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Non-surgical Management in Idiopathic Granulomatous Mastitis

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Abstract

Introduction: Idiopathic Granulomatous Mastitis; Despite its low incidence, is in high interest due to masquerading as carcinoma of the breast. In confirmed IGM case series, it's been reported that more than 50% of patients were initially misdiagnosed as affecting by carcinoma of the Breast. Herein we are introducing a non-surgical management of IGM with frequently aspiration of the masses accompanied by using bacteriostatics and close regular surveillance.

Material and Method: This was a before and after clinical trial looking at the effects of repeated aspirations coupled with antibiotic treatment on the natural course of IGM. Overall 55 patients met the inclusion criteria. These patients underwent clinical and imaging study as well as Core Needle Biopsy (CNB) of the lesion with a 14-16 Gauge needle. Patients' presenting sign and symptoms were categorized into six variable ones, including inflammation, Erythma, mass, pain and sinus formation. Confirmed cases of IGM were treated with antibiotic therapy (Ciprofloxacin 500 mg, or Trimethoprin-Sulfamethoxazol 400+80 mg every 12 hours) until either the relief of symptoms or a maximum of 3 weeks. One or two Weeks follow up visits were conducted in the first three months, monthly visits in the first six months, and then no matter when the last visit was done, it was recorded.

Results: 44 patients (80% of cases), elucidated signs of inflammation, whereas solely 18 patients (32% of cases) were presented with inflamed breasts at final visit. (P value=0.03) 45 patients (81% of cases) presenting symptom was erythema, ultimately there were 14 cases (25%) in whom erythema persists. (p value=0.03) Mass presence was the dominant sign being discovered in 45 (72%) of enrolled cases at the time of first visit. The reported results has experienced a decline curve, finally 10 cases (18%) has remained symptomatic with a mass. (P value=0.02) Furthermore pain was elucidated in more than half of those who entered the study, 25 cases (56%). Sinus formation has complicated 14.5% (8 cases) of the patients, interestingly followed by a minimal rise at second visit during 1-3 weeks, the number of affected patients was consistently reported as 7 patients (12%) during the further visits.

Discussion and Conclusion: Because of the nature of the disease which is an inflammatory reaction, any form of surgical intervention will be an unsuitable procedure and may become a disaster for both patient and the physician. As a result, the procedure of recurrent drainage may resolve the symptoms of pain, erythema and possibly the sinus formation, ultimately the mass will be resolved; therefore the recurrent drainage is highly recommended.

Keywords: Idiopathic granulomatous mastitis; Breast cancer

Introduction

The misery of affecting by Breast cancer, leads to one of the most common cause of surgical clinic referrals by women. All other differentials capture great attention till being excluded by clinical, radiological and pathological documents.

Idiopathic Granulomatous Mastitis; Despite its low incidence, is in high interest due to masquerading as carcinoma of the breast though finalizing an appropriate management is crucial. It is a rare, non-neoplastic chronic inflammatory disease of the breast [1]. This self-limiting, non-case eating benign disorder also known as Idiopathic Granulomatous Lobular Mastitis, a breast disease of unknown etiology that was first described by Kessler and Wolloch in 1972 [2,3].

It is reported to occur predominantly in parous young woman and is usually unilateral, mainly affects women between the ages of 25 to 55. The time interval between the last childbirth and presentation of the first symptoms ranges from 1 to 15 years [4,5].

The lesions are usually unilateral, presenting as a single, firm, palpable, painful mass varying in size from 0.5 to 10 cm mostly in sub and peri areolar region. It may occur in any of the four quadrants and be accompanied by regional lymphadenopathy [3,5].

Patients are almost always afebrile and might present with multiple areas of simultaneous peripheral infection with abscesses and or inflammation of the skin overlying the region and ulceration or sinus formation. These findings can be accompanied by peau d'orange like changes, nipple inversion, nipple retraction and sinus formation skin changes [6].

