Effect of Topical Steroid Treatment on Idiopathic Granulomatous Mastitis: Clinical and Radiologic Evaluation

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Abstract: Idiopathic granulomatous mastitis (IGM) is a rare inflammatory, noncaseating, chronic granulomatous benign disease. The etiology of IGM is still unknown. It is postulated to be an autoimmune localized response. The use of a course of oral steroids provides an important regression of breast mass and skin lesions. Topical corticosteroids are used to treat many skin diseases, but no study is available on the sole use of topical steroids for treating IGM. Eleven women with IGM were treated with topical steroid and evaluated using mammography, ultrasonography, and dynamic MRI. At the end of the 12th week, patients were clinically and radiologically evaluated for the regression of breast and skin lesions. Pre- and post-treatment time-intensity curve patterns (TICs) were also compared. During the topical steroid treatment, the inflammation signs in the affected breast had markedly disappeared, the fistulas had become inactive, and the fistula orifices and/or skin erosions had closed in nine patients. The median follow-up period was 17 months (range: 12–48 months). Recurrence was observed in two patients (2/11) at 5 and 8 months, which were treated again topically. The inflammatory findings of the breast skin completely resolved after 8 weeks of treatment, and no side effects or steroid-related complications occurred. In the pretreatment period, TICs from enhancing areas showed a Type 1 pattern in three cases, a Type 2 pattern in five cases, and a Type 3 pattern in three cases. After topical steroid treatment, TIC was not changed only in one patient (Type 2). Type 1 patterns were determined in seven cases and Type 2 patterns in two cases. In addition, in two patients, TICs were not determined due to complete healing. Our MRI findings showed that topical steroid therapy may be useful because it affects mammary parenchyma as well as mammary skin. Further studies with a greater number of patients are needed to determine the topical steroid therapy dosing and duration, and to better understand the efficacy for treating IGM.

Key Words: dynamic MRI, idiopathic granulomatous mastitis, steroid treatment

Idiopathic granulomatous mastitis (IGM) is a rare inflammatory breast disease which was first described in 1972 (1). It is characterized by the presence of noncaseating chronic granulomatous breast lobules, in which no microorganisms are found (2,3). Damage to the ductal epithelium produced by local trauma, extravasated secretions, an underlying autoimmune process, or an unknown infective etiology is thought to induce a localized immune response which may elicit a local granulomatous response (4). However, the etiology of IGM is still unknown (5). Other causes of granulomatous mastitis, such as tuberculosis, sarcoidosis, Wegener’s granuloma, should be excluded before diagnosing IGM (6).

There is no clear clinical consensus regarding the ideal therapeutic management of IGM. Today, the most commonly applied treatment options are surgical excision and steroid therapy. Limited excision has a strong tendency of recurrence; however, wide local excision of breast tissue may have unfavorable cosmetic results. Thus, surgical excision should be reserved for recurrent disease that does not respond to medical therapy.

In studies published, to date, the mainstay of nonsurgical treatment is corticosteroids which provide important regression of breast mass and skin lesions. Unfortunately, aside from the well-established side effects of corticosteroid therapy, patients often relapse with cessation of therapy with studies reporting recurrence rates as 16–50%. Thus, we feel that the minimum dose of a steroid should be recommended.
In this report, we described a clinical and radiologic evaluation of 11 IGM cases successfully treated with topical steroid, suggesting that this is a promising therapeutic option which has not been reported yet.

**METHODS**

**Study Population and Treatment**

From September 2008 to March 2013, 11 cases diagnosed as IGM by pathologic examination were included in this study. All patients were studied in terms of lesion site, age, lactating status, history of contraceptive pills use, presentation, mammogram, ultrasound and MRI findings, as well as treatment and post-treatment follow-up.

