Gingival Manifestations of Orofacial Granulomatosis

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Background: Orofacial granulomatosis is a clinical entity presenting with swelling of the facial and/or oral tissues in association with histologic evidence of noncaseating granulomatous inflammation. Labial swelling is the most common finding. Compromise of the gingival and periodontal tissues may occur but has rarely been described in the literature. Our objective was to characterize granulomatous gingivitis in patients with orofacial granulomatosis.

Observations: The study included 29 cases of orofacial granulomatosis seen in our clinic between January 1, 1989, and December 31, 2006. Of these 29, 5 had clinical evidence of gingival tumefaction and underwent gingival biopsy. Histologic examination of all the gingival biopsy specimens showed noncaseating granulomas, edema of the superficial lamina propria, and a chronic inflammatory infiltrate consisting predominantly of lymphocytes and multinucleated giant cells. Treatment options included anti-inflammatory therapy associated with periodontal care.

Conclusion: Gingival tumefaction with histologic evidence of granulomatous inflammation may occur in orofacial granulomatosis and might be more common than reported in the literature.

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The term orofacial granulomatosis describes a clinical entity presenting with swelling of the facial and/or oral tissues in association with histologic evidence of noncaseating granulomatous inflammation. This classification includes idiopathic disorders such as Melkersson-Rosenthal syndrome and Miescher chronic granulomatous cheilitis, as well as the localized orofacial presentations of Crohn disease and sarcoidosis.1-4

This condition has no sex or racial predilection and the age at onset is highly variable, being more frequent in the second and third decades of life. Orofacial swelling may be intermittent initially but tends to become chronic with fluctuations in severity. It may also affect various sites or be oligosymptomatic. Labial swelling is the most common finding, and it may involve one or both lips, often in an asymmetrical manner.2,5-6 Specific gingival manifestations (granulomatous gingivitis) have rarely been described in the literature but may occur in 21% to 26% of patients.1,5,7-9 Detailed descriptions of these manifestations are scarce, with few publications dealing with this issue.8

The objective of this study was to detect gingival manifestations in patients with orofacial granulomatosis in a dermatology clinic and to present a detailed description of clinical and histopathological features of this particular presentation.

METHODS

The study included 29 patients with orofacial granulomatosis (14 females and 15 males), examined between January 1, 1989, and December 31, 2006, in the Oral Diseases Clinic of the Department of Dermatology, University of São Paulo. Patients included in the study had no sign of disseminated granulomatous disease. All patients underwent biopsy and, in those presenting with clinical gingival changes, a gingival biopsy was also performed. Biopsy specimens were fixed in 10% buffered formalin and embedded in paraffin. Sections were stained with hematoxylin-eosin for histologic examination and with the histochemical techniques of periodic acid–Schiff, acid-fast bacilli, and Grocott for detection of infectious microorganisms.

RESULTS

Gingival-specific manifestations were detected in 5 of the 29 patients with orofacial granulomatosis examined. Their clinical characteristics and outcome are summarized in the Table. The Figure illustrates the clinical and histologic findings.
Orofacial granulomatosis is a descriptive term used for a broad group of disorders affecting soft tissues of the face and oral cavity. It is characterized clinically by chronic orofacial swelling and histologically by noncaseating epithelioid granulomas. The term orofacial granulomatosis is nonspecific and is used to encompass clinical and histologic features of more than 1 underlying etiology.1,3 Melkersson-Rosenthal syndrome is the triad of recurrent or persistent orofacial swelling, peripheral facial nerve paralysis, and plicated tongue.5,7 However, few patients present with the complete syndrome. Hornstein2 reported that only 6 of 73 patients (8%) showed the complete triad. Cheilitis granulomatosa is the most frequent finding and may occur as an isolated feature. Fissured tongue (or plicated tongue) is not considered a pathognomonic sign of Melkersson-Rosenthal syndrome because it is common in the general population, and facial nerve palsy is usually of sudden onset and clinically indistinguishable from Bell palsy.2,4 Several other symptoms, including intraoral, neurologic, ophthalmologic, and otologic manifestations, have been described in association with orofacial granulomatosis/Melkersson-Rosenthal syndrome.2,4,8

