Original Article

Corticosteroid and Azithromycin in Idiopathic Granulomatous Mastitis

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Abstract

Background: Mastitis is an inflammatory disorder in breast tissues due to bacterial factors, mycobacterial infections or autoimmune diseases. Idiopathic granulomatous mastitis (IGM) is a form of mastitis which may be affected by systematic diseases such as sarcoidosis, and infectious causes such as mycobacterium and fungus. This study evaluates the efficacy of medical therapy with a combination of corticosteroid and Azithromycin in patients with IGM. **Materials and Methods:** This study is a clinical trial research carried out in Alzahra Hospital (Isfahan, Iran) in 2013 on granulomatous mastitis patients. It was administered 250 mg of Azithromycin per 12 hour and 60 mg of Prednisolone per day within 2 weeks. Next, they took 40 mg/day within 8 weeks, and this dosage was tapered during 6 months and the patients clinically and radiologically followed up. The studied patients were examined within 1 week, 2 weeks, 1 month, 3 months, and 6 months, from the beginning of treatment. **Results:** This study investigated granulomatous mastitis patients in Alzahra hospital in 2013. The mean age of these patients was 33.6 ± 8.9, and their age range was 18–56 years old. Among 26 studied patients, 24 persons (92.3%) according to follow-up the patients by physical examination and sonography responded to treatment of corticosteroid and Azithromycin. The remaining (7.7%) underwent surgery. Treatment periods in case of drug use were respectively, 8.5 ± 0.71 months. **Conclusion:** Treatment with corticosteroid and Azithromycin is an effective and appropriate treatment for IGM.

Keywords: *Azithromycin, idiopathic granulomatous mastitis, prednisolone, treatment*

Introduction

Mastitis is an inflammatory disorder in breast tissues due to bacterial factors (*Staphylococcus aureus* and *Corynebacterium*), mycobacterial infections, or inflammatory factors (autoimmune). Almost 10% of women from bacterial infection, which is caused by *S.aureus* after postpartum period and during lactation and is recovered by conservative treatments such as paregoric and febrifuge consumption and continuation of lactation. In addition, antibiotics should be administered in case of systemic symptoms.[1] Franklin and Lowly observed this disorder in 1–3% of women.[2] In breast mastitis, surgical debridement is hardly done when mastitis is changed into abscess. Periductal mastitis is a recurrent subareolar abscess which is also called squamous metaplasia and Zuska disease and is not associated with lactation. Perhaps, it is an inflectional process which is interrelated with smoking in 90% of cases and may be observed in males.[3]

Idiopathic granulomatous mastitis (IGM) is involved in relatively 1% of breast biopsies,[4,5] which may be affected by systemic diseases such as Wegener disease, sarcoidosis, and infectious causes such as mycobacterium and fungus as well as by nipple piercing. Furthermore, it may be influenced by hypersensitive reactions to epithelial antigens of breast lobules.[6] Systematically, IGM is a benign disease of the breast, which afflicts breast feeding women taking oral contraceptive pills and usually emerges in the form of lobulated Granulomatous without calcification and with unknown etiology. In addition, in case of inaccurate diagnosis, this disease may be confused with breast cancer. However, some cases of it cause mastectomy or open biopsy.[7,8] IGM symptoms usually are breast mass, pain, and local erythema, which are regarded as neoplastic inflammations.[9] Mammographic and sonographic results are not specified in this regard and histopathologic manifestations including non calcified granulomata which

