Low-level laser as a complementary therapy in orofacial granulomatosis management: a case report

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Orofacial granulomatosis (OFG) is a chronic inflammatory disease that typically affects the soft tissues of the orofacial region. The most common clinical manifestation of OFG is lip swelling, which may be associated with intrabuccal ulcerations and increased growth of the gingiva and mucosa, as well as cutaneous erythema and facial edema. The treatment for OFG is challenging, and sometimes considered unsatisfactory. Thus, this study presents a case report of OFG and the therapeutic regimen applied. A 47-year-old man presented with increased lip volume which had started 10 months earlier. His lips were thick with a fibroelastic consistency, which were painless upon palpation. Incisional biopsy and histopathological analysis of the upper lip revealed non-specific granulomatous inflammation and the diagnosis of OFG was subsequently made. Low-level laser therapy was successfully used to treat OFG in this case, and appears to be an efficient treatment for OFG when corticosteroid therapy is not enough. (Oral Surg Oral Med Oral Pathol Oral Radiol 2019;128:e1–e5)

Orofacial granulomatosis (OFG) is a rare, chronic inflammatory disorder that typically affects the soft tissues of the orofacial region.[1] It was first described in 1985 by Wiesenfeld as the presence of granulomas in the orofacial region in the absence of other known causes of granulomatous inflammation, including mycobacterial infection, deep fungal infection, sarcoidosis, rosacea, and Crohn disease.[2,3] The name is synonymous with granulomatous cheilitis and Miescher cheilitis, which were previously identified as isolated changes, and also represents the granulomatous disorder present in Melkersson-Rosenthal syndrome.[2]

The most common clinical manifestation of OFG is lip swelling,[4,5] which may be associated with intraoral ulcerations and increases in the gingival and mucosal volumes, resulting in a cobblestone-like appearance. Skin erythema and swelling of the face can also be observed.[4] OFG seems to have predilection for young adults, although it can affect patients of any age, race, or gender.[6]

The etiology and pathogenesis of OFG are not well understood. Numerous studies have shown varied results, suggesting a multifactorial disorder, and several processes have been hypothesized to play a role in its pathogenesis, including genetic, immunologic, allergic (food or dental materials), and infectious etiologies.[6]

Histopathologic examination is an important tool for obtaining the correct diagnosis because OFG typically presents as granulomas consisting of epithelioid histiocytes surrounded by lymphocytes. Multinucleated giant cells and inflammatory infiltrate, including the presence of noncaseating granulomas, can also be observed.[7] Treatment of OFG is quite challenging, with variable efficacy among patients,[6,8] and current treatment is considered unsatisfactory by some authors.[7,9] Historically, treatments often involved surgery, but immunosuppressive agents have been used more recently with success, often involving topical, intralesional, and systemic corticosteroids, such as thiopurines, and occasionally others, such as clofazimine, thalidomide, and anti–tumor necrosis factor-α therapies.[10-12] A multi-therapy approach may be effective in some cases, but the treatment must be tailored to individual cases.[6] Intralesional injection of corticosteroids has been demonstrated to induce remission of lesions with remarkable results. Low-level laser therapy (LLLT) may be used as a complementary therapy when conventional treatment is not effective.[8,13]

Considering the variable efficacy of treatments for OFG and the importance of management and care related to this condition, we present a case report of OFG managed with intralesional corticosteroids and LLLT as a complementary therapy.

CASE REPORT

A 47-year-old man was referred to the Department of Stomatology and Oral and Maxillofacial Surgery of the

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Hospital Metropolitano Odilon Behrens in Belo Horizonte, Brazil, with a complaint of increased lip volume that had started to appear 10 months earlier. In the anamnesis, the patient reported no systemic disorders. Clinical extraoral examination revealed evident swelling of both the upper and lower lips and extending to the cheeks, causing facial asymmetry and affecting facial harmony (Figures 1A and 1B). On palpation, the lips showed thickening and a fibroelastic consistency, but the patient did not report any pain. Hyperkeratotic ulcerations were observed in the oral mucosa, which were thought to be related to occlusal trauma. The clinical hypotheses included OFG, Melkersson-Rosenthal syndrome, angioedema, sarcoidosis, and paracoccidioidomycosis.

