

Diffuse Lip Swelling

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The following Case Challenge is provided in conjunction with the American Academy of Oral and Maxillofacial Pathology.

Case Summary

A 44-year-old man presented with a diffuse, asymptomatic swelling of the lower lip which he claimed had been present for nine months. The patient reported a previous episode of swelling that occurred in the same location but then resolved. He was not experiencing pain, facial nerve palsy, tenderness, or pruritus associated with the lesion, and he was afebrile. No history of trauma to the area was admitted. Antihistamines and aclometasone dipropionate cream .05%, prescribed by his dermatologist, had failed to reduce his swelling.

After you have finished reviewing the available diagnostic information, make the diagnosis.

Diagnostic Information

Medical Work-Up

The patient was taking levothyroxine sodium. His medical history included a thyroidectomy for the treatment of childhood hyperthyroidism. Medical evaluation for this patient's lesion included North American patch testing which revealed a positive response only to thimerosal (a preservative in vaccines and skin test antigens). The patient's serum angiotensin converting enzyme levels were normal, and chest films revealed no pulmonary involvement. He denied any gastrointestinal symptoms.

Oral Examination

The patient's lower lip was markedly larger than his upper lip, and his tongue was mildly fissured (Figures 1 and 2).

His oral hygiene was fair, and all of his first and second molars had amalgam restorations. Bitewing and periapical radiographs showed no evidence of significant periodontal bone loss or apical rarefaction. All mandibular anterior teeth responded to cold and electric pulp testing, and

no evidence of a draining sinus or parulis could be detected. Periodontal probing revealed a 5 mm sulcus depth on the mesial of #14, but no other probing depths were beyond 4 mm.

Biopsy Findings

A 0.3 x 0.3 x 0.4 cm punch biopsy was obtained from the patient's lower labial mucosa. Sections showed unremarkable surface epithelium in association with underlying connective tissue and lobules of accessory salivary glands (Figures 3 and 4).

Scattered chronic inflammatory cells were seen in the connective tissue as well as several well-defined, non-necrotizing granulomas consisting of collections of epithelioid histiocytes and multinucleated giant cells. Special stains were negative for fungal and mycobacterial organisms. No evidence of foreign material was observed in the submitted specimen.



Figure 1. Diffuse bilateral swelling of the lower lip.

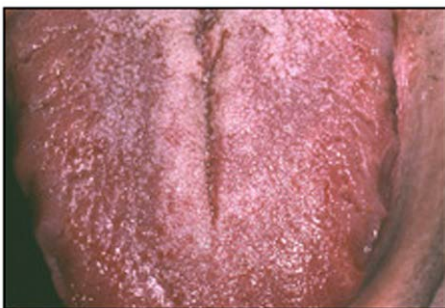


Figure 2. The tongue exhibits a central midline fissure, plus mild fissuring along the lateral borders.

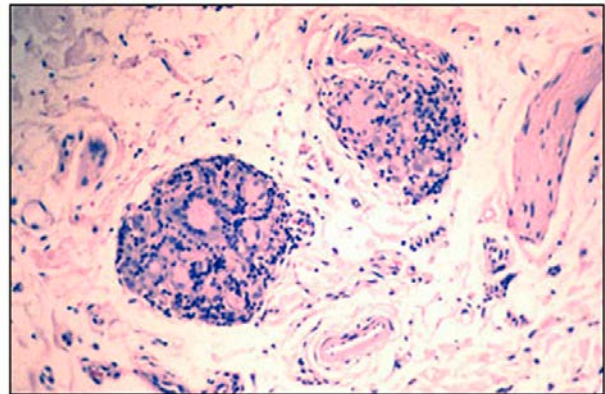


Figure 3. Medium-power photomicrograph showing focal granuloma formation within a background of loose, edematous connective tissue. (Hematoxylin and eosin stain)

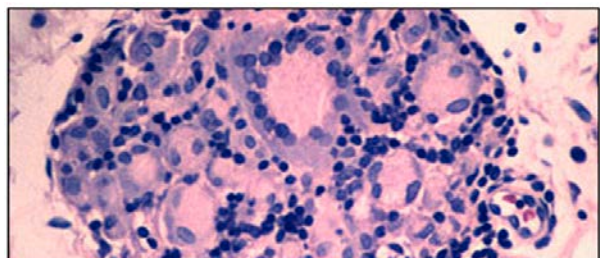


Figure 4. High-power photomicrograph of a granuloma which is characterized by a well-circumscribed collection of epithelioid histiocytes, multinucleated giant cells, and lymphocytes. (Hematoxylin and eosin stain)

Can you make the diagnosis?

A 44-year-old man presented with a diffuse, asymptomatic swelling of the lower lip which he claimed had been present for nine months. The patient reported a previous episode of swelling that occurred in the same location but then resolved.