Patients with inflammatory findings, but without abscess, were initially treated with pomade (30 g, Mustafa Nevzat Drug Industry, Istanbul, Turkey), which was applied to the breast by the patient twice a day on alternate days for 4 days, with a subsequent interval of 3 days. The same cycles were repeated. The topical steroid treatment was given for 12 weeks. Of our 11 patients who received topical steroids, nine showed resolution after a single course of therapy. Two patients underwent a second course of treatment. All patients followed for a minimum period of 12 months to observe recurrence or other complications. No complications were noticed, but two patients developed recurrence after 5 and 8 months. Patients who had recurrences were continued on topical prednisolone until complete clinical response was observed.

For pre- and post-treatment (at the end of 12 weeks), clinical and radiologic evaluation was made in patients who underwent topical steroid therapy.

**Radiologic Evaluation**

Routine mammographic evaluation was performed in both the craniocaudal and the mediolateral oblique views using a mammography device (Lilyum, Metaltronica, Italy).

All patients were evaluated for the pre- and post-treatment period with duplex ultrasonography using the same USG device (Aplio MX; Toshiba, San Jose, CA, USA). The ultrasonographic features of IGM were analyzed by assessing the internal echoes of the masses, as well as the shape of masses, skin changes, subcutaneous fat obliteration, and parenchymal distortion and presence of axillary adenopathy.

MR imaging was performed with 1.5 T MR imaging system (1.5-Tesla whole-body scanner, with a dedicated breast coil; Signa Horizon; GE Medical Systems, Milwaukee, WI). Precontrast turbo spin-echo T1-weighted (T1W) and fat-saturated T2W axial images were obtained. An axial dynamic contrast-enhanced MR imaging sequence was applied to cover the entire breast. A power injector with an injection flow rate of 2 mL/seconds was used to start the intravenous administration of 0.2 mmol/kg body weight of gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) followed by a 20-mL saline flush. TICs from enhancing areas, nodule formations, and abscess walls at several points were calculated. The system was applied to classify TICs into three different types.

**RESULTS**

The mean age of patients was 35 years (range, 24–46 years). Most of the patients (10/11) were at a reproductive age. Nine patients had a history of lactation, three patients had a history of oral contraceptive use, one had a history of gestational diabetes and chronic hypertension, three had a history of smoking. Clinical presentations were palpable nontender mass in four patients and palpable painful mass in seven patients. The left breast was affected in five cases. Their size ranged between 2 and 13 cm. Six patients presented with erythema. The mean duration of symptoms was 8 ± 2 weeks. In four cases, the clinical impression prior to therapy was that of a malignant neoplasm. In the remaining seven cases, a benign lesion was considered. Three patients also had draining sinuses fistula orifice in the skin and axillary adenopathy was noted in 4 of 11 women. None of the patients have a family history of breast cancer. There was no previous history of systemic disorders, tuberculosis, sarcoidosis, or other infectious or granulomatous disease in any of the patients. The clinical features of these study cases are summarized in Table 1.

During the topical steroid treatment, the inflammation signs in the affected breast had markedly disappeared, the fistulas had become inactive, and the fistula orifices and/or skin erosions had closed in nine patients. The inflammatory findings of the breast skin completely resolved after 8 weeks of treatment. Two patients underwent a second course of treatment.
(completely resolved after 17 and 20 weeks). The median follow-up period was 17 months (range: 12–48 months) and the median time to resolution in patients with complete symptom resolution was 10 weeks with a range of 8 and 20 weeks. Recurrence was observed in two patients (2/11) at 5 and 8 months, which were treated again topically. No side effects or steroid-related complications occurred.

In this study, the preoperative histopathologic diagnosis was established with ultrasound-guided fine-needle aspiration (2 patients) or true-cut biopsy (9 patients) in all cases. No excisional biopsy was performed. Other diagnostic studies involved mammogram, ultrasound, and MRI. A mammogram was obtained from patients older than 35 years. Eight patients were examined by mammography (only pretreatment period), and all patients were examined by both USG and MRI.

