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# Efficacy of topical clobetasol propionate in the treatment of idiopathic granulomatous mastitis

## İdiyopatik granülatöz mastit tedavisinde yerel klobetazol propionatın etkinliği

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### ABSTRACT

**Objectives:** To evaluate the efficacy of topical clobetasol propionate 0.05% pomade in the treatment of idiopathic granulomatous mastitis.

**Patients and Methods:** Twenty-one idiopathic granulomatous mastitis patients' clinical and histopathological findings were retrospectively reviewed. Those patients excluded from other etiologies were categorized as idiopathic granulomatous mastitis and treated with topical clobetasol propionate 0.05% pomade as an initial treatment.

**Results:** All 21 patients with a final diagnosis of idiopathic granulomatous mastitis were women with the average age of 36.2±5.2 years. Of the 21 patients; erythema, induration and pain problems of 6 (28.5%) patients totally resolved without recurrence in 3 months follow-up period. Erythema, induration and pain problems of 7 (33.5%) patients were minimalized and stay stable in 3 months follow-up period. The symptoms of 8 (38%) did not change under topical clobetasol propionate treatment. None of the patients developed side or adverse effects due to topical steroid treatment and 6 of 18 patients with non-steroidal anti-inflammatory drugs (NSAIDs) complained of gastric pain.

**Conclusion:** Topical steroid treatment is a safe treatment option for idiopathic granulomatous mastitis patients before systemic steroid and immunosuppressive treatments and also surgery.

**Keywords:** Idiopathic granulomatous mastitis, Granulomatous mastitis, Mastitis, Topical Steroid, Steroid

### ÖZ

**Amaç:** İdiyopatik granülatöz mastit tedavisinde topikal klobetazol propionat %0,05 pomadın etkinliğini değerlendirmek.

**Hastalar ve Yöntemler:** Klinik ve histopatolojik olarak idiyopatik granülatöz mastit tanısı konulan 21 hastanın dosyası retrospektif olarak incelendi. Altta yatan başka patoloji saptanmayan hastalar idiyopatik granülatöz mastit olarak sınıflandırıldı ve ilk tedavi olarak topikal klobetazol propionat % 0,05 pomad uygulandı.

**Bulgular:** İdiyopatik granülatöz mastit tanılı 21 kadın hastanın yaş ortalaması 36,2 ± 5,2 yıldır. Yirmi bir hastanın 6 (% 28,5)'sinin eritem, sertlik ve ağrı problemleri tamamen geriledi ve 3 aylık takip döneminde tekrarlamadı. Hastaların 7 (% 33,5)'sinde eritem, sertlik ve ağrı şikayetleri tama yakın geriledi ve 3 ay süreli takiplerinde artış izlenmedi. Sekiz (%38) hastada iyileşme gözlenmedi. Hastalarda yerel steroid tedavisine bağlı yan etki görülmezken, ek olarak non-steroid antiinflamatuar (NSAI) ilaç kullanan 18 hastanın 6'sında mide ağrısı şikayetleri gelişti.

**Sonuç:** Yerel steroid tedavileri idiyopatik granülatöz mastit tedavisinde etkili ve güvenli tedavi seçenekleridir.

**Anahtar kelimeler:** İdiyopatik granülatöz mastit, Granülatöz mastit, Mastit, Yerel steroid, Steroid

### Introduction

Idiopathic granulomatous mastitis (IGM) is a benign inflammatory condition of the breast with unknown etiology. Several mechanisms have been proposed, including autoimmune process, infectious diseases and hormonal disruption [1]. The localized autoimmune inflammatory response to retained milk secretions in the duct has been postulated in the pathogenesis of IGM [2-4]. IGM occurs most commonly in parous young women, it may be seen also in nulliparous women and rarely men [5,6]. There is no increased risk of subsequent breast cancer in patients with IGM [7]. The breast mass, abscesses, erythema, induration and tenderness are the common clinical findings

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of IGM. The nipple retraction, sinus formation, fistula and axillar adenopathy may accompany these findings. The malignancies, bacterial mastitis, tuberculosis, sarcoidosis, deep fungal infections, foreign body granulomas and autoimmune diseases should be considered in the differential diagnosis of IGM [1,2,4]. The challenging diagnosis of IGM requires exclusion of all other possible disorders with a multidisciplinary approach. There are studies reporting about association between IGM and *Corynebacterium kroppenstedtii* infection and elevated prolactin levels [8,9].

