An 83-year-old man presented with a new-onset 1.2-cm eroded plaque on the vermilion border of the right lower lip that reportedly developed 2 weeks prior and was increasing in size. The plaque was moist and was composed of confluent glistening papules. Medical history was notable for the presence of both basal cell and squamous cell carcinomas.

WHAT’S THE DIAGNOSIS?

a. aphthous ulcer
b. bullous oral lichen planus
c. herpes simplex labialis
d. solitary keratoacanthoma
e. squamous cell carcinoma

PLEASE TURN TO PAGE E2 FOR THE DIAGNOSIS
PHOTO CHALLENGE DISCUSSION

THE DIAGNOSIS:
Squamous Cell Carcinoma

The initial clinical presentation suggested a diagnosis of herpes simplex labialis. The patient reported no response to topical acyclovir, and because the plaque persisted, a biopsy was performed. Pathology demonstrated squamous cell carcinoma (SCC) that was moderately well differentiated and invasive (Figure).

Approximately 38% of all oral SCCs in the United States occur on the lower lip and typically are solar-related cancers developing within the epidermis. Oral lesions initially may be asymptomatic and may not be of concern to the patient; however, it is important to recognize SCC early, as invasive lesions have the potential to metastasize. Some factors that increase the chance for the development of metastases include tumor size larger than 2 cm; location on the ear, lip, or other sites on the head and neck; and history of prior unsuccessful treatment. Any solitary ulcer, lump, wound, or lesion that will not heal and persists for more than 3 weeks should be regarded as cancer until proven otherwise. Although few oral SCCs are detected by clinicians at an early stage, diagnostic aids such as vital staining and molecular markers in tissues and saliva may be implemented. Toluidine blue is a simple, fast, and inexpensive technique that stains the nuclear material of malignant lesions, but not

Differential Diagnosis of Squamous Cell Carcinoma of the Vermilion Border

<table>
<thead>
<tr>
<th>Condition</th>
<th>Characteristic</th>
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<tbody>
<tr>
<td>Herpes simplex labialis</td>
<td>Most common manifestation of recurrent herpes simplex virus type 1, which involves a prodrome of pain or tingling at the site followed by the development of erythematous papules and then by vesiculation; histopathology shows necrotic keratinocytes that result in profound edema and vesiculation as well as characteristic multinucleated giant cells*</td>
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<tr>
<td>SCC</td>
<td>Malignant epithelial tumor that often presents as a shallow ulcer covered by a plaque and most commonly located in sun-exposed areas of the head and neck; may be preceded by the presence of actinic keratoses; malignant keratinocytes are pleomorphic and atypical, resulting in tumors that may be well or poorly differentiated and also can sometimes exhibit basaloid features^2</td>
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<tr>
<td>Bullous oral lichen planus</td>
<td>Rare variant of oral lichen planus that exhibits a clinical and histopathological occurrence of blister formation accompanied by burning and pain; lesions most commonly are seen on the buccal mucosa and lateral margins of the tongue; histopathology resembles the findings observed in cutaneous lichen planus, with the key characteristic of lichenoid inflammation and subepidermal clefting^13</td>
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<tr>
<td>Aphthous ulcer</td>
<td>Clinically presents as multiple, recurrent, round ulcers with erythematous halos; histopathologic appearance is not pathognomonic^11</td>
</tr>
<tr>
<td>Solitary keratoacanthoma</td>
<td>Common cutaneous neoplasm that occurs most often on sun-exposed sites with a histologic pattern resembling SCC; lesion undergoes rapid growth over 4–5 wk but typically regresses spontaneously and only rarely progresses into an invasive SCC; pathology reveals an exophytic-endophytic architecture with a central keratotic horn and glassy keratinocytes^12</td>
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Abbreviation: SCC, squamous cell carcinoma.

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Shave biopsy revealed irregular acanthosis of the epithelium. Many keratinocytes had glassy cytoplasm and there is a brisk lymphohistiocytic inflammatory infiltrate. Perineural and vascular invasion were not identified (A)(H&E, original magnification ×4). Higher-power examination revealed keratinocytes with hyperchromatic nuclei as well as nuclear pleomorphism (B)(H&E, original magnification ×400). Multinucleated giant cells were not identified.
normal mucosa, and may be a worthwhile diagnostic adjunct to clinical inspection.4

Our patient presented with a lesion that clinically looked herpetic, though he reported no prodromal signs of tingling, burning, or pain before the occurrence of the lesion. Due to the persistence of the lesion and lack of response to treatment, a biopsy was indicated. The differential diagnoses include aphthous ulcers, which may occasionally extend on to the vermilion border of the lip and exhibit nondiagnostic histology.5 Bullous oral lichen planus is the least common variant of oral lichen planus, is unlikely to present as a solitary lesion, and is rarely seen on the lips. Histologically, the lesion demonstrated lichenoid inflammation.6 Solitary keratoacanthoma, though histologically similar to SCC, typically presents as a rapidly growing crateriform nodule without erosion or ulceration.7 The differential diagnoses are summarized in the Table.

The patient underwent wide excision with repair by mucosal advancement flap. He continues to be regularly seen in the clinic for monitoring of other skin cancers and is doing well. Clinicians encountering any wound or ulcer that does not show signs of healing should be wary of underlying malignancy and be prompted to perform a biopsy.

REFERENCES