An incisional biopsy of the upper lip was performed under local anesthesia, and the material was fixed in 10% buffered formalin. Histopathologic analysis demonstrated nonspecific granulomatous inflammation (Figures 2A and 2B). Hematology, serology, and chest radiography did not show any alterations. Therefore, an association with gastrointestinal inflammatory or respiratory diseases was excluded, and a diagnosis of OFG was made.

The treatment of choice was initially triamcinolone hexacetonide (Triancil; 20 mg/mL), administered as a 5-mL intralesional infiltration into the lips and equally distributed between the upper and lower lips. Three infiltration sessions were performed, with a 15-day interval between each session. After 3 treatment sessions, hardening of the lips was observed. The patient developed a chronic abscess with an internal fistula on the upper left labial mucosa; therefore, we decided to suspend the infiltrations and, instead, start weekly LLLT sessions (3 sessions per week, performed every other day). In addition, oral antibiotic therapy (500 mg amoxicillin + 125 mg potassium clavulanate; 8 per 8 hours for 14 days) was provided (Figure 3). A total of 12 LLLT sessions were performed and resulted in significant resolution of the infection and disappearance of the fistula, as well as partial resolution of the OFG. After 6 months of follow-up, the patient is disease-free (Figures 1C and 1D).

DISCUSSION

Orofacial granulomatosis is a rare, idiopathic, granulomatous disease involving the face and oral cavity and

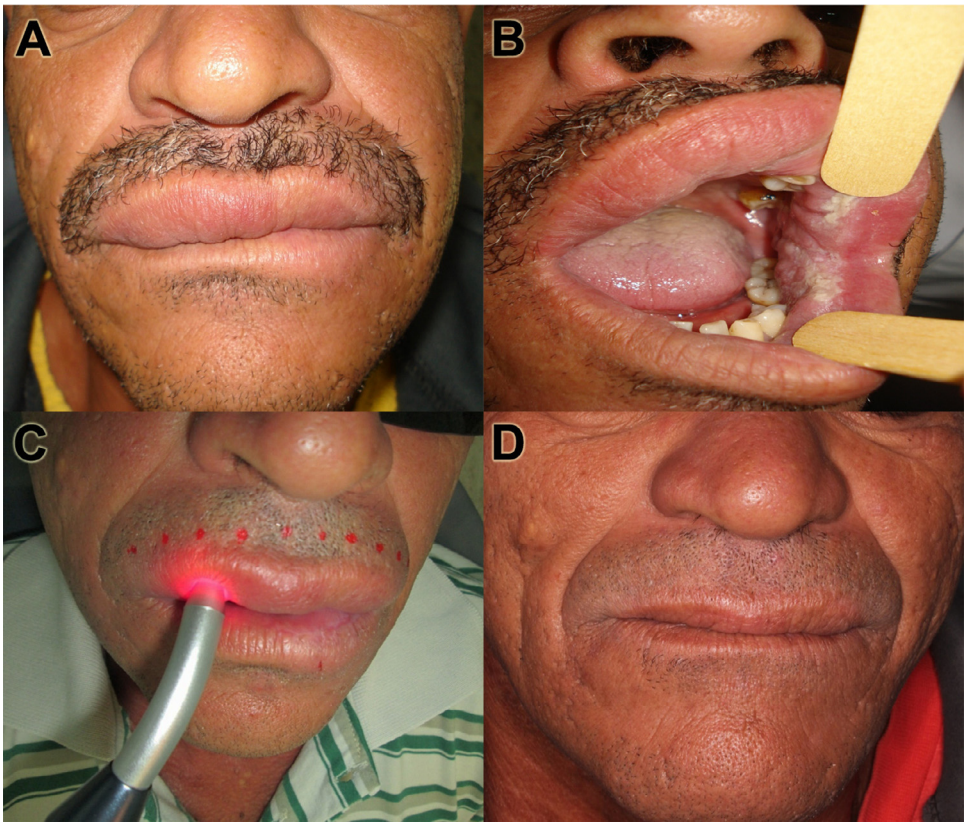

Fig. 1. **(A)** Upper lip swelling, presenting fibroelastic consistency. **(B)** Intraoral hyperkeratotic areas of the jugal mucosa, extending to the lips. **(C)** Low-level laser therapy session, with irradiation at established points (1 cm apart) along the entire orofacial granulomatosis (OFG) committed area. **(D)** Complete remission of the OFG at follow-up 6 months after treatment.