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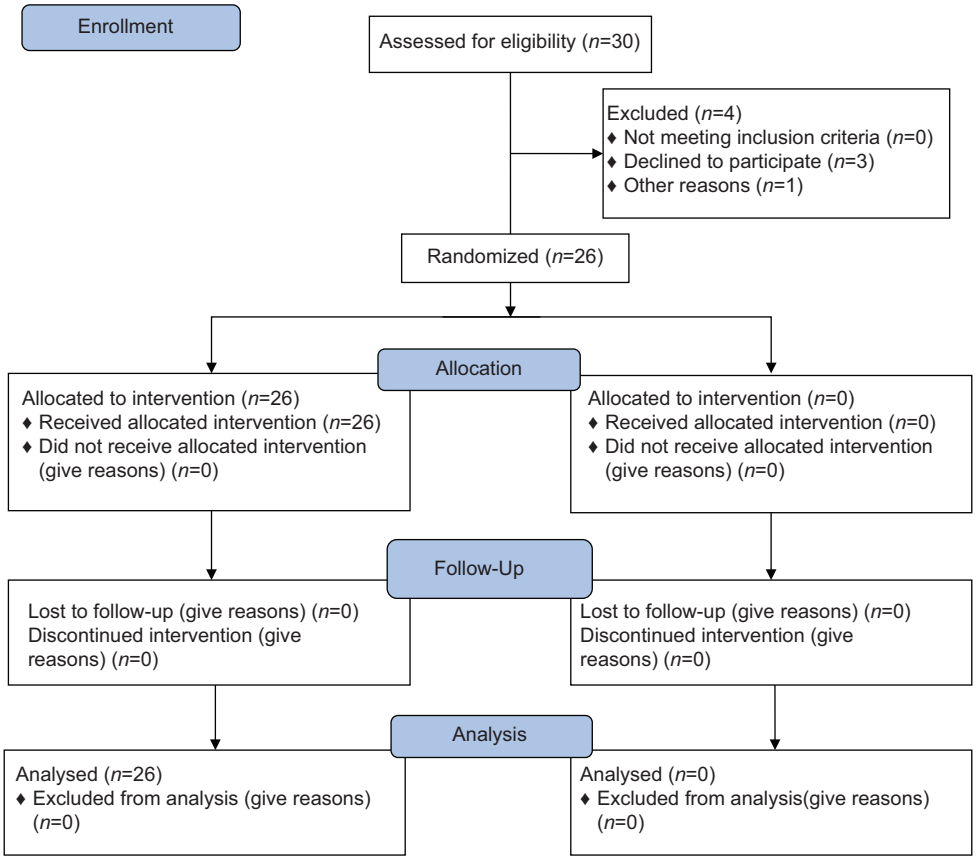
make changes in lobular regions can suggest a lack of malign conditions[2,10,11] while etiology of this disease is in an unclear state. Most cases of IGM are aseptic and have autoimmune pathogenesis.[5,12] However, there are some reports about its simultaneity with microorganisms. Therefore, perhaps, it is a starting point of pathology.[8,13] Specifically, strains of *Corynebacterium* (Gram-positive bacilli of skin flora) may occur with IGM.[1,14] Due to difficulty of clinical diagnosis of IGM, IGM is diagnosed by excluding prevalent causes of breast Granulomata diseases. IGM likely has the highest level of prevalence as compared with infectious cause of mycobacterium tuberculosis.[15] IGM is also described as a local reaction to biochemical secretions.[16]

Disagreements as to this disease center are not only etiology but also treatment. Before the 1980s, removal of whole damaged tissues was the conventional method for its treatment, which concurred with skin ulceration, abscess, fistula, and recurrence.[14] In two decades ago, DeHertogh *et al*. Suggested surgery of whole damaged tissues along with Prednisolone (60 mg/day).[17] Similarly, at the present time, surgery is recurrently done by some surgeons. The optimal treatment has not been yet established where as antibiotic therapy, local excision, and abscess drainage are currently the favored treatment options for IGM. Su *et al*. Propose low dosage of steroid for cure of this disease.[7] Some beneficial strategies are close and precise following up, surgery, antibiotic therapy, and corticosteroid treatment can be exploited. There are articles that evaluate the role of medical treatment in IGM. This study evaluates the efficacy of therapy with a combination of corticosteroid and Azithromycin in patients with IGM.

Materials and Methods

This study is a clinical trial research, carried out in Alzahra Hospital (Isfahan, Iran) in 2013 and was registered in Iranian Registry of Clinical Trial (IRCT number: IRCT 2013123015999N1).

