A Young Patient With Persistent Gingival Bleeding

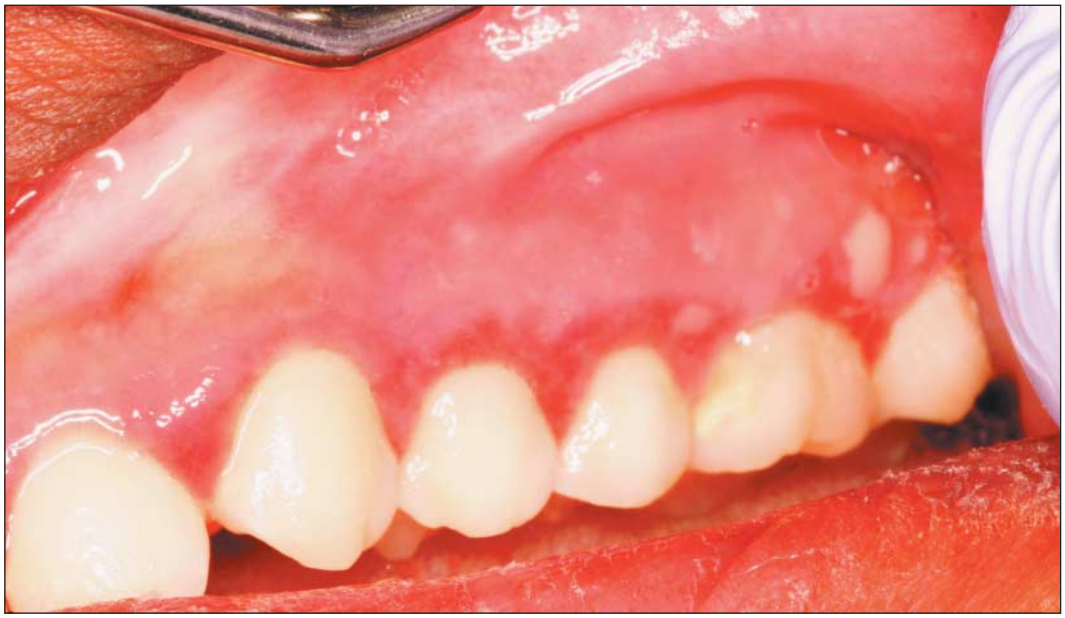

Figure 1. Gingival erythema and ulcerations in a 13-year-old patient.

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A 13-YEAR-OLD GIRL COMES TO YOUR OFFICE FOR EVALUATION OF ULCERS, erythema, and a "peeling off" sensation in her gums. Her gums have been sore and red for at least 6 years. Initially she was diagnosed as having generalized gingivitis despite a low level of local irritants such as dental plaque or calculus. Her medical history is not significant and she is not taking any medication except cetirizine for seasonal allergies. Findings from a general physical examination are within normal limits. Her intraoral examination reveals ill-defined ulcers with marked erythema in the gums (FIGURE 1). The epithelium "peels" easily, leaving a thin membrane around the teeth. There is no evidence of significant dental plaque accumulation or the presence of local irritants such as calculus. Pertinent laboratory values (complete blood cell count, platelet count, liver panel) are within normal limits.

What Would You Do Next?

A. Obtain a biopsy from the affected gums
B. Order human immunodeficiency virus and coagulation tests
C. Prescribe topical steroids
D. Recommend better oral hygiene including the use of dental floss

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JAMA Clinical Challenge Section Editor: Huan J. Chang, MD, Contributing Editor. We encourage authors to submit papers for consideration as a JAMA Clinical Challenge. Please contact Dr Chang at tina.chang@jama-archives.org.

Diagnosis

Pemphigus vulgaris

What to Do Next

A. Obtain a biopsy from the affected gums.

The key clinical feature is persistent bleeding and easy peeling of the gingiva despite good oral hygiene. Pemphigus vulgaris represents an uncommon but important condition because, if left untreated, it can progress systemically, often resulting in death. Oral lesions are often the first sign of disease. The critical point in this case is making an early diagnosis through biopsy of the affected tissues.