The treatment options are controversial. The reports of spontaneous remissions lead observation or conservative treatments such as symptomatic treatments, systemic antibiotics, steroids and immunosuppressive drugs [10]. In some reports; for recurrent cases excision of the affected tissue have been proposed as a treatment option [10].

## Material and Methods

We conducted a retrospective study to evaluate the efficacy of topical clobetasol propionate 0.05% pomade in the treatment of IGM. The files of 21 IGM patients treated with topical clobetasol propionate at least for 2 months in the general surgery and the dermatology outpatient clinics from April 2014 to July 2017 were analyzed. The patients were included in this study if they had histopathologic confirmation of granulomatous mastitis and excluded the other possible disorders by breast ultrasonography, polymerase chain reaction (PCR) for *Mycobacterium tuberculosis*, chest radiography, bacterial and fungal tissue cultures. Those in whom no underlying etiology was found were categorized as having IGM and treated with topical clobetasol propionate with or without oral non-steroidal anti-inflammatory drug (NSAID) at least 2 months.

All statistical analyses were performed with the Statistical Package for Social Sciences (SPSS) Statistics 20.0 software. The descriptive data were analyzed according to the frequency, percentage, average and standard deviation. Chi-Square and Mann – Whitney U tests were used to compare qualitative data.

## Results

The files of 21 patients with IGM those applied topical clobetasol propionate 0.05% pomade twice a day, at least for 2 months were analyzed retrospectively. Eighteen

of 21 patients were also treated with oral steroidal anti-inflammatory drugs (NSAIDs). The most common presenting symptoms and signs were unilateral erythema, infiltration, mass and mastalgia in the patients. All patients had the histologic findings consistent with granulomatous mastitis without caseous necrosis. All had normal chest radiography. The breast cancer was assessed in all patients with ultrasonographic imaging.

No identifiable etiology was found in any of the patients who were diagnosed with IGM. All patients were women with an average age of 36.2+/- 5.2 years. None of them has personal or family history for the breast cancer or tuberculosis. Six of 21 (28.5%) were cigarette smokers. Six of 21 (28.5%) used oral contraceptives at any time in the last 3 years. All women had nursed their children with double breast at least 4 months. Three (14.3%) women presented during breastfeeding. None of 21 patients were pregnant at the time of presentation. There were abscess drainage histories in 4 of 21 (19%) patients. None of the patients except 1 had systemic symptoms. One patient suffered coexisting erythema nodosum and arthralgia. All patients had erythema, infiltration and tenderness on affected breast's skin. All patients except 1 had unilateral findings. Nine patients had abscess and fistula formation. The patient characteristics are summarized in Table I.

**Table I.** Characteristics of patients with idiopathic granulomatous mastitis (n=21)

	Min	Max	Average	Standard Deviation
Age	26	47	36.2	5.2
Duration of disease (month)	3	36	11.22	9.05
Number of pregnancy	1	4	2.76	1.38
Time from last pregnancy (month)	14	180	75.00	36.29
Total breastfeeding duration (month)	4	72	24.73	12.37

All histopathological examinations were established with ultrasound-guided tru-cut biopsy. The initial treatment with topical clobetasol propionate 0.05% pomade was given to all patients for at least 2 months. Of the 21 patients; 6 patients' (28.5%) erythema, induration and pain totally resolved within 2 months of treatment without recurrence after 3 months off-therapy period. Seven patients' (33.5%) erythema, induration and pain resolved with minimal erythema and induration and did not worsen for 3 months follow-up period. Eight patients' (38%) symptoms did not improve with topical clobetasol propionate treatment. Total 62% of patients had complete or partial remission off-therapy. None of the patients developed side or adverse

effects due to topical steroid treatment. Six of 18 patients treated with NSAID had complaints of gastric pain.

