Effectiveness of Small-volume, Intralesional, Delayed-release Triamcinolone Injections in Cheilitis Granulomatosa: A Pilot Study

Rizwan Hamid[1], Altaf Chalkoo[2], Bashir Wani[3], Gazanfer Shah[4], Ubaid Ullah Gul Salmani[5]

ABSTRACT

Introduction: Orofacial granulomatosis is an uncommon disease, which presents as recurrent or persistent swelling of the soft tissues of oral and maxillofacial region, predominantly lips - termed as Cheilitis Granulomatosa (granulomatous cheilitis). It may give rise to significant cosmetic and functional problems. Treatment with high-volume triamcinolone injections has been shown to be effective but requires local anesthesia (nerve block) and causes a dramatic temporary increase of lip swelling. A non-comparative open-label pilot study using small volume of high-concentrate extended release intralesional triamcinolone injections were performed in 7 patients with cheilitis granulomatosis in order to evaluate its effectiveness in reducing lip swelling and preventing recurrences.

Material and Methods: Seven patients with granulomatous cheilitis were studied. Small-volume, intralesional, high-concentrate, extended release triamcinolone was injected on a weekly basis. A standard cycle consisted of 2 or 3 injection sessions over 2 or 3 weeks, depending on the clinical response.

Results: After cycle completion, all patients remained without recurrences or with cosmetically acceptable slight lip enlargement for a mean time of 13.5 months (range, 8-19 months). No side effects were seen, except in one patient who developed hypopigmentation of the skin of the upper lip.

Conclusion: Intralesional, high-concentrate, extended-release triamcinolone injections in small volume appears to be an effective treatment in reducing the enlargement of lips in patients with granulomatous cheilitis and at the same time do not require nerve block anesthesia or cause a temporary troublesome increase of swelling. A long disease-free period is generally obtained.

Keywords: Effectiveness of Small-volume, Intralesional, Triamcinolone Injections, Cheilitis Granulomatosa:

INTRODUCTION

Orofacial granulomatosis (OFG) is a descriptive term used for a wide group of granulomatous disorders affecting the soft tissues of the face and oral cavity that are characterized histologically by noncaseating epithelioid granulomas and clinically by recurrent chronic orofacial swelling. [1] Although several areas of the face and oral cavity can be affected,[2,3] the classic and most frequent clinical feature of OFG is a painless, non-erythematous, nonpruritic oedema of the lips (upper and lower, unilateral and bilateral, symmetric and asymmetric).[4] After recurrent attacks at irregular intervals, the swelling becomes firm, indurated,[5] and permanent. Thus, it may cause significant cosmetic problems and enormous embarrassment and can interfere with speaking and eating.[2] Cheilitis granulomatosa (granulomatous cheilitis) is characterized by persistent idiopathic swelling of the lip due to granulomatous inflammation. It is thought to be a subset of orofacial granulomatosa and is frequently used in the literature to describe the monosymptomatic presentation of Miescher cheilitis. Because a clear etiologic factor driving the granulomatous tissue response of OFG has not been identified, rational therapy is not available.[6] Treatment of cheilitis granulmatosa is aimed at preventing and curing its unsightly sequelae,[7] but if delayed diagnosis occurs, treatment is often unrewarding and burdened by poor outcomes.[8] Corticosteroids have been shown to be effective in reducing facial swelling and preventing recurrences and are considered the (single) most effective drugs in the treatment of OFG.[1,6-8] Nevertheless, because the chronic course of the disorder requires long-term treatment, the usefulness of systemic corticosteroid therapy is limited by its potentially serious side effects. Thus, intralesional injections have been proposed.[9] Initially, triamcinolone acetonide was used in small quantities (0.5-1 ml of 10 mg/mL) so as to avoid patient discomfort, soft tissue atrophy, and hypopigmentation. In fact, these well-known potential side effects of corticosteroid therapy may cause significant cosmetic problems if the lips and perioral area are affected. The clinical response was favourable but temporary, with multiple repeated injections required for months or, in certain cases, years, causing relevant pain and distress in patients.[10,11] In 1992, Sakuntabhai, MacLeod, and Lawrence[12,13] suggested treating OFG patients with high volume steroid injections after first numbing the lips by means of mental and infraorbital nerve blocks with 2% lignocaine. In this way, the injections were pain free and easy to give because the patient was not distressed, and it was possible to inject a high volume of triamcinolone acetonide (10 mg/mL; range, 30-100 mg; mean, 60 mg). Even if lip swelling increases immediately after the injection of such a high volume of drug,[12] this therapy has been shown to be very effective. It has led to almost complete clinical remission and a long-term disease-

