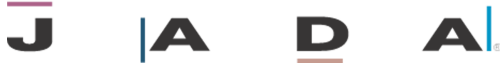


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Chronic lesions of the gingiva and mucosa

Scott S. DeRossi, DMD; German Salazar, DMD; Jaya Sarin, DMD; Faizan Alawi, DDS

THE CHALLENGE

A 43-year-old man was referred to the Division of Oral Medicine at the University of Pennsylvania Medical Center, Philadelphia, for evaluation and treatment of multiple sore oral lesions affecting the gingiva, buccal mucosa and labial mucosa. The patient reported that oral lesions had been present for four months before his initial visit to the lead author (S.S.D.). He reported having mild, but increasing, gastrointestinal pain and distress, including diarrhea. He initially noticed mild soreness and increased bleeding of the gingiva, which gradually progressed to swelling and soreness of the gin-

giva and buccal mucosa (Figures 1 through 3).

The patient's medical, family and social histories were noncontributory. He was not taking any medications, nor did he report having any drug allergies. A comprehensive review of systems revealed episodic stomach discomfort and diarrhea that were controlled with over-the-counter antidiarrhea medication. The clinical examination revealed no cervical adenopathy or lesions on exposed skin surfaces or conjunctivae. Evaluation of the oral cavity revealed generalized erythema, thickening and "cobblestone" plaques and superficial erosions of the buccal mucosa, as well as edema of the gingiva with multiple yellowish pustules (Figures 1 through 3).



Figure 1. Swollen gingiva with "pebbly" appearance.



Figure 2. Mandibular gingiva exhibiting small, yellowish pustules.



Figure 3. Shallow erosions and folds can be seen on the right buccal mucosa.

Can you make the diagnosis?

- A. erythema multiforme
- B. primary herpetic gingivostomatitis
- C. oral lichen planus
- D. pyostomatitis vegetans
- E. pemphigus vulgaris

THE DIAGNOSIS

D. pyostomatitis vegetans

Pyostomatitis vegetans (PV) is a relatively rare, chronic, nonneoplastic disorder of unknown etiology. The significance of PV lies in its association with inflammatory disease of the bowel, including ulcerative colitis, Crohn disease, spastic colitis and chronic diarrhea. Several case reports and literature reviews have estimated that PV is associated with gastrointestinal disease in 75 percent of cases.¹⁻⁶ Often, bowel disease precedes the onset of oral lesions by months or years.¹

Clinically, PV is characterized by miliary pustules, erosions and a vegetating dermatosis of the skin and mucous membranes.² Oral lesions typically involve the anterior attached gingiva as well as the labial and buccal mucosa and are distinct in character. Hard- and soft-palate and tonsillar areas also may be affected. Multiple small, superficial, yellowish pustules (2 to 3 millimeters in diameter) may be present on an erythematous base. These pustules can coalesce to form necrotic lesions with a typical "snail tracks" appearance.³ Deep folds in the buccal mucosa are common, and small vegetating papillary projections may be seen over the surface of friable mucosa. Despite the extensive involvement, patients usually describe having only mild-to-moderate soreness or discomfort.

Men are affected by PV nearly twice as often as are women. The peak age range is between the third and sixth decades. Laboratory values generally are within normal limits, although many patients may have mild anemia, zinc deficiency⁴ or peripheral eosinophilia.⁵ A search for an infectious etiology has persistently yielded negative or inconsistent results.

Our patient returned seven days after his initial visit for a biopsy of the buccal mucosa. Multiple sections showed ulcerated, markedly spongiotic, stratified squamous epithelium that exhibited acantholysis and intraepithelial blister formation. A pronounced inflammatory infiltrate of eosinophils and neutrophils was present within areas of clefting, and a dense submucosal infiltrate consisted of eosinophils, neutrophils, lymphocytes and plasma cells (Figure 4).

On the basis of the histologic diagnosis, combined with the patient's complaints of diarrhea, we referred him to a gastroenterologist. A stool sample and sigmoidoscopy revealed ulcerative col-

itis. The gastroenterologist prescribed an aminosalicylate, which was helpful in controlling the patient's gastrointestinal symptoms. The lead author treated his oral cavity lesions with topical corticosteroid gel, which helped to control the gingival and mucosal soreness.

