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J Am Dent Assoc 2008;139;587-590

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Lip swelling in a teenage boy

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THE CHALLENGE

A pediatric admitting physician contacted clinicians from the oral medicine consulting service of the Children's Hospital of Philadelphia regarding evaluation of a 16-year-old boy who was admitted because of painful lower lip swelling. The patient reported a three-day history of lower lip swelling, which had become acutely painful during the previous 24 hours. His medical history was significant for asthma, chronic acne, multiple environmental and food allergies (apple, banana, carrot, pear, peach) and a penicillin allergy. He had seen his primary care physician, who prescribed methylprednisolone in a dose pack at the onset of the lip swelling for a presumed allergic reaction to isotretinoin, which he had been taking for several months before the onset of the lesion. The patient also was using a moisturizing balm for cracked lips secondary to acne treatment.

Despite the patient's stopping the isotretinoin treatment and use of the lip balm and starting methylprednisolone treat-

ment, the swelling did not subside and the pain worsened. On the third day of the systemic corticosteroid regimen, the patient came to the emergency department, where he was treated with morphine and ketorolac to control the pain. In addition, the primary medical team administered acyclovir and hydrocodone.

On physical examination, we found an agitated and anxious boy who gripped his lower lip in acute discomfort. The lip was desquamated and had several superficial pustular areas (Figure 1). We did not find any gingival or pharyngeal involvement. The patient's tongue was dry but free of lesions or exudate. He did not have lesions elsewhere on his body. He was warm and well-perfused, and his vital signs were normal on admission, with the exception of moderate tachycardia and fever (38.5°C). The results of the screening laboratory tests, including a complete blood cell count with differential and hepatic panel, were significant for marked neutrophilia (neutrophil count of 78 percent). The results of a rapid strep test were negative.



Figure 1. Swelling, desquamation and the presence of multiple vesicles on the lower lip are seen.

Can you make the diagnosis?

- | | |
|----------------------------|--------------------|
| A. angioneurotic edema | C. impetigo |
| B. cheilitis granulomatosa | D. herpes labialis |

THE DIAGNOSIS

C. impetigo

Impetigo is a highly contagious bacterial skin infection predominantly affecting children. Steer and colleagues¹ reported that impetigo affects between 20 and 30 percent of the pediatric population. Although it mostly affects the young, impetigo is seen in people of all ages. It is the third most common dermatologic disease among children (after atopic dermatitis and viral warts).¹ The disease is transmitted via direct contact, with a reported incidence of 1.6 percent in children between 5 and 15 years of age, and it has a greater occurrence in the summer months.^{1,2}

Impetigo is classified as bullous and nonbullous. Seventy percent of cases correspond to the nonbullous category, and the lesions begin on the face or on limbs that have been subjected to trauma. Common lesions preceding the onset of the infection include scratches, burns and insect bites. Vesicles and pustules develop later in the course of the infection. With the exception of pruritus, constitutional symptoms usually are not present, unless the infection is complicated by the onset of progressive cellulitis.

Etiologic factors for impetigo include *Staphylococcus aureus* and group A β -hemolytic streptococci.³ The former is spread from the nose to the perioral skin, and the latter have been associated with the onset of impetigo in the respiratory tract. Bullous impetigo is caused exclusively by *S. aureus*, and it occurs mainly in infants and young children. Lesions of bullous impetigo can form on intact skin and as a component of scalded skin and toxic shock syndromes. Both types of impetigo usually heal without significant scarring, although a delay in initiating antibiotic therapy will affect the prognosis. The time to resolution depends on whether the patient receives prompt medical attention; however, typically it is no longer than one week.³

Clinicians base the diagnosis of impetigo on the patient's clinical presentation and on a culture or Gram's stain of the superficial dermal lesions. A great proportion of cases, however, are diagnosed on the basis of the clinical presentation and symptoms alone. Nonbullous impetigo starts as a single erythematous macule or papule that rapidly turns into a vesicle that ruptures, leaving an eroded surface. Secondary impetigo complicates systemic conditions such as diabetes and

HIV infection. Moreover, viral infections with mucosal involvement can precede the onset of impetigo. The lesions of bullous impetigo are characterized by superficial vesicles that progress into large bullae. This subtype favors mucosal folds and moist dermal areas.