## Discussion

Idiopathic granulomatous mastitis (IGM) is a chronic inflammatory disorder of the breast tissue without proven etiology [1,2,4]. Although, patients do not have systemic findings, in some reports erythema nodosum and arthritis were associated with IGM [11]. IGM is generally seen in young-or middle-aged women unilaterally after giving birth. Autoimmune reactions against milk which leak from breast lobules is the suspected mechanism of the disease. The patients generally present with breast mass that should be differentiated from breast cancer by imaging and histopathological examination.

The IGM shows non-caseating granulomatous inflammation in the lobules on histopathological examination. After exclusion of malignancies, etiology for granulomatous mastitis as *Mycobacterium* infections, foreign body granulomas, fungal infections, *Corynebacterium* infection, sarcoidosis, Sjögren's disease, vasculitis and other autoimmune diseases should be evaluated. Clear screening for differential diagnoses leads for the diagnosis of IGM. The combination of clinical history, histopathology, laboratory and imaging findings with multidisciplinary approach is critical in the diagnosis and treatment of the IGM.

There is no consensus on treatment however, step by step treatment by antibiotics, steroids and then immunosuppressives and finally excision is suggested in the literature. The prognosis of the IGM is variable.

The successful results with systemic corticosteroid therapy was first reported in 1980 [12]. There are 1 case report and 1 prospective and 1 retrospective study by the same group in the literature on IGM treatment with topical steroid therapy [13-15]. The latest report analyzed topical prednisolone 0.125% pomade from 28 patients with biopsy-proven IGM, retrospectively. After initial complete remission, during 4 months follow-up period, only 10.7% of the patients had disease recurrence in whom a repeated course of topical prednisolone treatment resulted with complete healing in most patients. According to results of this study, topical steroid treatment seemed to be very effective in the treatment of IGM [15].

A meta-analysis in 2017 reviewed the complete remission (CR) and recurrence rates of various reported

treatments for IGM [10]. According to this study; a pooled estimate of complete remission and recurrence rates for surgical managements were 90.6% and 6.8%, oral steroids were 71.8% and 20.9%, oral steroids+surgical managements were 94.5% and 4%, oral steroids+methotrexate were 71.4% and unknown, observation were 95.1% and 9.2% and finally of topical steroids were 98.8% and 14.3%, respectively. All the studies about topical steroid efficacy in the treatment of IGM which also analyzed in this meta-analysis were mentioned above [14,15]. This meta-analysis assessed 4 reports of observation in IGM [16-19]. The number of patients were between 3 and 8 in the 3 of these 4 reports [16,18,19]. There were 27 patients, with 100% CR rate and 11.1% recurrence rate during average 7.4 months follow-up period, in the report of Bouton et al. [17].

The success rate of observation without treatment, topical steroids and advanced treatment options were reported similar and high in the literature. Despite the fact that strength of topical clobetasol propionate is superior than topical prednisolone, the remission rates are inferior relatively in our study. This might be due to lower number of patients, shorter medication period, resistance of our cases or the prolonged activity of various antibiotics those used in previous study. Our study has a 62% total complete and partial remission rate and it is still an effective response result for IGM.

There is still no consensus on how to manage this benign condition properly. This is mostly due to its rarity and lack of well-designed studies. Previous studies and our study showed that topical steroid treatment is a safe alternative for the modalities with more adverse event risks such as systemic steroid, immunosuppressive agents and surgery. In the light of recent studies surgical treatments and medical treatments with possible side effects might be reserved for those in whom conservative modalities such as observation and topical steroids are not effective or who ask to have a rapid amelioration.

The limitations of our study are retrospective design of the study, the lack of longer follow-up period and the lack of an observational arm results. Our study and previous studies show the necessity of the randomised, placebo controlled studies and that it is worth observing and/or trying topical steroids in the treatment of IGM before advanced options in the selected cases.

## Conclusion

Our study suggests to treat IGM with topical steroids before the options with more adverse event risks and also less cosmetic results as systemic steroids, immunosuppressive agents and surgery.

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