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free period (10-12 months). Side effects have not been seen by the authors. A non-comparative open-label pilot study using small volume of high-concentrate extended release intralesional triamcinolone injections were performed in 7 patients with cheilitis granulomatosis in order to evaluate its effectiveness.

MATERIAL AND METHODS

Seven patients (5 females and 2males; age range,19-35 years) with granulomatous cheilitis were studied in Dept. of Oral Medicine and Radiology, GDC, Srinagar, Kashmir. Diagnosis was made performing clinical examination, hematologic and microscopic investigations in each patient in addition to imaging techniques, radio-allergo-sorbent and patch tests. Thus, we excluded local and systemic diseases that can have similar clinical manifestations, including hypersensitivity reactions, acquired and hereditary C1INH-related angioedema, sarcoidosis, tuberculosis, leprosy (Hansen's disease), deep fungal infections, leukemic infiltrate, Crohn's disease, Anderson-Fabry disease, and Ascher's syndrome. After fulfilling the inclusion criteria (based on clinical features and histologic criteria),[1] seven (7) subjects were selected with granulomatous cheilitis. Swelling of the lips was the main clinical feature in all patients; 3 patients had lower lip involvement, whereas in other 4 patients the upper lip was affected. All patients were treated with small volume of high concentrate, delayed / sustained release intralesional corticosteroid injections. The concentrations of delayed-release triamcinolone was 40 mg/mL. If there was unilateral lip swelling, we performed 2 injections each amounting to 0.1ml (4mg) introducing the needle vertically next to the median line and at the corner of the lip (total dose, 0.2 mL [8 mg]). If swelling affected the whole lip, we added two more injections at the opposite side (total dose, 0.4 mL [16 mg]) (Figure 1). The needle was introduced at junction of pro-labium and labial mucosa, and the needle was directed deeply toward the oral mucosa with the aim of avoiding atrophy and hypopigmentation of the labial skin. Injections were performed with an Insulin syringe 30 gauge (40 IU) syringe for subcutaneous use. Therapy was performed on a weekly schedule; a standard cycle consisted of 2 or 3 injection sessions over 2 or 3 weeks depending on the clinical response (maximum of 3 injections, 0.6-1.2 mL [24-48 mg]). This small volume of triamcinolone injected did not cause significant pain and was generally well tolerated, with very low discomfort. Only two patients reported significant pain at the needle introduction. Thus, they required the application of topical anaesthetic gel on the lip a few minutes before the injections.

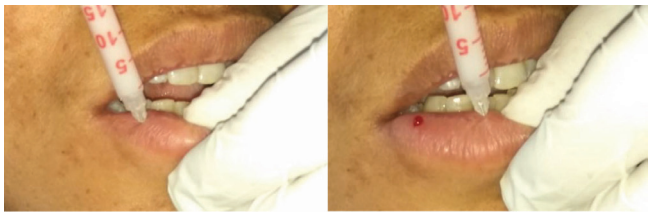

Figure-1: Points of needle insertion in a patient with granulomatous cheilitis affecting the lower lip. If swelling affected the whole lip, we added two more injections at the opposite side.