Topical antibiotics are effective in the treatment of localized lesions. Mupirocin and fusidic acid (not available in the United States) are effective and relatively safe.³ Less effective topical antibiotics include bacitracin and bacitracin/neomycin compounds. Narrow-spectrum beta-lactamase systemic antibiotics also appear to be an effective treatment for impetigo. Cephalosporins and amoxicillin/clavulanate potassium are more effective than other types of penicillins and macrolides. Antistaphylococcal antibiotic agents, such as clindamycin, are the preferred therapy for patients with severe cases. Clinicians decide whether to prescribe an oral versus a systemic antibiotic on the basis of the extension of the infection and the presence of systemic symptoms. The role of topical disinfectants remains controversial, as their efficacy in treating impetigo varies.⁴

DIFFERENTIAL DIAGNOSIS

Lip swelling or macrocheilia may be localized or diffuse in appearance. In addition to angioneurotic edema, other causes of diffuse macrocheilia include various granulomatous inflammatory conditions and genetic or congenital diseases. The granulomatous conditions include Crohn disease, Melkersson-Rosenthal syndrome, orofacial granulomatosis (OFG) and cheilitis granulomatosa.⁵ In patients with these conditions, the labial swelling often is painless and may be associated with mucosal fissuring. In most cases, and in contrast to angioedematous reactions, macrocheilia usually involves a gradual onset. Histologic examination of a tissue biopsy specimen typically reveals discrete, noncaseating granulomas.⁶

Oral manifestations of Crohn disease may precede the onset of the more classical gastrointestinal manifestations by months or, in some cases, several years. Linear ulcerations in the mucobuccal folds, aphthouslike ulcers, generalized mucosal erythema and cobblestoned mucosa also may be apparent in patients with Crohn dis-

ease.⁷ A fissured tongue and facial palsy are characteristic of Melkersson-Rosenthal syndrome. In the absence of any other manifestations or etiologies, clinicians often render a diagnosis of OFG. Thus, OFG essentially is a diagnosis of exclusion.

Infectious organisms. Although rare, infectious organisms such as tuberculosis and leprosy have been associated with diffuse lip swelling, and they appear in a manner similar to that of noninfectious granulomatous diseases.⁸ Clinicians typically perform histochemical studies, including acid-fast stains and stains used to detect fungal organisms, to identify any infectious agents. In the absence of detectable organisms, and because extrapleural primary tuberculosis is quite rare, chest radiographs may be necessary to make a diagnosis. A complaint of paresthesia or tingling of the extremities should increase the clinician's suspicion of leprosy. Other cutaneous infectious diseases found in infants and young children are atopic dermatitis and generalized lesions of bullous impetigo in scalded skin syndrome. Atopic dermatitis is characterized by chronic pruritic lesions and abnormally dry skin.^{1,2} Viral infections can affect the lips, causing erosion, crusting and swelling, as seen in lesions caused by members of the herpesvirus family.

Various genetic or congenital conditions also may be associated with diffuse lip enlargement, including lipoid proteinosis and Ascher syndrome. In the latter case, the swelling is characterized more appropriately as a "double lip," because the enlargement is a consequence of redundant tissue folds. Patients with Ascher syndrome typically experience no pain in the lips.

Foreign material. Foreign material, which also may elicit granulomatous inflammation, can contribute to diffuse or localized lip enlargement. For instance, various injectable substances used for lip augmentation, including hyaluronic acid, have been associated with foreign body-type reactions. The clinical presentation often is one of painless nodularity that may be associated with labial erythema. In cases of localized swellings, the foreign material often is introduced into the lip after a traumatic event. Other causes of localized macrocheilia include trauma (hematoma) and various reactive or neoplastic proliferations.

Our patient was admitted to the hospital because of pain and dehydration. On consultation with the primary medical service, we focused the differential diagnosis primarily on an infectious etiology, owing to the presence of malaise and



Figure 2. Lower lip 24 hours after drainage of a pustule.

