

# Hemorrhagic bullae of the oral mucosa



Karina Paci, BS,<sup>a</sup> Katherine M. Varman, MD,<sup>b</sup> and Christopher J. Sayed, MD<sup>b</sup>  
Chapel Hill, North Carolina

**Key words:** bullous disease; mucous membrane/oral disease and dental; pemphigoid; pemphigus; ulcers.

## INTRODUCTION

Angina bullosa hemorrhagica (ABH) is a rare benign disorder characterized by sudden onset of painless, blood-filled, blisters of the oral cavity that quickly expand and rupture spontaneously within 24 to 48 hours. First reported in 1967,<sup>1</sup> ABH has been noted under other diagnostic terms including *recurrent or traumatic oral hemophlyctenosis* and *benign hemorrhagic bullous stomatitis*.<sup>2</sup> Localization of blisters is usually restricted to the soft palate, yet the buccal mucosa, tongue, and lips may also be involved.<sup>3</sup> Associated symptoms have been noted in some cases, including hoarseness and blood-tinged sialorrhea. Blisters tend to heal without scarring. Most cases occur in adults, ages 50 to 70, with no differentiation in incidence between men or women.<sup>2,4</sup> Because it is infrequently encountered in the clinical setting and sparsely reported in the dermatologic literature, its recognition and diagnosis make it challenging for providers. We report a recent case of ABH in a middle-aged man with idiopathic thrombocytopenia, including its emergent presentation and relevant histopathology.

## CASE

A 45-year-old man presented to clinic with a 4-day history of multiple, tender hemorrhagic bullae of the oral cavity. He reported the first lesion appeared on the left buccal mucosa after he consumed an apple, followed by acute rupture and subsequent bleeding. Two more lesions appeared successively leading to a hospital admission where he was treated empirically with oral clindamycin at a dose of 300 mg 3 times daily and discharged. An additional bulla appeared on the right buccal mucosa the evening before his visit, which was present at the time of the

### Abbreviations used:

ABH: angina bullosa hemorrhagica  
H&E: hematoxylin-eosin



**Fig 1.** A tense hemorrhagic bulla on the buccal mucosa.

examination. Examination found a 1-cm hemorrhagic tense bulla overlying edematous mucosa and a shallow, atrophic erosion with ragged border at the site of the previous bullae on the left buccal mucosa (Fig 1). No other papules, plaques, or ulcers were appreciated in the oropharynx. His medical records showed a recent history of thrombocytopenia, congestive heart failure, and shortness of breath and a medication regimen including aspirin (81 mg/d), losartan, levothyroxine, gabapentin, furosemide, esomeprazole, docusate sodium, and amiodarone. Complete review of systems was otherwise unremarkable. Laboratory test results highlighted a platelet count of 98,000/L (normal range, 150–440  $10^9/L$ ) and a lymphocyte count of 1.4/L (normal range, 1.5–5.0  $10^9/L$ ). Four-millimeter punch biopsy specimens were taken

From the University of North Carolina at Chapel Hill School of Medicine,<sup>a</sup> and the Department of Dermatology, University of North Carolina at Chapel Hill School of Medicine.<sup>b</sup>

Funding sources: None.

Conflicts of interest: None declared.

This article was presented as an E-Poster at the 2016 Summer American Academy of Dermatology Meeting, Boston, Massachusetts.

Correspondence to: Christopher J. Sayed, MD, University of North Carolina School of Medicine, Department of Dermatology, 410