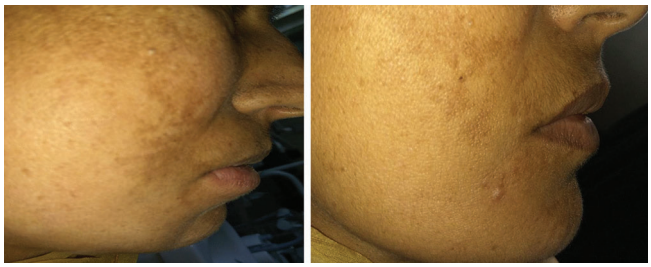

Figure-2: Orofacial granulomatosis involvement of the lower lip with obliteration of mento-labial sulcus before (A) and after (B) therapy.

STATISTICAL ANALYSIS

Microsoft office 2007 was used for the statistical ananlysis. Descriptive stiatistics like mean and percentages were used for the analysis.

RESULTS

After cycle completion, lip swelling started to settle within a few days in all patients, returning to normal size within 2 to 4 weeks (Figure 2). The patients remained without recurrence, or with cosmetically acceptable slight lip enlargement for a mean time of 13.5 months (range 8-19 months). During the cycle, recurrences were usually observed but did not exceed 3 in number. Accordingly, in those patients showing two initial recurrences, a long disease-free period was reached with a cycle of two injection sessions over a period of 2 weeks (0.4-0.8 mL [16-32 mg] depending on the lip area affected). In

	Patient Number						
	1	**2**	**3**	**4**	**5**	**6**	**7**
Sex/Age (y)	M/32	F/25	M/23	F/20	F/21	F/28	F/19
Lip involved	Whole lower	Whole upper	Half lower	Whole upper	Whole upper	Whole upper	Half lower
First cycle (recurrences and injection sessions)	3	3	2	3	3	3	2
Total volume injected [mL (mg)]	1.2 (48)	1.2 (48)	0.4 (16)	1.2 (48)	1.2 (48)	1.2 (48)	0.4 (16)
Disease-free period after first cycle (mo)	10	19	12	8	14	17	16
Further recurrences/injection sessions	1	-	1	1	-	-	1
Follow-up after last injection (mo)	3	19	7	9	14	17	5
Side effects	No	Yes *	No	No	No	No	No
* Hypopigmentation of the upper lip skin; mo - Months							

Table-1: Clinical data and treatment response of patients with granulomatous cheilitis

those showing 3 recurrences, another session was necessary, with a total dose of 0.6 to 1.2 mL (24-48 mg). Subsequent recurrences were observed in 4 patients and treated with a single injection session. No side effects were observed, with the exception of one patient having hypopigmentation of the upper lip skin. Clinical data are summarized in Table 1.

DISCUSSION

Permanent facial swelling of OFG may cause significant cosmetic problems and enormous embarrassment and can interfere with speaking and eating. Its early recognition is a key factor in controlling its unsightly sequelae. Patients with long-term, misdiagnosed, nontreated disease present with a firm, indurated, fibrous enlargement of the lips that has no tendency to resolution and generally does not respond well to corticosteroid therapy. In these cases, plastic surgical reduction of the swelling has been suggested[10,14,15] but is probably not warranted or reliably effective.[8] Furthermore, intralesional triamcinolone injections are useful only in reducing further lip enlargement. On the contrary, if the disease is recognized early, intralesional corticosteroid injections have been shown to be very effective. They reduce acute face swelling and prevent chronic recurrences, obtaining a long disease-free period and representing the cornerstone of OFG therapy.[7,12] Right now, the best results have been obtained with high-volume intralesional triamcinolone (3-10 mL of 10 mg/mL) injections as proposed by Sakuntabhai, MacLeod, and Lawrence,[13] with a very long disease-free period of about 10 months. However, it has two main drawbacks. One is nerve block anaesthesia is necessary to make the injections pain free and second is, as a consequence of the high volume injected, the lip swelling was reported to increase to a ''dramatic size''[12] in the first 4 to 5 days before starting to subside. On the contrary, the use of delayed-release high concentrate triamcinolone (40 mg/mL) as we have described in our study enables us to obtain several advantages. First, the total volume of triamcinolone is significantly reduced, allowing us to use an insulin syringe of 30 gauge (40 IU) for subcutaneous infiltration with a small thin needle. This makes the injections relatively painless. For those patients who experience pain and discomfort, however, application of a topical anaesthetic gel on the lip a few minutes before the injections is effective in eliminating the pain from needle introduction as we observed in two patients. In addition, the delayed release of the drug and its high concentration work in synergy, being effective for both resolution of acute swelling and prevention of recurrence for a long period. As we have reported previously, in the course of acute phases, the disease has a high tendency to present recurrences, which are generally controlled with 2 to 3 injection sessions over 2 to 3 weeks. After this cycle, lip size remains stable for a long period even if recurrences are variable and unpredictable. Our best outcome was obtained in patient 2, with a disease-free period of 19 months. The worst outcome was in patient 4, with the first subsequent recurrence observed 8 months after cycle completion. Potential well-recognized side effects of intralesional corticosteroid include skin atrophy and hypopigmentation, the latter of which was observed in only one patient.