The population consisted of granulomatous mastitis patients in this hospital. In this study, 26 patients were included. They were selected on the basis of granulomatous mastitis diagnosis; the diagnosis was confirmed with biopsies. Local excision was performed for a minimum lesion-free radial margin 5–10 mm. In patients with abscess after drainage, incision biopsy was performed, and at least four tissue samples were obtained. Concurrent excision done if there was fistula formation. Lack of allergy to drug, and consent to participation in this research were the inclusion criteria. In addition, they were excluded from research in case of allergic reactions, non referral to research setting, and use of other drugs such as antibiotics or contraceptives. We selected patients who went into this hospital within 9 months of 2013 using census sampling [Flowchart 1].



Flowchart 1: Study flowchart

Then, we administered 250 mg of Azithromycin per 12 hour and 60 mg of prednisolone per day within 2 weeks. Then, they took 40 mg/day within 8 weeks, and this dosage was tapered during 6 months. During treatment process, patients who did not respond or with progression were sent to the surgeons for removal of damaged tissue. Azithromycin treatment was administered in this study because according to other studies, in a large number of patients with no harbored germ in their cultures, *Corynebacteriums* were triggered as skin flora and were treated with azithromycin. The studied patients were examined within 1 week, 2 weeks, 1 month, 3 months, and 6 months from the beginning of treatment. In other words, treatment or recurrences of disease symptoms were considered. Data were analyzed by SPSS for Windows version 20 (SPSS Inc., Chicago, IL, USA) using Fisher exact test for comparing the frequency distribution of the variables in the both groups.

Results

This study investigated granulomatous mastitis patients in Alzahra hospital in 2013. The mean age of these patients was 33.6 ± 8.9, and their age range was 18–56 years old. Among 26 studied patients, 24 persons (92.3%) according to follow-up the patients by physical examination (such as fever, abscess number, lymphadenopathy, and side of lesions), and also sonography (such as size of lesions) responded to treatment of corticosteroid and Azithromycin alone. The remaining (7.7%) underwent surgery. Table 1 shows demographic details of these patients.

Frequency of lymphadenopathy in the medical and surgical patients were 1 and 2, respectively (8.3% vs. 16%; $P = 0.99$).

Mean and range of damaged tissue size in the whole population of studied patients were 3.63 ± 0.77 cm and 2.5–5.5, respectively. Damaged tissue sizes in drug treatment group were 3.75 ± 0.35 cm and 3.63 ± 0.8 cm. Results of *t*-test did not show any significant difference between two groups ($P = 0.83$). Figure 1 shows frequency of clinical symptoms among patients. Our findings reveal one case of mass, one case of lymph node, 13 cases of abscess, and 3 cases of fever.

Mean of the treatment period and time range were 6.4 ± 1.1 months and 4–9 months, respectively. Treatment periods in case of drug use and surgery were 8.5 ± 0.71 months and 6.29 ± 0.1 months, respectively. Results of *t*-test did not show any significant difference in mean treatment period between these two groups ($P = 0.001$).

Discussion

This study evaluates the clinical response to combination of corticosteroid and Azithromycin in granulomatous mastitis patients. Current trends in treatment of this disease are antibiotic therapy, anti-inflammatory medication; recent studies show a relative improvement in the state of granulomatous mastitis patients. Furthermore, in a large number of patients, mass size is not reduced perhaps due to distinct nature of granulomatous mass. Nevertheless, because of idiopathic nature of a large number of granulomatous mastitis, no particular case is usually reported in mass pathology. Therefore, as biopsy is an aggressive procedure, which is hardly accepted by patients in one hand and it incurs extra expense for patients and health care system, on the other hand, biopsy should only be done when there is a malign state of disease or tuberculous mass. Furthermore, surgery of granulomatous mastitis mass is proposed when malignity is reported in