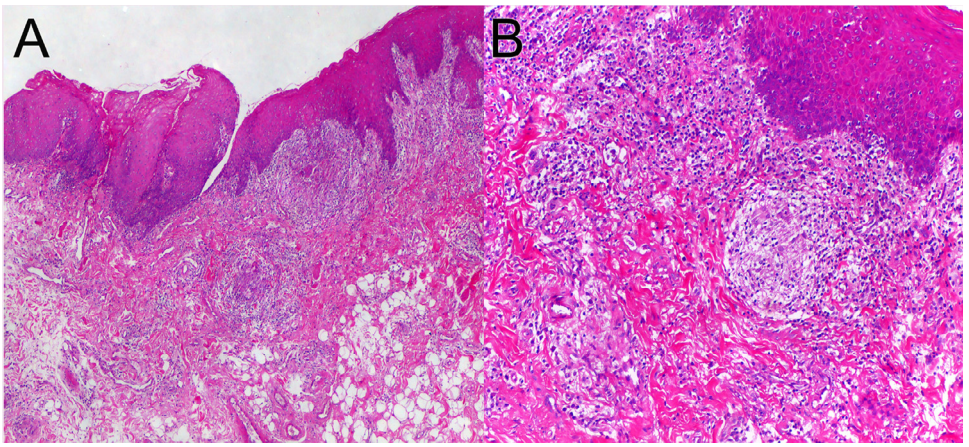

Fig. 2. **(A, B)** Histopathologic appearance, showing intense subepithelial and diffuse mononuclear infiltrate, in addition to the presence of vasculitis with granuloma formation (hematoxylin and eosin [H & E]; original magnification × 40 [A] and × 100 [B]).

is clinically characterized by a diffuse, nontender, soft-to-firm, painless swelling that is restricted to one or both lips and to intraoral sites, such as the tongue, gingiva, and buccal mucosa. It is histologically characterized by noncaseating granulomatous inflammation.[8] OFG is an increasingly recognized entity; however, its exact etiology remains unclear.[5]

Treatment for OFG is challenging and presents variable prognostic outcomes among that are sometimes considered unsatisfactory, specifically with regard to single therapeutic protocols that have often failed to reduce the orofacial swelling and mucosal inflammation.[6,8] Traditionally, the first-line treatment for most cases of OFG is corticosteroid administration.[5] If the underlying cause of OFG can be identified and the lesion effectively removed, the symptoms may be alleviated sooner—that is, the dosage and duration of steroid treatment can be reduced.[14] In a large case series of patients with OFG, Al Johani et al.[4] reported that they based treatment on the severity of the case; less severe cases were treated with topical corticosteroids or tacrolimus, whereas more severe cases or those that did not respond to initial treatment were treated with systemic or intralesional corticosteroids. These authors found complete remission of the lesion in only half the cases after 3 years of treatment. In a cohort study, Fedele et al.[12] demonstrated the long-term effectiveness of using intralesional corticosteroid injections to reduce facial edema.