CONCLUSION

In conclusion, small-volume, intralesional, delayed- release, high-concentrate triamcinolone is an effective and relatively painless therapy in patients with granulomatous cheilitis. It resolves the acute swelling within 2 to 3 weeks, produces long-term remission, can be easily repeated in cases of recurrence, and has very few minor side effects.

REFERENCES

1. Wiesenfeld D, Ferguson MM, Mitchell DN, MacDonald DG, Scully C, Cochran K, et al. Oro-facial granulomatosis: a clinical and pathological analysis. Q J Med 1985;54:101-13.
2. Mignogna MD, Fedele S, Lo Russo L, Lo Muzio L. Orofacial granulomatosis with gingival onset. J Clin Periodontol 2001;7: 692-5.
3. Mazen SD, Rogers RS III. Melkersson-Rosenthal syndrome. Semin Dermatol 1995;14:135-9.
4. Zimmer WM, Rogers RS III, Reeve CM, Sheridan PJ. Orofacial manifestations of Melkersson-Rosenthal syndrome: a study of 42 patients and review of 220 cases from the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1992;74:610-9.
5. Ziem PE, Pfrommer C, Goerdt S, Orfanos CE, Blume-Peytavi U. Melkersson-Rosenthal syndrome in childhood: a challenge in differential diagnosis and treatment. Br J Dermatol 2000;143: 860-3.
6. Rogers RS III. Granulomatous cheilitis, Melkersson-Rosenthal syndrome, and orofacial granulomatosis. Arch Dermatol 2000; 136:1557-8.
7. Rogers RS III. Melkersson-Rosenthal syndrome, and orofacial granulomatosis. Dermatol Clin 1996;14:371-9.
8. Orofacial granulomatosis. [editorial]. Lancet 1991;338:20-1.
9. Eisenbud L, Hymowitz S, Shapiro R. Cheilitis granulomatosa: report of a case treated with injection of triamcinolone acetonide aqueous suspension. Oral Surg 1971;32:384-9.
10. Krutchkoff D, James R. Cheilitis granulomatosa: successful treatment with combined local triamcinolone injection and surgery. Arch Dermatol 1978;114:1203-6.
11. Allen CM, Carnisa C, Hamzeh S, Stephens L. Cheilitis granulomatosa: report of six cases and review of the literature. J Am Acad Dermatol 1990;23:444-50.
12. Sakuntabhai A, MacLeod RI, Lawrence CM. Intralesional steroid injection after nerve-block in orofacial granulomatosis. Lancet 1992;340:969.
13. Sakuntabhai A, MacLeod RI, Lawrence CM. Intralesional steroid injection after nerve block anesthesia in the treatment of orofacial granulomatosis. Arch Dermatol 1993;129:477-80.
14. Glickman LT, Gruss JS, Birt BD, Kohli-Dang N. The surgical management of Melkersson-Rosenthal syndrome. Plast Reconstr Surg 1992;89:815-21.
15. Rey R, Carreau JP, Gola R, Berbis P. Sindrome de Melkersson- Rosenthal. Inte´reˆ t de la che´ iloplastie de re´duction. Ann Dermatol Venereol 1996;123:325-7.

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