Since the clinical and imaging findings of the IGM have high resemblance to those in breast cancer, it can be mistaken and moreover the management might be planned based on this misdiagnosis [7,8].

In many cases, it hasn't been possible to differentiate between an inflammatory process and malignancy and the disease mimicking Breast carcinoma worsens the scenario [4,9].

In confirmed IGM case series, it's been reported that more than 50% of patients were initially misdiagnosed as affecting by carcinoma of the Breast [10].

Due to this masquerade as Breast carcinoma and its resemblance to infection; primarily exclusion of infectious causes of breast disease and malignancy is mandatory [2,11-16].

The imaging details of Idiopathic Granulomatous Mastitis are not well-documented and multiple small masses or a large focal asymmetrical density seen suggests malignancy. Ultrasound usually

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reveals a, large homogenous hypoechogenicity with interstitial tubular lesions, central necrosis and abscess formation maybe also included [7,8].

Doppler examination reveals increased vascularity of lesions and surrounding tissue, unfortunately not helping in the differentiation from malignancy and infection.

Patients often present with a distinct firm mass with or without skin changes, preceding findings can be accompanied by axillary lymphadenopathy, each one with the high probability of being confused with an ongoing infectious granulomatous process or an underlying malignant lesion, the ultimate method for differentiating, is tissue diagnosis by core-needle biopsy.

Sarcoidosis or tuberculosis of the breast can also induce a granulomatous reaction in the breasts with almost cheating feature. Histopathologically in IGM, the tissue is predominantly composed of inflammatory cells, mostly lymphocytes associated with epithelioidhistocytosis mixed with langhans giant cells. The typical Histopathologic feature of IGM and characteristic for it is the presence of multinucleated giant cells and epithelioidhistocytes around lobules. As a non-caseating granulomatous feature of the disease, often minor ductal and periductal inflammation is evident.

Although etiology of Granulomatous Lobular Mastitis is not well determined yet, several theories regarding its pathogenesis have been postulated including infectious, autoimmune process while some have attributed that to a local reaction to chemical secretions or foreign bodies, also probable association with recent pregnancy and breast feeding has been noted.

The disease might be evaluated as breast cancer and its management might be planned based on this incorrect evaluation, thereby increasing the amount of unnecessary excisional biopsies and even mastectomies adding to the load on health care system.

Understanding IGM, is important in guiding clinical decision making while dealing with breast lumps can save both the patient and the physician from unnecessary diagnostic and treatment procedures.

Complications seem to be related to both the disease process as well as the surgical procedures including skin ulceration, abscess and sinus formation, fistulae, wound infection, recurrent of disease post treatment and chronic mastitis followed by excisional biopsies. In some cases there are systemic signs and symptoms such as arthralgia, skeletal pain, multiple lymphadenopathies, even in mediastinum.

As far as the treatment of IGM is concerned, no single best intervention; neither surgical nor pharmacological has been proposed. The different managements used varying from conservative pharmacological therapy with antibiotics, glucocorticoids and methotrexate administration; excisional biopsies and even mastectomies haven't been promising enough to become the treatment of choice and it remains a clinical challenge.

Keeping in mind the self-limiting nature of the disease without subsequent increase in risk of the breast cancer in patients with IGM, it seems both logical and cost-effective to primarily confirm the diagnosis by histopathological examination often exclusion of other more important and dangerous differentials and then use a non-invasive pharmacological treatment accompanied by close regular surveillance based on the strategy of expectant management.

Herein we are introducing a non-surgical management of IGM with frequently aspiration of the masses accompanied by using bacteriostatics;

such as Ciprofloxacin or trimetoprim-sulfamethoxazole known as cotrimoxazole and close regular surveillance.

Material and Method

This was a before and after clinical trial looking at the effects of repeated aspirations coupled with antibiotic treatment on the natural course of IGM. Overall 55 patients met the inclusion criteria.