The major mammographic radiographic finding was an irregular ill-defined mass in seven patients, focal asymmetric density with no distinct margins in three patients, and diffusely increased density in one patient. Skin thickening was seen in six patients and axillary lymph nodes were detected in three patients. None of the lesions showed calcification (Table 2).

The pretreatment USG findings were a large irregular hypoechoic mass with multiple tubular extensions in a patient; multiple irregular hypoechoic mass with multiple tubular extensions in three patients; multiple irregular hypoechoic masses with tubular extensions and abscess cavities, fistula tracts in three patients; multiple central hypoperipheral hyperechoic lesions in a patient; heterogeneous hypo- and hyperechoic areas with parenchymal distortion in three patients. We also observed skin thickening (7 of 11 lesions) and axillary adenopathy (4 of 11 lesions). On Doppler examination, increased arterial and venous vascularity was detected in four cases. The lesions ranged from 2 to 13 cm in diameter. After the treatment, ultrasonography showed a single lobulated hypoechoic mass with minimal parenchymal distortion in five patients, multiple lobulated hypoechoic masses with tubular extensions in two patients, heterogeneous hypo- and hyperechoic areas with parenchymal distortion in two patients and normal in two patients. In addition, we detected no skin thickening and axillary adenopathy only in one patient (Table 2).

The most detected pretreatment nonenhanced MRI findings were focal or diffuse asymmetrical T1W hypo- and T2W hyperintense signal intensity changes with or without mass effect. Dynamic-enhanced MRI findings were heterogeneously tubular enhancing areas, diffuse enhancement, ring-like enhancement of abscesses, skin thickening, and parenchymal infiltration. In addition,
enlargement of the axillary lymph node was present in five patients. In the post-treatment period, generally, the number and size of lesions was decreased, and skin thickening and parenchymal infiltration healed. Axillary node was present only in one patient (Figs. 1 and 2).

In the pretreatment period, TICs from enhancing areas showed a Type 1 pattern in three cases, a Type 2 pattern in five cases, and a Type 3 pattern in three cases. After topical steroid treatment, TIC was not changed only in one patient (Type 2). Type 1 patterns were determined in seven cases and Type 2 patterns in two cases (Fig. 3). In addition, in two patients, TICs were not determined because of completely healing. These findings are summarized in Table 3.

**DISCUSSION**

Systemic corticosteroid therapy was first proposed by DeHertogh et al., who reported successful results (7). Several reports of using high- and low-dose prednisolone to treat IGM have also been published (5,8). However, no study is available on the sole or combined use of topical steroids for treating IGM except for a case report (9).

Topical corticosteroids are used to treat many skin diseases, particularly atopic dermatitis, due to their anti-inflammatory, vasoconstrictive, antiproliferative, and immunosuppressive effects (10). Although steroids can be easily absorbed through normal skin, their absorption increases during skin inflammation. Although the duration of topical steroid use should be short, studies have reported the absence of side effects such as skin thinning, atrophy, or hypothalamic-hypophyseal-adrenal axis suppression as a result of 16–24-week-long therapies (11). In this report, we described 11 cases of IGM successfully treated with topical steroids, suggesting that this is a promising therapeutic option which has not been reported yet.

The clinical presentation frequently mimics breast abscess, infective mastitis, and breast cancer. This has led to several examples of unnecessary operations in the medical literature. Thus, differential diagnostic methods are quite valuable (12,13).

The imaging findings such as ultrasound, mammogram, and contrast-enhanced MRI can be helpful in the diagnosis (14). Engin et al. reported that neither mammography nor Doppler sonography played a significant role in the differential diagnosis of granulomatosis versus carcinoma (15). MRI is a useful imaging test for the differential diagnosis. It also could be useful in order to indicate active lesions and to locate the extent of the lesions, but it is impossible to differentiate an active inflammatory process from a neoplastic process as the technique focuses on the morphology rather than on the vascular physiology. A “dynamic contrast-enhanced magnetic resonance mammography” focuses on the dynamic attributes of the lesion and thereby reveals the vascular nature. It is therefore supposed that this is the only technique having the potential for discriminating between benign and malignant lesions, but it cannot discriminate tumor from inflammatory causes (16,17). In this report, we presented the mammography, USG, and MRI findings.
together with the measurement of time–signal intensity curves (TICs) in 11 patients with the histologic diagnosis of IGM comparing preoperative and postoperative period.