The primary objective in the treatment of PV must be identifying and/or controlling the associated bowel disease. Lesions frequently improve when the colitis is controlled; likewise, an exacerbation of colitis usually is followed by a similar flare in oral lesions. A modified diet and systemic medications such as antispasmodics, antibiotics, aminosalicylates (such as sulfasalazine and mesalamine), corticosteroids, azathioprine or dapsone may be used to treat the bowel disease.⁶

Oral lesions often are treated effectively with topical corticosteroids in a gel or mouthwash formulation. However, systemic corticosteroids, dapsone and other immunosuppressive therapy may be indicated for moderate-to-severe symptomatic lesions in the oral cavity that are recalcitrant to topical therapy.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of chronic multiple lesions of the oral cavity can be extensive and requires a careful medical history (including systemic signs and symptoms of illness), a physical examination, a histologic evaluation and, occasionally, laboratory testing to narrow the diagnostic possibilities.

Erythema multiforme. Erythema multiforme (EM) usually is a self-limiting, occasionally severe and recurrent type of hypersensitivity (allergic) reaction that develops in response to medications, infections or illness. Medications associated with EM include sulfonamides, penicillins, barbiturates and phenytoin. Associated infections include herpes simplex and mycoplasma infections. The exact etiology is unknown, but the disorder is believed to involve a vasculitis of the skin and mucous membranes, with subsequent damage to tissues leading to ulceration. Approximately 90 percent of cases of EM are associated with herpes simplex or mycoplasma infections.⁷ The disorder develops primarily in children and young adults (< 40 years of age).

Clinically, the lesions of intraoral EM are char-

acterized by irregular ulcerations affecting any region of the oral cavity, but usually sparing the gingiva. Hemorrhagic crusting of the lips is common. The diagnosis of EM is based on the patient's medical history and clinical manifestations. The results of laboratory and histologic evaluations often are nonspecific. Clinicians treat EM with supportive therapy, systemic corticosteroids and antiviral drugs for recurrent cases precipitated by herpes.

Primary herpetic gingivostomatitis. Primary herpetic gingivostomatitis is an infection caused by herpes simplex virus. Clinicians often diagnose it according to the patient's medical history and a clinical finding of acute-onset lesions, usually seen in children and adolescents. Occasionally, cultures and cytologic smears can aid in the diagnosis. Patients often complain of generalized prodromal symptoms—fever, headache, malaise, nausea and vomiting—that precede clinical lesions by one to two days. A negative history of recurrent herpes labialis and a positive history of direct intimate contact with someone who has primary or recurrent herpes are helpful in making the diagnosis.⁸

Shortly after the onset of prodromal symptoms, small, thin-walled vesicles appear that quickly rupture, leaving shallow discrete ulcers on any areas of the oral mucosa. An important diagnostic criterion in this disease is the appearance of generalized, acute, marginal, edematous and inflamed gingiva. Primary herpetic gingivostomatitis primarily is a self-limiting disease, with fever resolution in three to four days and oral lesions healing within 10 to 14 days. Supportive treatment is helpful; however, systemic antiviral therapy may shorten the course of the disease if instituted within 48 to 72 hours of vesicle eruption.

Oral lichen planus. Oral lichen planus (OLP) is a common mucocutaneous disease that affects