A couple of patients who had presented with systemic constitutional symptoms of malaise, arthralgia and myalgia were excluded from the study and were referred to rheumatologists for further evaluations. After initial evaluation with mammography and ultrasonography in patients complaining of breast mass, those in whom imaging studies revealed heterogeneous unilateral densities were referred to the Cancer Research Center at Shohaday-e-Tajrish hospital. IGM was suspected in patients presenting with the conglomerate of signs and symptoms which include breast mass, breast inflammation, pain and no evidence of febrile disease. These patients underwent clinical and imaging study as well as Core Needle Biopsy (CNB) of the lesion with a 14-16 Gauge needle. Any aspirated fluid was cultured, gram stained, and checked for antibiotic susceptibility. At this time the patients were all put on Ciprofloxacin 500 mg, or Trimethoprin-Sulfamethoxazol 400+80 mg (Cotrimoxazole) every 12 hours.

Cases with a positive culture result were treated as breast abscess and being excluded from the study. Cases with a negative culture which experienced improved symptoms were followed up, while those with persistent symptoms or recurrent disease were aspirated again and evaluated with fungal, aerobic and anaerobic cultures. The latter also underwent CNB for evidence of IGM if any doubts persist for definite diagnosis.

The criterion for pathologic confirmation of the diagnosis was the presence of non-caseous non-vascular granules, giant cells, epithelioid cells, leukocytes, and microabscess. If the diagnosis was still uncertain Complete Blood Count, Chest X-ray, Purified Protein Derivative, Erythrocyte Sedimentation Rate, Angiotensin Converting Enzyme were checked in order to rule out other causes of granulomatous disease. Patients with pathologic evidence suggesting IGM and no other diagnosis were included in the study.

A questionnaire including patient's demographic information, past medical, surgical, and obstetric history, presenting illness, symptoms at presentation, physical examination findings, and a detailed description of the condition was filled by a trained researcher. In cases with a past history of treatment for IGM, the type, length and success of past treatment was also documented. Pain was measured using the simple method of evaluating the patients based on Visual Analogue Scale.

Confirmed cases of IGM were treated with antibiotic therapy (Ciprofloxacin 500 mg, or Trimethoprin-Sulfamethoxazol 400+80 mg every 12 hours) until either the relief of symptoms or a maximum of 3 weeks. One or two Weeks follow up visits were conducted in the first three months, monthly visits in the first six months, and then no matter when the last visit was done, it was recorded. In each visit if a mass or accumulation of inflammatory products was palpated; the aspiration was done. On each follow up visit the patients were assessed for edema, erythema, mass lesions, pain, sinus formation, and personal satisfaction. Any further intervention at the time of the visit was also recorded.

During the course of follow up, known confounding factors that might influence the success of treatment including corticosteroid use for other indications was also documented and excluded from the study.

Signs and symptoms of disease before and after the treatment were compared in order to reveal the treatment success. Also the relationship between different demographic variables and the success of treatment was analyzed. Statistical analysis was performed using the SPSS software.

Results

55 patients met the inclusion criteria and enrolled the study.

Patients presenting sign and symptoms were categorized into six variable ones, including Six following variables were evaluated; inflammation, erythema, mass, pain and sinus formation, also patient satisfaction was evaluated in a predicted manner of 30-50% for mild satisfaction, 60-80% for moderate satisfaction while those who declared the percentage of 90-100% ,were recorded as excellent satisfaction.

Patients were followed up in a regular manner of a single visit during first to third weeks after first visit, followed by 1-3 months, 4-6 months and final visit which varied from 12 to 90 months.

44 patients (80% of cases), elucidated signs of inflammation, whereas solely 18 patients (32% of cases) were presented with inflamed breasts at final visit. The inflammation rate at first and final visit were 80% (44 out of 55) and 32% (18 patients) respectively (P value=0.03).

Among those who fulfill the inclusion criteria, 45 patients (81% of cases) presenting symptom was erythema, ultimately there were 14 cases (25%) in whom erythema persists (p value=0.03).

