndrome, avascular necrosis, diabetes mellitus, hypertension, peptic ulcer disease, neuropsychiatric symptoms, and aggravation of undetected underlying infections. Also, it has a variable clinical response and problems with recurrence after steroid withdrawal. In some cases, excision of recurrence not be an adequate treatment and low-dose steroid therapy may be tried. We did not use steroid therapy for the first line treatment because of wide local excision with negative surgical margins. In the literature recurrence rate of IGM is reported to be 16-50% even if complete resection is obtained. Most of the recurrence occurred following abscess drainage and relapse rate of surgical excision and steroid therapy were low and similar (8,3%). The exact etiology of the IGM is not known since that the possible reason of recurrence is also obscure.

Recurrence developed in three patients (25%) in our series. In the first two patients, a mass lesion appeared in the same location of the breast 36 months and 60 months after excision, and in the third patient abscess and fistula formation developed only 12 month after excision. All the patients with recurrent IGM have been admitted with breast abscesses and fistula primarily. All patients with recurrence were successfully treated by reexcision and low-dose prednisolone (20 mg/day) therapy. Mean follow up duration of 3 cases operated due to recurrence was 28 months and no pathologic finding is seen so far.

Conclusions

IGM is a rare and challenging condition. Therefore, a proper treatment method should be chosen on a case-by-case basis. IGM is a diagnosis of exclusion with histology of breast cancer. Surgical intervention in the form of wide local excision is necessary and there is a place for adjuvant treatment, as steroids, in selected and recurrent cases.

References


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