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ORIGINAL ARTICLE

A Diagnostic Approach to Recurrent Orofacial Swelling: A Retrospective Study of 104 Patients

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Abstract

Objective: To identify patients evaluated in an outpatient setting at our institution with a presentation of recurrent orofacial swelling and to review the spectrum of causes to outline a diagnostic approach.

Patients and Methods: A retrospective study of 104 patients with more than 1 episode of orofacial swelling lasting for more than 5 days identified through a keyword search of the electronic health record from January 2, 2000, through July 5, 2011.

Results: Patients were categorized according to final cause of orofacial swelling: idiopathic orofacial granulomatosis, solid facial edema due to rosacea and acne vulgaris, Crohn disease, contact dermatitis, sarcoidosis, exfoliative cheilitis, lichen planus, actinic cheilitis, cheilitis glandularis, lymphedema, miscellaneous, and multifactorial. Granulomatous inflammation was noted on biopsy in 40 of 85 patients (47%). Oral involvement was associated with Crohn disease ($P<.001$), and facial and periorbital swelling was associated with solid facial edema in the setting of rosacea and acne vulgaris ($P<.001$).

Conclusion: The broad range of diagnoses responsible for recurrent orofacial swelling underscores the diagnostic challenge and importance of a thorough multidisciplinary evaluation to identify underlying causes.

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Recurrent orofacial swelling may be a presenting sign for multiple disease processes from acute infections to chronic inflammatory diseases, and identification of the underlying cause can be integral to determining prognosis and appropriate treatment. Angioedema and acute infectious causes of recurrent orofacial swelling often have typical clinical presentations, laboratory findings, and systemic symptoms. Angioedema typically lasts hours to days and may be associated with a positive family history, urticaria, laboratory abnormalities (eg, complement C4), and clear inciting factors.[1] Acute infectious causes of swelling including cellulitis and erysipelas often present with skin erythema, tenderness, and constitutional symptoms that are frequently managed in the emergency setting.

The greater diagnostic challenge is recurrent orofacial swelling without erythema, pain, or systemic symptoms. In current practice, many clinicians use the term *orofacial granulomatosis* (OFG) as a clinicopathologic descriptor, similar to the use of *dermatitis*, triggering a search for etiologic factors. Orofacial granulomatosis is characterized clinically by orofacial swelling that may be mild and recurrent but can be progressive and persistent.[2,3] The lips are most commonly affected. Additional features may include oral ulceration, gingivitis and gingival overgrowth, angular cheilitis, scaling and vertical fissuring of the lips, and cobblestone appearance of the buccal mucosa.[2,4-7] Histopathologic features include scattered tuberculoid noncaseating granulomas, tissue edema, ectatic lymphatic vessels, and a perivascular lymphohistiocytic infiltrate.[2,3,8,9] The underlying causes of OFG presentation are unclear and are likely multifactorial with genetic, immunologic, allergic, and infectious contributions being postulated.[8,10]

Orofacial granulomatosis is increasingly used to describe multiple entities with varying causes responsible for recurrent and often persistent orofacial swelling. In addition, OFG likely encompasses a spectrum of known granulomatous diseases, including localized swelling in granulomatous cheilitis (Miescher cheilitis) and more extensive inflammation

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leading to facial nerve palsy and lingua plicata (fissured tongue) in Melkersson-Rosenthal syndrome (MRS).[4,7,11-13] Accordingly, nomenclature is confusing given considerable clinical and histopathologic overlap among causative entities. A reluctance to biopsy affected areas and the inconsistent presence of granulomatous inflammation in biopsy specimens obtained from patients presenting with recurrent orofacial swelling add to the diagnostic challenge. A dynamic clinical presentation and often unclear relationship to underlying medical conditions make creation of a standardized diagnostic approach to patients with recurrent orofacial swelling difficult. The aims of this study were to identify the clinical and histopathologic characteristics of patients presenting in an outpatient setting with signs and symptoms categorizable as OFG and to classify underlying causes to outline a diagnostic approach in affected patients.

PATIENTS AND METHODS

After approval of the study by the Mayo Clinic Institutional Review Board, a search of the electronic health record identified a total of 105 patients evaluated in the Department of Dermatology from January 2, 2000, through July 5, 2011, at Mayo Clinic in Rochester, Minnesota, who had more than 1 episode of orofacial swelling lasting more than 5 days. One patient declined participation in research. The following keywords were used for the search: oral granulomatosis, oral granuloma, oral sarcoidosis, oral sarcoid, orofacial granulomatosis, Melkersson-Rosenthal syndrome, granulomatous cheilitis, cheilitis granulomatosa, and Miescher cheilitis. Duration of swelling and keywords were chosen to exclude angioedema and acute infectious causes of recurrent orofacial swelling. Associations between clinical or histopathologic features and diagnosis were evaluated with chi-square or Fisher exact test. All tests were 2-sided, and *P* values of less than .05 were considered statistically significant.

RESULTS

Of the 104 patients, 66 (64%) were women. Mean age at initial consultation was 43.6±20 years (median, 46.5 years; range, 7-87 years). Mean duration of symptoms was 36.6±47 months (median, 18 months; range, 0.5-240 months). The most common locations of orofacial swelling were the lips (76 patients), face (32 patients), periorbital region (17 patients), gingivae (12 patients), oral mucosa (9 patients), and tongue (3 patients). Asymmetric swelling was described in 22 patients. Recurrent swelling with eventual persistence occurred in 55 patients (53%). Nineteen patients had oral erosions. Patients were placed into categories on the basis of final diagnostic cause of orofacial swelling (Table). Of the 43

TABLE. Cause of Orofacial Swelling and Presence of Granulomatous Inflammation in 104 Patients[a]

Category	No. of patients	Biopsy, n (%)	Granulomas on biopsy, n (%)	Biopsy diagnostic, n (%)
Idiopathic OFG	43	40 (93)	27 (68)	28 (70)
SFE (rosacea/acne vulgaris)	12	7 (58)	3 (43)	5 (71)
Crohn disease	10	8 (80)	6 (75)	6 (75)
Contact dermatitis	8	4 (50)	0 (0)	0 (0)
Sarcoidosis	3	3 (100)	3 (100)	3 (100)
Exfoliative cheilitis	3	3 (100)	0 (0)	0 (0)
Lichen planus	2	2 (100)	0 (0)	2 (100)
Actinic cheilitis	2	2 (100)	0 (0)	1 (50)
Cheilitis glandularis	2	1 (50)	0 (0)	0 (0)
Lymphedema	2	2 (100)	0 (0)	0 (0)
Multifactorial	7	6 (86)	1 (17)	4 (67)
Miscellaneous[b]	10	7 (70)	0 (0)	3 (43)

[a]OFG = orofacial granulomatosis; SFE = solid facial edema.

[b]The following were each found in 1 patient only: orbital pseudolymphoma, plasma cell gingivitis, aphthous stomatitis, idiopathic eosinophilia, photosensitized cheilitis, superior vena cava syndrome, pressure-induced urticaria, atypical erythema multiforme, cystic hygroma, and plasma cell cheilitis.

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