

## What Is Your Diagnosis?



A 95-year-old woman was admitted to the hospital for hip fracture repair with a course complicated by pneumonia and transfer to the intensive care unit. On hospital day 11, several days prior to surgery, she developed multiple, slightly tender, yellow papules on her tongue and inner lip. She denied odynophagia.

PLEASE TURN TO PAGE 185 FOR DISCUSSION

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The authors report no conflict of interest.

## The Diagnosis: Acute Herpes Simplex Virus Type 1 Stomatitis

Physical examination of our patient revealed approximately 15 soft yellowish papules (4–8 mm in diameter) on the tongue, some with slight hemorrhage (Figure 1). There was a solitary, 4×8-mm, fleshy oval papule on the right central inner lip mucosa not extending to the vermilion border (Figure 2). There also were several smaller vesicles (1–2 mm in diameter) on the floor of the mouth, soft palate, and buccal mucosa. The patient was afebrile with a white blood cell count within reference range and no cervical lymphadenopathy.

Histologic examination of a shave biopsy specimen from the papule on the inner lip showed ulceration of the mucosa and underlying dermal necrosis with numerous neutrophils and extravasated fibrin. There were small foci containing epithelium with cytopathic viral changes and formation of multinucleate giant cells (Figure 3). A direct fluorescence assay conducted on vesicles from the soft palate was positive for herpes simplex virus type 1 (HHV-1) infection. Serum taken for routine blood chemistries several days prior to the onset of oral lesions was retrieved; HHV-1 IgG titers were positive. Acute HHV-1 stomatitis was diagnosed and treatment was initiated with intravenous acyclovir sodium (5 mg/kg every 8 hours for 5 days) followed by oral acyclovir (400 mg every 8 hours for 5 days). Over these 10 days of treatment, all oral lesions gradually resolved.

Herpes simplex virus type 1 stomatitis primarily occurs in children aged 6 months to 5 years but can occur at any age. Humans are the primary reservoir for HHV-1 and up to 90% of the worldwide population is seropositive for HHV-1 by 40 years of age; however, most immunocompetent hosts infected with HHV-1 do not manifest disease symptoms.<sup>1</sup> The typical presentation of primary HHV-1 stomatitis is multiple vesicles on the oral mucosa and gingiva, some with edema and ulceration; patients often exhibit fever, malaise, and lymphadenopathy.<sup>2</sup> In contrast, recurrent HHV-1 infection in the immunocompetent host typically manifests as herpes labialis, with relatively small numbers of grouped vesicles near the vermilion border, perioral region, or on facial skin; recurrent oral mucosa lesions usually are unilateral on the palate. However, one study demonstrated that recrudescent intraoral HHV-1 infection in immunocompetent hosts can clinically mimic



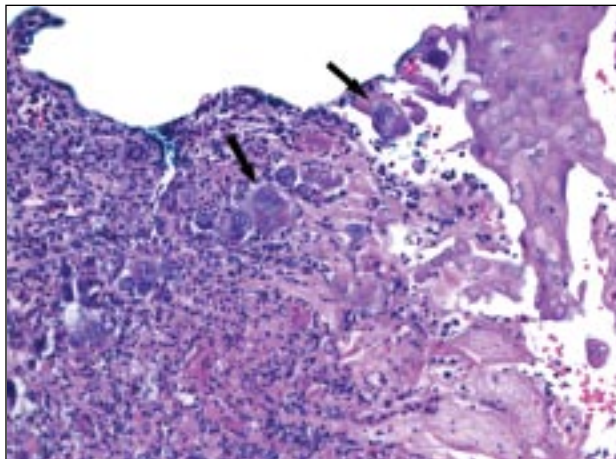
**Figure 1.** Yellowish papules measuring 4 to 8 mm in diameter on the tongue, some with slight hemorrhage.



**Figure 2.** Fleshy oval papule (4×8 mm) on the right central inner lip mucosa.

primary HHV-1 stomatitis.<sup>3</sup> While our patient did not describe a history of herpes lesions, HHV-1 IgG titers were positive on serum obtained prior to the onset of oral lesions, indicating prior exposure and subclinical disease. Given the extent and severity of involvement in this patient, her disease is best characterized as acute HHV-1 stomatitis.

The papules on our patient's tongue represent an atypical presentation of HHV-1 stomatitis. Descriptions of tongue involvement of HHV-1 in immunocompromised patients include herpetic geometric glossitis<sup>4</sup> and a tongue mass.<sup>5</sup> Atypical tongue manifestations of HHV-1 also have been described in oncology patients as tongue nodules and erosions.<sup>6,7</sup>



**Figure 3.** Ulceration of the mucosa and underlying dermal necrosis with numerous neutrophils and extravasated fibrin. There were small foci containing epithelium with cytopathic viral changes and formation of multinucleate giant cells (arrows)(H&E, original magnification  $\times 200$ ).

Given positive HHV-1 IgG titers, one would have expected to observe clinical features of recurrent HHV-1 infection in our patient, with typical lesions on the lip, perioral region, face, or unilateral palate. Instead, her presentation is more akin to acute HHV-1 stomatitis with vesicles on the soft palate and atypical tongue lesions; multiple tongue papules in acute HHV-1 infection have not been previously reported.

Trauma and stress of a prolonged intensive care unit course with multiple medical procedures are known triggers for recurrent HHV-1 infection.

Our patient's more florid and atypical presentation may be attributed in part to immunosenescence, the relative immunocompromise associated with advanced age.<sup>8</sup>

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