Among our initial cohort of 29 patients with orofacial granulomatosis, 5 (17%) presented with specific gingival lesions. We found a wide range of gingival aspects in these cases. One patient (case 4) had mild gingival involvement with edema of interdental papillae, and patients 2 and 5 had a diffuse infiltration. Two patients showed massive gingival enlargement (cases 1 and 3), associated with bleeding. In addition, patient 3 showed periodontal fistulas and tooth mobility. All of these cases were confirmed to be due to specific infiltration of noncaseating granulomas.

Only a few studies describing gingival manifestations of orofacial granulomatosis/Melkersson-Rosenthal syndrome are available in the literature, especially regarding histologically confirmed granulomatous

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### Table. Patients With Orofacial Granulomatosis Manifesting Granulomatous Gingivitis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patient No. 1 (Figure, A and B)</th>
<th>Patient No. 2 (Figure, C and D)</th>
<th>Patient No. 3 (Figure, E and F)</th>
<th>Patient No. 4 (Figure, G and H)</th>
<th>Patient No. 5 (Figure, I and J)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient age, y/sex</td>
<td>28/F 3</td>
<td>18/F 3</td>
<td>52/M 4</td>
<td>24/F 2</td>
<td>13/M 3</td>
</tr>
<tr>
<td>Specific clinical manifestation</td>
<td>Upper lip edema</td>
<td>Upper lip edema</td>
<td>Upper and lower lip edema</td>
<td>Upper and lower lip edema</td>
<td>Upper and lower lip edema</td>
</tr>
<tr>
<td>Gingival manifestation</td>
<td>Gingival hyperplasia</td>
<td>Marked hyperplasia of upper anterior gingivae including interdental papillae</td>
<td>Marked hyperplasia of upper and lower gingivae, abscesses, and fistulas; severe periodontal disease and tooth mobility</td>
<td>Marked hyperplasia of upper anterior gingivae including interdental papillae</td>
<td>Marked hyperplasia of upper anterior gingivae including interdental papillae</td>
</tr>
<tr>
<td>Tongue manifestation</td>
<td>No</td>
<td>No</td>
<td>Yes (plicated and geographic tongue)</td>
<td>Yes (geographic tongue)</td>
<td>No</td>
</tr>
<tr>
<td>Treatment</td>
<td>Dapsone (100 mg/d), intralesional corticosteroid infiltration (lip), and gingivoplasty</td>
<td>Dapsone (100 mg/d), intralesional corticosteroid infiltration (lip), and gingivoplasty</td>
<td>Dapsone (100 mg/d), oral prednisone (40 mg/d), intralesional corticosteroid infiltration (lip), and gingivoplasty</td>
<td>Dapsone (100 mg/d), intralesional corticosteroid infiltration (lip), and gingivoplasty</td>
<td>Dapsone (100 mg/d), intralesional corticosteroid infiltration (lip), and gingivoplasty</td>
</tr>
<tr>
<td>Outcome</td>
<td>Mild improvement (lost to follow-up after 1 y)</td>
<td>Good improvement (2-y follow-up)</td>
<td>Good improvement (3-y follow-up)</td>
<td>Good improvement (2-y follow-up)</td>
<td>Good improvement (1-y follow-up)</td>
</tr>
</tbody>
</table>
According to these previous reports, the incidence of gingival alterations in Melkersson-Rosenthal syndrome ranges from 21% to 26% and may antedate or occur simultaneously with lip manifestations. The main clinical characteristics of gingivae affected by Melkersson-Rosenthal syndrome differ from those of nonspecific inflammatory gingivitis. Gingival and periodontal alterations include gum edema and erythema, often with a patchy distribution. These alterations can be associated with erosion and pain. Gingival manifestations of Melkersson-Rosenthal syndrome occur particularly in the anterior parts of the mouth and may extend from the gingival margin to the nonkeratinized alveolar mucosa. Histologically, gingival biopsy specimens are reported to show noncaseating epithelioid granulomas.