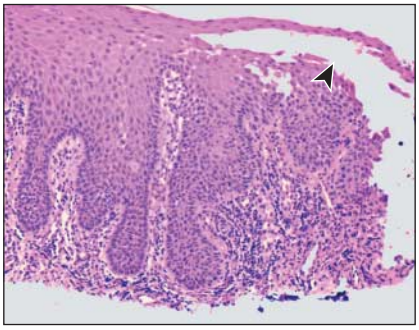

Figure 2. Gingival punch biopsy showing the characteristic intraepithelial separation (arrowhead), which occurs just above the basal layer of the epithelium (hematoxylin-eosin, original magnification ×40).

Comment

Pemphigus is a group of potentially life-threatening autoimmune diseases characterized by cutaneous blistering, mucosal blistering, or both. Pemphigus vulgaris is the most common variant (80% of cases) and oral lesions are the initial manifestation about half of the time.[1] In approximately 18% of patients with pemphigus, the oral cavity is the only place affected.[2] This condition typically affects adults between the ages of 40 and 60 years; prevalence is generally slightly higher in women.[3] The annual incidence of pemphigus vulgaris is 1 to 5 per million population per year in the United States.[4] The diagnosis of pemphigus vulgaris in young patients is rare and few cases have been reported in the literature.[5]

The etiology of pemphigus vulgaris is unknown. However, there is evidence that the epithelial disruption in pemphigus vulgaris is mediated by IgG autoantibodies. Blisters occur in the epidermis and the mucous membranes, where the IgG autoantibodies target 3 different proteins of the desmosomes (Dsg 1, Dsg3, and Dsg4).[6] Loss of tolerance for autoimmune target molecules may play a role in triggering this condition.[7] External factors that can potentially induce or perpetuate pemphigus vulgaris in genetically predisposed individuals include medications, diet, and environmental factors.

Pemphigus vulgaris affects the mucosa and the skin, resulting in superficial blisters that rapidly rupture and result in painful ulcerations. While any area in the oral cavity can be involved, the soft palate, buccal mucosa, and gingiva are predominantly affected.[8] Patients usually report oral soreness unresponsive to routine oral hygiene therapy for several months before consulting with their dentist or primary care physician. Often, tissue fragility becomes overt in areas of trauma from toothbrushing or from frictional forces caused by removable oral prosthetics. The formation of a lesion after gentle mechanical pressure on affected tissue may be used as a diagnostic tool (Nikolsky sign). The clinical differential diagnosis of pemphigus vulgaris includes paraneoplastic pemphigus, erosive lichen planus, mucous membrane pemphigoid, epidermolysis bullosa, linear IgA disease, lupus erythematosus, chronic erythema multiforme, and graft-vs-host disease.

In this patient with persistent gingival bleeding despite good oral hygiene, performing a biopsy was reasonable. A gingival punch biopsy showed the characteristic intraepithelial separation, which occurs just above the basal layer of the epithelium (FIGURE 2). The diagnosis of pemphigus vulgaris is based on 3 independent sets of criteria: clinical features, histology, and immunological testing.[9] The diagnosis should be made as early as possible, because symptom control is generally easier to achieve and because of the serious consequences of untreated disease progression.[10] Pemphigus vulgaris is a systemic disease; therefore, treatment consists of systemic corticosteroids often in combination with other immunosuppressive medications. The potential adverse effects associated with long-term use of prednisone must be considered at the time of starting therapy. Topical treatment cannot replace systemic medications but may be useful for palliation of painful oral ulcers. Maintaining oral hygiene and minimizing irritation of the lesions are part of general supportive treatment. Pemphigus vulgaris may undergo complete resolution, although exacerbations are common.

Patient Outcome

The patient was referred to a dermatologist. Treatment included rituximab and topical steroids with resolution of symptoms in 6 months. The patient sees her dermatologist every 6 months.

Conflict of Interest Disclosures: Both authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr White reported holding a patent from UK HealthCare, receiving textbook royalties, and receiving compensation for expert testimony and serving on speakers' bureaus from UK HealthCare. Dr Yepes reported no disclosures.
Additional Contributions: We thank the patient's mother for providing permission to share her story.

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