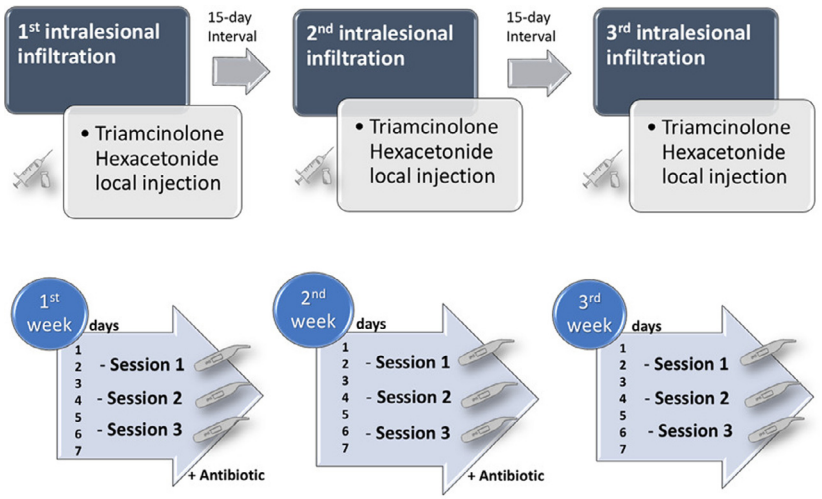

Fig. 3. The therapeutic sequence, using corticosteroid, followed by low-level laser therapy (LLLT) sessions and simultaneous use of antibiotic in the first 2 weeks. The orofacial granulomatosis (OFG) treatment was performed with 3 intralesional corticosteroid injections followed by LLLT sessions at established points, each point receiving 40 seconds of irradiation (with Laser Duo, MMO; potency of 100 mW; dose 133 J/cm^2). The LLLT was performed for a total of 12 laser session appointments (3 appointments per week).

Many studies have reported that triamcinolone is an effective agent in OFG treatment, with the outcomes ranging from moderate to satisfactory disease remission.[15-19] Other agents used to treat OFG have also shown acceptable results in previous studies.[20-23] However, the success rate is highly variable, and sometimes adjustment of therapy is needed.

In the literature, LLLT has been widely reported to be used for the treatment of several oral diseases,[13] including radiotherapy/chemotherapy−induced oral mucositis, herpetic lesions, and bullous (e.g., pemphigoid) and erosive-ulcerative (e.g., oral lichen planus and recurrent aphthous stomatitis) diseases.[24-28] This type of therapy has several advantages: (1) the security of the application, (2) absence of adverse effects, (3) the characteristic of being noninvasive, (4) the absence of discomfort and pain during the application of light, (5) the duration of the sessions, and (6) the achieved analgesia.[13] The use of LLLT in the management of OFG is still in its infancy; however, LLLT seems to present anti-inflammatory and healing properties.[4] Moreover, the positive effect of LLLT in OFG treatment may be related to the effect of LLLT on tumor necrosis factor-α, which seems to play a pivotal role in the action of other inflammatory mediators.[29]

On the basis of the properties and advantages of LLLT, we chose to use LLLT as a complementary therapy in the case presented here because the initial treatment (corticosteroid) was not effective in reducing the swelling in OFG. Most studies do not mention the use of LLLT as a therapeutic option for cases that are nonresponsive to conventional therapy.[30] Nevertheless, Merigo et al.[13] reported success with LLLT with the use of a 4-cm defocalized lens and 1 W power after failure of conventional therapy in the treatment of a patient with OFG. The treatment was administered in sessions consisting of 5 irradiations of 1 minute duration each, with a 1-minute interval between irradiations (0.08 W/cm^2 power density; 4.8 J/cm^2 fluence/application; 24 J/cm^2 fluence/session). Laser therapy was repeated a total of 12 times (3 times per week), and there was an improvement in symptoms and edema after 2 weeks, and complete healing was evident after 1 month. No signs of recurrence were observed after 2 years of follow-up.

In the present report, we described a treatment for OFG consisting of corticosteroid intralesional injections followed by LLLT sessions, with irradiation performed at established points (1 cm apart) along the area affected by OFG, with each point receiving 40 seconds of irradiation (using Laser Duo, MMO, at a potency of 100 mW and dose 133 J/cm^2). The LLLT treatment was performed over 12 sessions (3 appointments per week). The patient was followed up after the therapy, and complete OFG remission was observed 6 months after completion of the treatment. Spontaneous remission of OFG is very rare,[29] and LLLT appears to be a good complementary therapy in cases where intralesional corticosteroid application does not work as expected or in those cases where it is not indicated (e.g., large facial area affected). Therefore, considering the particularities of the case, LLLT is an important part of optimal therapy for OFG. However, more studies are needed to support the use of LLLT as a therapy for OFG.

CONCLUSIONS

The combination of corticosteroid and LLLT was effective in the treatment of OFG in the case reported here, and it seems to be effective in cases where conventional therapy (corticosteroid) is not successful. However, the general condition of the individual must to be considered when planning the intervention, and new approaches are necessary for the effective treatment and management of OFG. After 6 months of follow-up, our patient showed no signs of recurrence.

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