Select the Correct Diagnosis

- A. Crohn's Disease (regional enteritis)
- B. Angioedema
- C. Sarcoidosis
- D. Cheilitis Granulomatosa/Orofacial Granulomatosis

Crohn's Disease (regional enteritis)

Choice A. Sorry, this is not the correct diagnosis.

Crohn's disease, or regional enteritis, is a chronic, granulomatous inflammatory condition of unknown cause that can affect any portion of the gastrointestinal tract from the mouth to the anus. The most common site to be affected is the ileum, although extra-intestinal sites of involvement, such as the skin, eyes, and joints, have been described.¹ Crohn's disease is usually diagnosed in teenagers, and the symptoms include abdominal cramping, malnutrition, diarrhea, weight loss, and anemia.¹

Dentists may be the first healthcare providers to identify Crohn's disease because oral lesions

have been reported to precede gastrointestinal symptoms in as many as 31% of cases.² Shallow linear ulcers in the buccal vestibule have been reported to be a common finding in patients with regional enteritis.¹ In addition, several examples of regional enteritis initially presenting with orofacial swelling have been documented.³⁻⁷ For this reason, the possibility of regional enteritis should be considered for a patient who presents with non-tender orofacial swelling (e.g., swelling of the lower lip) that cannot be readily explained otherwise.

In this case the patient did not have any other signs of Crohn's disease, so this diagnosis was considered unlikely.

Please re-evaluate the information about this case.

Angioedema

Choice B. Sorry, this is not the correct diagnosis.

Angioedema is a localized, non-pitting edema that is a result of plasma extravasation. The swelling that results from plasma extravasation is sudden, but it typically resolves in 24 to 72 hours.⁸ Any body part can be affected by angioedema, but the deep layers of the skin and mucosa are most frequently involved.^{8,9} When the skin is involved, the swelling will be diffuse, warm, and tender. A burning sensation may be present, and the patient may also report pruritus but this is uncommon. If angioedema occurs, identification of a trigger is important because swelling can cause occlusion of the airway and death. Death from hereditary angioedema can be as high as 30-40% and is usually the result of airway obstruction.⁹ Therefore, if a patient complains of swelling that comes and goes, angioedema should be considered in the differential diagnosis

and the patient should be referred to an appropriate medical professional for evaluation.

There are several causes for angioedema but most cases are idiopathic.⁹ A variety of medications and allergens have been documented as triggering agents for angioedema as well as exposure to cold or minor local trauma.

If exogenous causes for angioedema cannot be determined, the patient may have an acquired or hereditary susceptibility to develop angioedema. Genetic susceptibility to angioedema is related to a C1-esterase inhibitor (INH) deficiency. This is rare, however, with the prevalence reportedly varying from 1:10,000 to 1:150,000.

In this case challenge the patient's swelling was persistent, which is inconsistent with angioedema. Therefore, the diagnosis of angioedema was excluded.

Please re-evaluate the information about this case.

Sarcoidosis

Choice C. Sorry, this is not the correct diagnosis.

Sarcoidosis is a granulomatous systemic disease that can affect multiple organs.¹⁰ The cause of sarcoidosis is unknown, but a genetic predisposition to the disease has been confirmed.¹¹ In the United States the incidence of sarcoidosis is greater among the African-American population (35.5-64:100,000) than the Caucasian population (10-14:100,000).

The most common presentation of sarcoidosis is in the lungs, where hilar lymphadenopathy can often be detected on chest radiographs.^{10,11} Lymph nodes, skin, lacrimal glands, and salivary glands are also common sites of involvement. Cutaneous lesions occur in 25% of patients appearing as chronic, firm, and violet plaques.¹⁰

Oral lesions of sarcoidosis are rare. As of 2005, only 68 cases of oral sarcoidosis had been well-documented and reported in the English literature.¹¹ Both the soft tissues and jaw bones have been reported to be affected. Bony

lesions appear radiolucencies and may result in pain, nasal obstruction, and loosening of the teeth.² Mucosal lesions have been described as swellings, ulcers, and gingival hyperplasia.^{10,11}

Biopsy, chest radiographs, and angiotensin converting enzyme levels are helpful diagnostic tools for sarcoidosis. A biopsy of sarcoidosis will reveal aggregates of epithelioid histiocytes with a rim of lymphocytes.¹⁰ Although these histopathologic features are suggestive of sarcoidosis, they are not diagnostic. In 50-80% of patients with sarcoidosis, serum angiotensin converting enzyme (ACE) levels are elevated.¹¹ Like biopsy, ACE level alone is not diagnostic as it can be elevated in other systemic conditions (e.g., diabetes, cirrhosis).¹¹ However, ACE level is a tool that, when combined with chest radiographs and biopsy, can help with the diagnosis of sarcoidosis.

In this case the patient's chest radiograph was negative and his ACE levels were normal. Therefore, the diagnosis of sarcoidosis could essentially be excluded.

Please re-evaluate the information about this case.

Cheilitis Granulomatosa/Orofacial Granulomatosis

Choice D. Congratulations! You are correct.