More specifically in a couple of patients (3.6%), decrease in the surface involved by erythema was noted.

Mass presence was the dominant sign being discovered in 45 (72%) of enrolled cases at the time of first visit. The reported results has experienced a decline curve, finally 10 cases (18%) has remained symptomatic with a mass (P value=0.02).

Furthermore pain was elucidated in more than half of those who entered the study, 25 cases (56%). Likewise the couple of previous noted symptoms, number of patients experiencing pain at final visit demonstrated significant decline. pain has affected small number of patients at the final visit.

Sinus formation has complicated 14.5% (8 cases) of the patients, interestingly followed by a minimal rise at second visit during 1-3 weeks, the number of affected patients was consistently reported as 7 patients(12% of patients) during the further visits.

Satisfaction rate was recorded in a manner of mild (30-50%), moderate (60-80%) and excellent (90-100%). Following results were obtained, there were solely 3 patients (5.6%) in whom satisfaction rate varied from 30-50%.

The mainstay of performed study, intervention by recurrent aspiration and antibiotics administration was recorded as following, 19 patients (34% of cases) undergone aspiration of less than 2 cc in comparison with 48 patients (87% of cases) at final visit (p value=0.04).

The aspiration of significant amount of more than 6 cc was reported in 15 patients (27% of cases) at second visit followed by 4 patients (7% of cases) at final visit.

Antibiotics were administered for a duration of 2 weeks in the second visit of follow up for all the participants except 5 (90% of cases), and final visit were reported in 50 patients and 4 patients (7% of cases) respectively (p value=0.01).

Combinations of antibiotics were administered for duration of 3 weeks in 1 patient (1.8% cases) versus 18 patients (32% of cases) at second and final visits respectively.

Discussion

Idiopathic Granulomatous Mastitis is a rare clinical situation of breast affecting young women during reproductive period, which mimics breast cancer in clinical evaluations, imaging studies and even in pathological features.

Neither understood etiologically nor the best management is established, results in a great challenge.

The appropriate diagnostic procedure is core needle biopsy and pathological tissue evaluation.

After confirmation of pathological diagnosis, the management of cases are vested from excisional biopsy, lumpectomy and even mastectomy also the non-surgical management varied from different antibiotics, corticosteroids and anticellular agents such as methotrexate.

The most acceptable management for such cases in recent documents are combination of surgical interventions such as lumpectomy, open biopsy and using pharmaceutical agents such as antibiotics and corticosteroids.

Because of the nature of the disease which is an inflammatory reaction, any form of surgical intervention will be an unsuitable procedure and may become a disaster for both patient and the physician.

On the other hand using corticosteroid with long standing complications is not an acceptable and well tolerated prescription; therefore we recommend the procedure of recurrent and or multiple drainage with a 10 cc syringe, 22-23 gauge needles.

Rate of aspiration varied from a single to four time drainage. Patient's satisfaction was moderate to excellent in 94% at final visit and no more intervention was required.

Using some bacteriostatic antibiotics is based on the nature of the disease which is not a purulent disease but there is a clinical feature of inflammation.

In our cases there was neither drug reaction with ciprofloxacin nor with cotrimoxazole. Furthermore no systemic complication was seen, but regarding the natural history of the disease, Antibiotic administration may not be necessary and should be in consideration in further studies.

Conclusion

The current study elucidated that patients affected by Idiopathic Granulomatous Mastitis, suffer from the accumulation of the inflammatory products of mastitis.

As a result, the procedure of recurrent drainage may resolve the symptoms of pain, erythema and possibly the sinus formation, ultimately the mass will be resolved; therefore the recurrent drainage is highly recommended. On the other hand as the effectiveness of antibiotic administration is not absolutely documented, we have used a range of bacteriostatic antibiotics with cellular effects which may not be administered necessarily in the further studies.

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