Mammography and ultrasound identify an irregular and ill-defined mass in the majority of patients (13). Ultrasonographic findings of IGM have been relatively well described: an irregular mass with tubular connections, single or multiple hypoechoic tubular/nodular structures, focally or segmentally parenchymal heterogeneity and hypoechoigenicity (18). In this study, the most frequent USG findings were single or multiple irregular hypoechoic masses with tubular extensions. A tubular connection, which was a frequent finding in previous reports (19), was seen in seven cases in the present work. However, after treatment, we frequently described single lobulated hypoechoic masses with tubular connections. In addition, we also observed marked regression of parenchymal and skin lesions (Fig. 4).

The few studies using dynamic enhanced magnetic resonance imaging to evaluate granulomatous mastitis have also revealed a variety of radiological appearances and enhancement patterns. Specific patterns of dynamic contrast-enhanced MRI have been defined as persistent (Type 1), plateau (Type 2), and washout (Type 3). Type 1 (persistent) contrast enhancement, which is characterized by a monotonic increase, has been shown to be suggestive of a benign lesion, whereas Type 3 (washout) contrast enhancement is highly associated with malignancy. However, a Type 2 plateau enhancement pattern can be seen in both benign and malignant lesions (20–22). In our study, Gd-DTPA enhancing MRI showed that Type 1 pattern in three cases, Type 2 pattern in five cases, and Type 3 pattern in three cases. After topical steroid treat-

**Figure 2.** In comparison to Figure 1a, follow-up MRI reveals marked improvement in the number and size of the enhancing annular lesions, with only a few millimetric enhancing nodules remaining in the breast.

**Figure 3.** Patient 5. (a) Pretreatment dynamic contrast-enhanced MRI showed plateau (Type 2) time-intensity curve pattern. (b) Three months later, post-treatment MRI revealed marked improvement in the number and size of the lesion and the TIC obtained from the lesion showed a persistent (Type 1) pattern.

**Figure 4.** Patient 11. Significant clinical improvement was seen in the patient’s right breast after topical steroid treatment (from a to b).
ment, TIC was not changed only in a patient (Type 2). Type 1 patterns were determined in seven cases and Type 2 patterns in two cases. In addition, in two patients, TICs were not determined because of completely healing. Thus, we have determined that topical steroid therapy causes a tendency toward a benign pattern in IGM patients.

In conclusion, IGM is a rare benign breast condition that may be misdiagnosed as breast carcinoma. Because clinical or imaging diagnosis has often been difficult and inconclusive, increased awareness of this disease will improve understanding and management. In addition, we believe that non-invasive treatments should be preferred initially because of the self-limiting nature of IGM, and topical steroid therapy is a useful therapeutic approach, as it affects mammary parenchyma as well as mammary skin. Further studies with a greater number of patients are needed to determine the topical steroid therapy dose and to better understand the efficacy of topical steroids for treating IGM.

Limitation

Our study does not provide additional information for the differentiation of mastitis from carcinoma. In addition, long-term follow-up of patients is advised as there is a chance of relapse after medication has ceased. It is not clear yet if long-term topical steroid treatment can prevent a relapse or not.

REFERENCES

1. Kessler E, Woloch Y. Granulomatous mastitis: a lesion clinically simulating carcinoma. Am J Clin Pathol 1972;58:642–6.

2. Lee JH, Oh KK, Kim EK, Kwack KS, Jung WH, Lee HK. Radiologic and clinical features of idiopathic granulomatous lobular mastitis mimicking advanced breast cancer. Yonsei Med J 2006;47:78–84.