Orofacial granulomatosis (OFG) is a condition that is characterized by noncaseating granulomatous inflammation affecting the soft tissues of the oral and maxillofacial regions.¹²

The term orofacial granulomatosis is used when the granulomatous inflammation is not related to a specific condition (i.e., sarcoidosis, regional enteritis, allergy, foreign body reaction, fungal, or mycobacterial infection). Due to the fact that most granulomatous facial swelling is associated with a specific etiology, the diagnosis of orofacial granulomatosis can be made only after ruling out other possible conditions.

Cheilitis granulomatosa is a type of orofacial granulomatosis in which the patient presents with a persistent, painless swelling of one or both lips. When it is found with fissured tongue and facial nerve palsy, the patient is said to have Melkersson-Rosenthal syndrome.¹²

Biopsy of cheilitis granulomatosa histopathologically appears very similar to lesions of sarcoidosis and regional enteritis. The biopsy shows edema in the superficial lamina propria

with dilated lymphatic vessels and scattered lymphocytes.¹² Aggregates of non-necrotizing granulomas consisting of epithelioid histiocytes and lymphocytes are observed. Multinucleated giant cells may also be present.¹² As the granulomas are not the result of infection, special stains and cultures for fungal and mycobacterial organisms are negative.

In this case challenge no specific etiology for the granulomatous inflammation of the patient's lower lip could be identified. Therefore, the diagnosis of cheilitis granulomatosa was made.

Intralesional corticosteroid injection is the most effective treatment for orofacial granulomatosis, although the lesions will respond to systemic corticosteroids.¹³ Injections of up to one ml of triamcinolone acetonide (10 mg/ml) on each side of the swollen lip should be given, usually after block anesthesia for patient comfort. This patient's lip was treated with intralesional triamcinolone and, as is the case with most of these patients, the lip returned to normal size within 24 hours. The patient should be reevaluated at weekly and then monthly intervals to determine if there is a need for additional injections. Surgery to reduce the lip (cheiloplasty) should be performed only if repeated corticosteroid injections do not correct the disfigurement.¹²

References

1. Neville BW, Damm DD, Allen CM, Bouquot JE. Crohn's disease. In: Oral and Maxillofacial Pathology, 2nd edition. Philadelphia: WB Saunders, 2002, pp 733-734.
2. Williams JK, Wray D, Ferguson A. The clinical entity of orofacial Crohn's disease. Q J Med 1991; 79: 451-458.
3. Leão J, Hodgson T, Scully C, Porter S. Review article: orofacial granulomatosis. Aliment Pharmacol Ther 2004; 20:1019-1027.
4. Girlich C, Bogenrieder T, Palitzch KD, Scholmerich J, Lock G. Orofacial granulomatosis as initial manifestation of Crohn's disease: a report of two cases. Eur J Gastroenterol Hepatol 2002; 14: 873-6.
5. Bogenrieder T, Rogler G, Vogt T, Landthaler M, Stolz W. Orofacial granulomatosis as the initial presentation of Crohn's disease in an adolescent. Dermatology 2003; 206:273-8.
6. van de Scheur M, van der Waal R, Volker-Dieben H, Klinkenberg-Knol E, Starink T, van der Waal I. Orofacial granulomatosis in a patient with Crohn's disease. J Am Acad Dermatol 2003; 49: 952-4.
7. Tonovic-Capin V, Galbraith S, Rogers III R, Binion D, Yancey K. Cutaneous Crohn's disease mimicking Melkersson-Rosenthal syndrome: treatment with methotrexate. Euro Acad Derm Vener 2006; 20:449-452.
8. Neville BW, Damm DD, Allen CM, Bouquot JE. Angioedema. In: Oral and Maxillofacial Pathology, 2nd edition. Philadelphia: WB Saunders, 2002, pp 308-310.
9. Frigas E, Ugochukwu N. Angioedema. Clin Rev Allergy Immunol 2002; 23:217-231.
10. Neville BW, Damm DD, Allen CM, Bouquot JE. Sarcoidosis. In: Oral and Maxillofacial Pathology, 2nd edition. Philadelphia: WB Saunders, 2002, pp 292-294.
11. Suresh L, Radfar L. Oral sarcoidosis: a review of literature. Oral Diseases 2005; 11:138-145.
12. Neville BW, Damm DD, Allen CM, Bouquot JE. Orofacial granulomatosis. In: Oral and Maxillofacial Pathology, 2nd edition. Philadelphia: WB Saunders, 2002, pp 294-297.
13. El-Hakim M, Chauvin P. Orofacial granulomatosis presenting as persistent lip swelling: Review of 6 new cases. Eur Acad Derm Vener 2006; 20:449-452.
14. van der Waal R, Schulten E, van de Scheur M, Wauters I, Starink T, van der Waal I. Cheilitis granulomatosa. Eur Acad Derm Vener 2001; 15: 519-523.

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Note: Bio information was provided at the time the case challenge was developed.

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