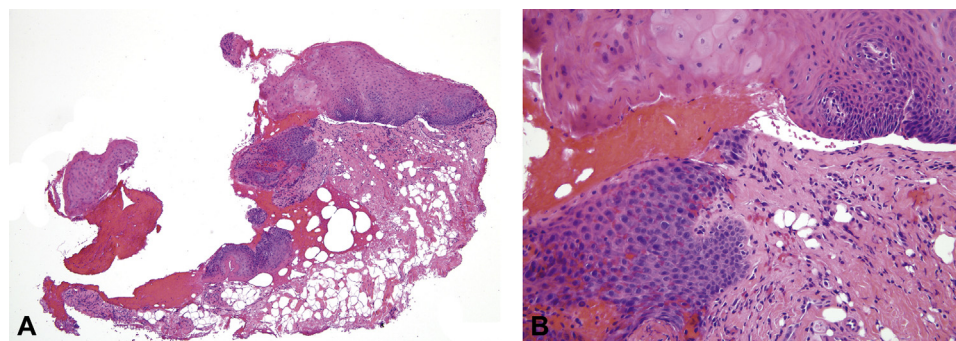
Market Street, Suite 400, CB#7715, Chapel Hill, NC 27516. E-mail: [christopher\\_sayed@med.unc.edu](mailto:christopher_sayed@med.unc.edu).

JAAD Case Reports 2016;2:433-5.

2352-5126

© 2016 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<http://dx.doi.org/10.1016/j.jidcr.2016.09.015>



**Fig 2.** **A**, Punch biopsy from the edge of the bulla. **B**, Punch biopsy specimen at greater specification. (**A** and **B**, H&E stain; original magnifications: **A**, 40 $\times$ ; **B**,  $\times$ 200.)

from the edge of the bulla for hematoxylin-eosin (H&E) staining and from perilesional skin for direct immunofluorescence. Before biopsy, the bullae was aspirated with an 18-gauge needle. Hemostasis was obtained with manual pressure and electrodesiccation. The clinical differential diagnosis included autoimmune blistering disorders, bullous lichen planus, and ABH. H&E staining of a punch biopsy from the oral mucosa found a pauci-inflammatory subepithelial cleft with hemorrhage (Fig 2, *A* and *B*). Direct immunofluorescence mapping of the mucosa was negative, showing no immunoreactants detected using specific antihuman IgG, IgM, IgA, C3, and fibrinogen conjugates. Indirect immunofluorescence of the serum did not detect any autoantibodies. Both the clinical history and histopathologic findings were directly in line with classic reports of ABH.<sup>5</sup> The patient's blisters healed with no scarring. His idiopathic thrombocytopenia remained stable. The patient died of unrelated causes without any recurrences 1 year after his initial presentation.

## DISCUSSION

Diagnosis of ABH highly depends on recognition of clinical features and is often delayed because of its resemblance to other similar-appearing conditions involving oral mucosa. Mucosal biopsies are inconclusive, usually yielding nonspecific findings such as hemorrhagic subepithelial bulla, chronic inflammatory cell infiltrate within the lamina propria,<sup>6,7</sup> and a decrease in elastic network leading to fragility of vessel walls.<sup>6-8</sup> Direct and indirect immunofluorescence consistently show negative results.<sup>3,4</sup>

The cause of ABH is still poorly understood.<sup>9</sup> However, several etiologic factors are identified as potential precipitating conditions, such as arterial hypertension, diabetes mellitus, long-term inhaled steroid use, and masticatory trauma.<sup>2,8,10</sup> Several isolated cases of drug-induced thrombocytopenia associated with ABH-like lesions have been

reported,<sup>11</sup> but it seems unlikely that our patient's stable idiopathic thrombocytopenia contributed to the development of his ABH given that it is typical for patients with ABH to have platelet counts and coagulation test results within normal range. A few reports of ABH showed a significant decrease in elastic fibers in microscopic sections of affected mucosa, thus, proposing that poor anchorage of small blood vessels could explain the appearance of hemorrhagic lesions in response to minor trauma.<sup>12</sup> Spontaneous ABH with no notable predispositions was noted to occur in up to 47% of patients reporting related clinical signs, including bullous blisters appearing most often on the soft palate and some in the buccal and lingual regions.<sup>3</sup>