Table 1: Frequency distribution of granulomatous mastitis patients

Variable	Level	Total	Surgery	Treatment	*P*
Age group	Under 30 years	10 (38.5)	0 (0)	10 (41.7)	0.66
	30-39 years	11 (42.3)	2 (100)	9 (37.5)	
	40 years and more	5 (19.2)	0 (0)	5 (20.8)	
Marital status	Married	23 (88.5)	2 (100)	21 (87.5)	0.99
	Single	3 (11.5)	0 (0)	3 (12.5)	
Number of children	0	4 (15.4)	1 (50)	3 (12.5)	0.71
	1	5 (19.2)	0 (0)	5 (20.8)	
	2	10 (38.5)	1 (50)	9 (37.5)	
	3	4 (15.4)	0 (0)	4 (16.7)	
	4	1 (13.8)	0 (0)	1 (4.2)	
	5	2 (7.7)	0 (0)	2 (8.3)	
Lactation	Yes	23 (88.5)	1 (50)	22 (91.7)	0.22
	No	3 (11.5)	1 (50)	2 (8.3)	
Lesion side	Right	13 (50)	1 (50)	12 (50)	0.99
	Left	12 (49.7)	1 (50)	11 (49.8)	
	Both sides	1 (3.8)	0 (0)	1 (4.2)	
Number of the lesions	1	24 (92.3)	1 (50)	23 (95.8)	0.15
	2	1 (3.8)	0 (0)	1 (4.2)	
	3	1 (3.8)	1 (50)	0 (0)	

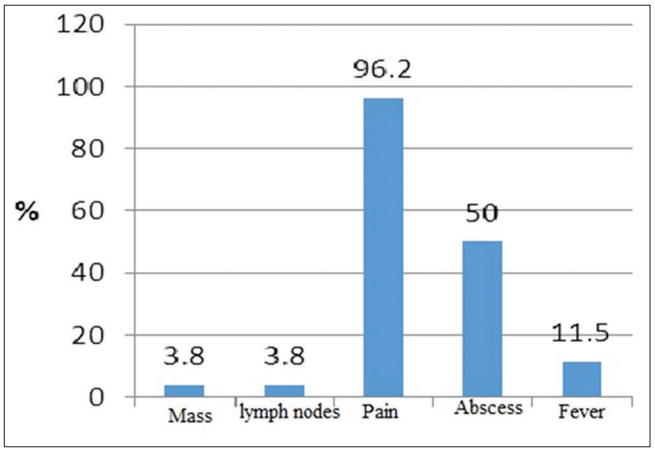


Figure 1: Frequency of local and systematic symptoms (%)

pathology or when the mass resists against the conventional treatment.

DeHertogh *et al*. in 1980 were the first who investigated the efficacy of different treatments, and they stated that corticosteroid is an appropriate treatment.[17] In a study by Sakurai *et al*. showed that corticosteroid could be efficient in 87% of patients without any relapse.[12] Another study by Su *et al*. showed that low doses of corticosteroids were useful and more investigations in this field were recommended by them.[7] Moreover, in 2010, it was showed that corticosteroids treatment is useful, whereas the first option should be specifics surgery in the case of relapse, abscess, and fistula.[6] However, there are some research providing different results. For example, Boufettal *et al*. testified different approaches, which include antibiotic therapy plus tumorectomy. This research showed that combination of corticosteroid and surgery was the most effective strategy. It is suggested that the different results of the later study might be justified by the difference of the samples in comparison with this study.[9]

The optimal treatment for IGM has not been accepted. Corticosteroid administration and wide local excision have been reported for the first line option in the treatment of IGM. The wide spectrums of clinical signs, symptoms of IGM make it difficult to choose a favorable treatment. Which one of these treatment modalities should be preferred? It is obvious that there is a need for more randomized trials comparing conservative approach, medical or surgical approach in IGM. Nevertheless, it may be possible to make an algorithm which is necessary for treatment of IGM.

Low level of the prevalence of IGM and time restriction in this study caused us not to investigate a high sample size of patients. Consequently, for evaluating more thoroughly, further studies should concentrate on larger sample size and on other parameters.

Conclusion

According to our article, it seems that medical treatment with corticosteroid and Azithromycin is an effective and appropriate treatment for IGM.

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Conflicts of interest

There are no conflicts of interest.

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