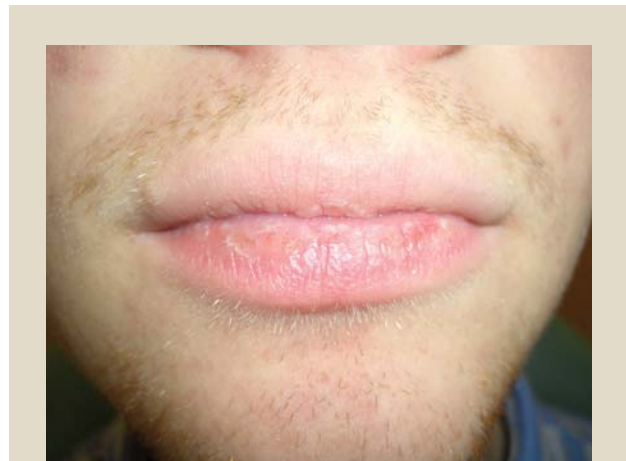


Figure 3. At the eight-week follow-up visit, the lip swelling, desquamation and vesicles had resolved.

fever, as well as to abnormalities in laboratory test results. We swabbed the lesions to rule out a fungal, bacterial or viral etiology. In addition, a purified protein derivative was placed to rule out tuberculosis-related cellulitis, and we ordered a C1 esterase screen to rule out angioneurotic edema.

We treated the most pressing problem (pain) with topical lidocaine, intravenous morphine, ketorolac and oxycodone. Approximately 12 hours after the patient's admission to the hospital, two of us (A.P., R.B.) drained an extensive pustule in the midline of his lower lip, resulting in some symptomatic relief (Figure 2). On admission to the hospital, the patient received intravenous acyclovir and clindamycin treatment, which was dosed per weight. The only significant screening

result was the bacterial culture, which was positive for *S. aureus*. We discontinued the antiviral medication on the third day after admission, and the patient continued to receive intravenous clindamycin treatment and warm compresses, as well as pain management for one more day. This resulted in rapid improvement in his condition. He was discharged from the hospital with prescriptions for clindamycin (150 milligrams three times a day), oxycodone (5 mg four times a day) and ibuprofen (600 mg four times a day).

A follow-up visit eight weeks after discharge from the hospital (Figure 3) revealed dramatic clinical improvement. The patient began using a new lip balm and again began isotretinoin therapy. Although this case was not typical of impetigo because of the acute symptoms and systemic involvement, it became apparent in retrospect that the symptoms and systemic involvement were caused by an aggressive local infection of the area. The initial corticosteroid treatment might have facilitated the progression of the local infection. The clinical appearance of the lesion and the results of the bacterial culture and other tests ruled out other possible diagnoses.

Although researchers and clinicians in the oral pathology, oral medicine and dermatology arenas disagree regarding the inclusion of lip lesions within the diagnosis of impetigo, we reached agreement on a final diagnosis of impetigo after consulting with a clinician (F.A.) in the Department of Dermatology, Hospital of the University of Pennsylvania, Philadelphia, as well as by considering the patient's clinical characteristics carefully. About 10 weeks after discharge, the patient developed a small vesicular-pustular area on his elbow, which also was positive for *S. aureus*. It is interesting to point out that an analysis of the antibiotic susceptibility of the culture revealed a resistance to clindamycin. A dermatologist treated the lesion with topical antibiotics, with excellent results.

CONCLUSION

Lip swelling can develop as a sign of multiple pathologic conditions. The differential diagnosis of lip swelling is based on the patient's history, his or her clinical appearance and hypothesis-driven testing that guides an astute clinician toward a diagnosis. Furthermore, more than one disease process can develop as part of the same clinical scenario. Clinicians should consider impetigo—the third most common dermatosis in the pediatric age group—in the differential diagnosis of infectious macrocheilia in children and adolescents. ■

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Disclosure: The authors did not report any disclosures.

Diagnostic Challenge is published in collaboration with the American Academy of Oral and Maxillofacial Pathology and the American Academy of Oral Medicine.

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