The differential diagnosis is broad when assessing ABH because of its nonspecific symptoms and clinical presentation. It includes mucous membrane pemphigoid, epidermolysis bullosa acquisita, linear IgA dermatosis, erythema multiforme, oral amyloidosis, pemphigus, dermatitis herpetiformis, and bullous lichen planus.<sup>2,3,5,13</sup> Many of these conditions differ histologically from ABH and tend to be associated with immunologic and autoimmune abnormalities. Hemorrhagic blisters can also arise in hematologic disorders, such as leukemia, vasculitis,<sup>14</sup> and thrombocytopenia,<sup>2</sup> but normal blood count and hemostatic function help distinguish between them. No treatment is necessary, although active blisters can be gently ruptured to prevent further separation of the epithelium, followed by the use of antibacterial mouthwash, chlorhexidine gluconate, to prevent infection.<sup>3</sup> Ascorbic acid/citroflavonoid (200 mg twice daily) has been reported to possibly prevent recurrences.<sup>2</sup> In one atypical case, intubation was required because of excessive bleeding from a large bulla that resulted in airway compromise.<sup>15</sup>

ABH is a rare yet benign condition affecting middle-age to elderly adults, both men and women

equally. Although several case series describing ABH do exist within dental and oral surgery research, relatively few reports exist within dermatologic literature. Our case emphasizes the need for dermatologists specifically to consider ABH in the differential diagnosis involving oral cavity blisters, as previous reports suggest knowledge of the condition is limited in the field.

#### REFERENCES

1. Badham NJ. Blood blisters and the oesophageal cast. *J Laryngol Otol*. 1967;81(7):791-803.
2. Grinspan D, Abulafia J, Lanfranchi H. Angina bullosa hemorrhagica. *Int J Dermatol*. 1999;38(7):525-528.
3. Stephenson P, Lamey PJ, Scully C, Prime SS. Angina bullosa hemorrhagica: clinical and laboratory features in 30 patients. *Oral Surg Oral Med Oral Pathol*. 1987;63(5):560-565.
4. Deblauwe BM, Van der waal I. Blood blisters of the oral mucosa (angina bullosa hemorrhagica). *J Am Acad Dermatol*. 1994;31(2 Pt 2):341-344.
5. Beguerie JR, Gonzalez S. Angina bullosa hemorrhagica: report of 11 cases. *Dermatol Reports*. 2014;6(1):5282.
6. Hopkins R, Walker DM. Oral blood blisters: angina bullosa hemorrhagica. *Br J Oral Maxillofac Surg*. 1985;23(1):9-16.
7. Edwards S, Wilkinson JD, Wojnarowska F. Angina bullosa hemorrhagica—a report of three cases and review of the literature. *Clin Exp Dermatol*. 1990;15(6):422-424.
8. Guillot B. Skin reactions to inhaled corticosteroids. Clinical aspects, incidence, avoidance, and management. *Am J Clin Dermatol*. 2000;1(2):107-111.
9. Yamamoto K, Fujimoto M, Inoue M, Maeda M, Yamakawa N, Kiritani T. Angina bullosa hemorrhagica of the soft palate: report of 11 cases and literature review. *J Oral Maxillofac Surg*. 2006;64(9):1433-1436.
10. High AS, Main DM. 'Angina bullosa hemorrhagica: a complication of long-term steroid inhaler use'. *Br Dent J*. 1988;165(10):357.
11. Abhinav C, Mahajan VK, Mehta KS, Chauhan PS. Angina bullosa hemorrhagica-like lesions: a rare presentation of drug-induced thrombocytopenia. *Int J Dermatol*. 2015;54(7):819-822.
12. Higgins EM, Du vivier AW. Angina bullosa hemorrhagica—a possible relation to steroid inhalers. *Clin Exp Dermatol*. 1991;16(4):244-246.
13. Domínguez JD, Rodríguez-peralto JL, Iglesias L. Recurrent oral blood blisters. *Arch Dermatol*. 1999;135(5):593-594, 596-597.
14. Vaillant L, Fontès V. [Bullous diseases of the oral mucosa]. *Rev Prat*. 2002;52(4):385-388.
15. Pahl C, Yarrow S, Steventon N, Saeed NR, Dyar O. Angina bullosa hemorrhagica presenting as acute upper airway obstruction. *Br J Anaesth*. 2004;92(2):283-286.