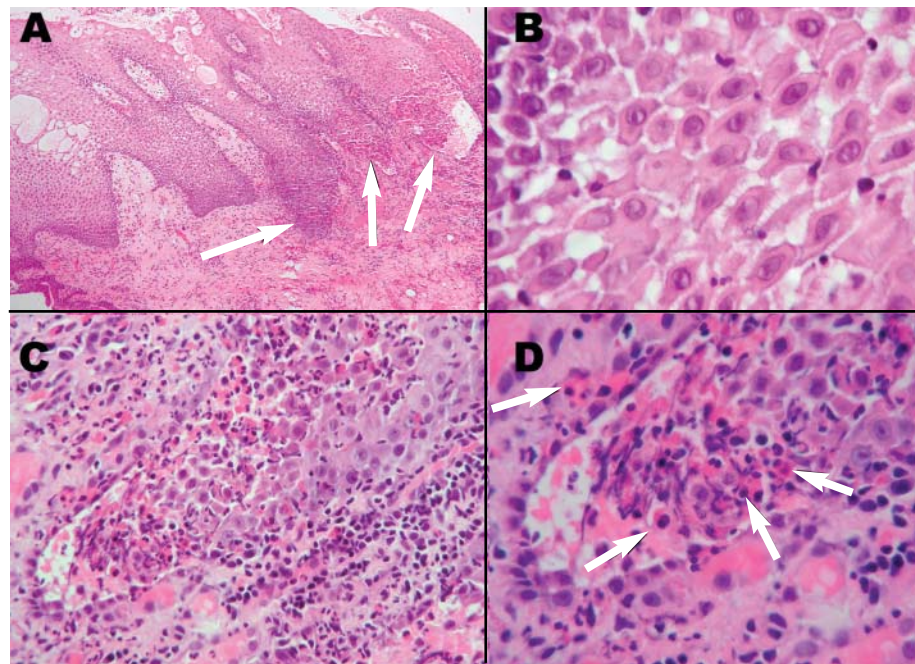


Figure 4. Pyostomatitis vegetans. **A.** Intraepithelial eosinophilic abscesses are seen in multiple areas (arrows) (hematoxylin-eosin stain, x20). **B.** Marked edema with acantholysis (hematoxylin-eosin, x400). **C, D.** Numerous eosinophils (arrows) are noted within the epithelium and underlying connective tissue (hematoxylin-eosin, x400).

1 to 2 percent of the population. It usually occurs in men and women between the ages of 30 and 70 years. OLP can vary clinically, appearing keratotic (plaquelike and reticular) or erythematous and ulcerative. The lesions of OLP are chronic, but spontaneous remission has occurred in less than 5 percent of cases.⁹ Although the exact cause of OLP remains unclear, recent research⁹ has yielded significant information about the immunological mechanisms that are fundamental to the initiation and perpetuation of the disease. Current evidence suggests that OLP is a T-cell-mediated process leading to basal keratinocyte breakdown in epithelium and ulceration in some cases. Clinically, OLP has a wide range of appearances that correlate with disease severity. The three most common presentations are the following:

- reticular form: white lacelike pattern of Wickham's striae;
- erosive form: mixture of intense erythema of mucosa and irregularly shaped ulcers with a yellowish pseudomembrane;
- plaquelike form: slightly raised or flat white patches.

The diagnosis of OLP varies according to presentation. Clinicians often diagnose reticular OLP on the basis of clinical examination findings

alone, because of the distinct characteristics of Wickham's striae. The erosive and plaque-like forms of OLP require histologic evaluation, because clinically they can resemble other oral mucosal lesions, including malignancy. Although no cure exists for OLP, treatment with topical corticosteroids remains the mainstay of therapy. Clinicians' goals in treating patients with OLP should be to alleviate symptoms and monitor for dysplastic changes leading to malignancy.

Pemphigus vulgaris. Pemphigus vulgaris is a mucocutaneous disease that occurs rarely, but is significant in consequence. It is a potentially fatal autoimmune disease caused by the production of autoantibodies against desmosomal proteins (that is, adhesive proteins that secure epithelial cells to one another), leading to vesicular eruptions and ulcerations of the skin and mucosa. There are one to five cases per million population per year, and the disease is seen most commonly in 40- to 60-year-old people.

As with many autoimmune diseases, there is a genetic predisposition to pemphigus; it is seen with increased frequency in certain ethnic groups, such as Ashkenazi Jews and people of Mediterranean origin, as well as within families. Pemphigus affects the skin and mucosa, resulting in superficial blisters that ulcerate quickly, leading to chronic erosions and ulcerations. Various mucosal surfaces of the body can be involved, including ocular, oral, nasal, pharyngeal, laryngeal and anogenital tissues. Almost 90 percent of patients with pemphigus develop oral lesions during the course of the disease and, in more than one-half of cases, the oral lesions are the first sign.

The classic lesion of pemphigus is a thin-walled blister that arises on otherwise normal skin or mucosa; the lesion extends rapidly and leaves an irregular ulceration. A biopsy specimen for routine and immunopathologic study is fundamental to the identification of pemphigus lesions.¹⁰ Treatment of pemphigus includes the use of systemic corticosteroids such as prednisone, systemic

immunosuppressive agents and topical palliative therapy for painful oral ulcerations.

CONCLUSION

Pyostomatitis vegetans is a relatively rare disorder of the oral cavity. However, a timely and accurate diagnosis is imperative, because approximately 75 percent of cases of PV are associated with gastrointestinal disease, some cases of which may not have been diagnosed. Often, significant similarities exist in the clinical presentation of oral lesions that require the oral health care professional to formulate a careful differential diagnosis and evaluation. ■

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