In orofacial granulomatosis/Melkersson-Rosenthal syndrome, the classic histologic features are noncaseating.
granulomas, multinucleated giant cells, and lymphoedema; however, these features may be absent, especially in initial lesions. The findings are the same in lip and gingival specimens, and these granulomas are histologically indistinguishable from those found in both gastrointestinal Crohn disease and systemic sarcoidosis. The histologic findings in our patients were similar in the lip and gingival specimens and showed a wide range of features. The most frequent change was edema of the superficial lamina propria with prominent dilated lymphatic vessels. In all 5 cases, chronic inflammatory infiltrate with granulomatous arrangement was observed. Most granulomas were ill-defined, consisting of epithelioid histiocytes and lymphocytes. Multinucleate giant cells were present in all 5 gingival biopsy specimens. Central necrosis was not observed in any of our cases.

Orofacial granulomatosis may be a manifestation of Crohn disease. In a study by Wiesenfeld et al,2 of a total of 60 patients with orofacial granulomatosis, 6 (10%) had gastrointestinal Crohn disease. Some authors recommend that patients presenting with orofacial granulomatosis be screened for the disease. None of the foregoing evidence was found in the patients presented herein.

Orofacial granulomatosis may also be a manifestation of sarcoidosis. In the same study by Wiesenfeld et al,2 2 of these 60 patients with orofacial granulomatosis (3%) had the diagnosis of sarcoidosis. This disease should be considered as well in all patients with orofacial granulomatosis. The absence of clinical signs suggestive of sarcoidosis, a normal chest radiograph, and normal levels of serum angiotensin-converting enzyme make sarcoidosis unlikely in the patients included in this study.

Tuberculosis and leprosy should also be considered as possibilities in patients with orofacial granulomatosis5; however, our patients had no clinical or histopathological evidence of these disorders either.

It is not clear how much investigation is appropriate for each patient with orofacial granulomatosis. It is important that suspected cases of orofacial granulomatosis be investigated appropriately to exclude other similar disorders. However, unwarranted and unpleasant investigations should be avoided when possible.11

In orofacial granulomatosis/Melkersson-Rosenthal syndrome the prognosis is difficult to predict. Occasionally the disease may have spontaneous regression, although the process may take years. In a long-term follow-up of 5 cases, Field and Tyllesley14 reported gradual resolution of buccal lesions and edema of the lips in all patients during a 10-year period. Treatment usually is necessary, and no single approach has been universally successful. Management of dental and periodontal conditions are important for patient outcome,10 as in patient 3 described herein.

In conclusion, orofacial granulomatosis may cause significant cosmetic and functional problems, has an uncertain cause, may be associated with systemic disease, and has an unpredictable response to treatment, which may be frustrating for the patient and physician. The gingiva may be involved in orofacial granulomatosis, and patients usually present with erythema and edema of the gingiva. The correct diagnosis and early treatment will be more comforting for the patient and yield better clinical results, making increased diagnostic awareness important.

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Author Contributions: Drs Lourenço, Lobo, Boggio, and Nico had full access to all of the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis. Study concept and design: Lourenço and Nico. Acquisition of data: Lourenço, Lobo, Boggio, Fezzi, Sebastião, and Nico. Analysis and interpretation of data: Lourenço, Lobo, Boggio, and Nico. Drafting of the manuscript: Lourenço, Lobo, Boggio, and Nico. Critical revision of the manuscript for important intellectual content: Lourenço, Lobo, Boggio, and Nico. Administrative, technical, and material support: Lourenço, Fezzi, Sebastião, and Nico. Study supervision: Lourenço and Nico.

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