3. Ocal K, Dag A, Turkmengolu O, Kara T, Sevit H, Konca K. Granulomatous mastitis: clinical, pathological features, and management. Breast J 2010;16:176–82.

4. Bani-Hani KE, Yaghani RJ, Matalka II, Shatanawi NJ. Idiopathic granulomatous mastitis: time to avoid unnecessary mastectomies. Breast J 2004;10:318–22.

5. Su FH, Liu SC, Suen JH, Chen DS, Sister Mary Ann Lou. Idiopathic granulomatous mastitis: a case successfully treated with a minimum dose of a steroid. Chang Gung Med J 2005;28:431–5.

6. Van Oorlagh C, Schrapen T, Van Steen A, Baez AL, Moerman P. Idiopathic granulomatous mastitis. Eur Radiol 1997;7:1010–2.

7. DeHertogh DA, Bossof AH, Harris AA, Economou SG. Prednisone management of granulomatous mastitis. N Engl J Med 1980;303:799–800.

8. Hovanessian Larsen LJ, Peyvandi B, Klipfel N, Grant E, Iyengar G. Granulomatous lobular mastitis: imaging, diagnosis, and treatment. AJR Am J Roentgenol 2009;193:574–81.

9. Alintopprak F. Topical Steroids to Treat Granulomatous Mastitis: a Case Report. Korean J Intern Med 2011;26:356–9.

10. Buys LM. Treatment options for atopic dermatitis. Am Fam Physician 2007;75:523–8.

11. Hanifi J, Gupta AK, Rajagopalan R. Intermittent dosing of fluticasone propionate cream for reducing the risk of relapse in atopic dermatitis patients. Br J Dermatol 2002;147:528–37.

12. Imoto S, Kitaya T, Kodama T, Hasebe T, Mukai K. Idiopathic granulomatous mastitis: case report and review of the literature. Jpn J Clin Oncol 1997;27:274–7.

13. Gurleyik Y, Aktoken A, Aker F, Karagulle H, Saglamc A. Medical and surgical treatment of idiopathic granulomatous lobular mastitis: a benign inflammatory disease mimicking invasive carcinoma. J Breast Cancer 2012;15:119–23.

14. Ozturk M, Mavili E, Kahirman G, Akcan AC, Ozturk F. Granulomatous mastitis: radiological findings. Acta Radiol 2007;48:150–5.

15. Engin G, Acunus G, Acunus B. Granulomatous mastitis: gray-scale and color Doppler sonographic findings. J Clin Ultrasound 1999;27:101–6.

16. Tunchilek N, Karakas HM, Okten OO. Imaging of granulomatous mastitis: assessment of three cases. Breast 2004;13:510–4.

17. Verfailie G, Breucl C, Sacre R, Bourgain C, Lamote J. Granulomatous lobular mastitis: a rare chronic inflammatory disease of the breast which can mimic breast cancer. Acta Chir Belg 2006;106:222–4.

18. Yilmaz E, Lebe B, Usal C, Balci P. Mammographic and sonographic findings in the diagnosis of idiopathic granulomatous mastitis. Eur Radiol 2001;11:2236–40.

19. Alndaal SM. Idiopathic granulomatous mastitis. Clinical presentation, radiological features and treatment. Saudi Med J 2004;25:1884–7.

20. Yaghaji RJ. The magnetic resonance image findings of idiopathic granulomatous mastitis. Saudi Med J 2004;25:1715–9.

21. Kocaoglu M, Somuncu I, Ors F, Bulakbas N, Tayfun C, Ilkakbar S. Imaging findings in idiopathic granulomatous mastitis. A review with emphasis on magnetic resonance imaging. J Comput Assist Tomogr 2004;28:635–41.

22. Kuhl CK, Mielcarek P, Klaschik S, et al. Dynamic breast MR imaging: are signal intensity time course data useful for differential diagnosis of enhancing lesions? Radiology 1999;211:101–10.