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# **Multiple Intraoral Ulcerations**

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The following Case Challenge is provided in conjunction with the UT Health San Antonio School of Dentistry faculty.

A 68-year-old Hispanic female presents with numerous intraoral ulcerations involving the lower labial mucosa, right and left lateral tongue, and ventral tongue.

After you have finished reviewing the available diagnostic information, make the diagnosis.

# **Diagnostic Information**

#### **History of Present Illness**

Mrs. Cabello is a 68-year-old Hispanic female who presents to your office for a new patient examination. She states that she last visited a dentist approximately four years ago. She relates no acute dental problems but complains of significant pain of several months duration involving multiple areas of her mouth.

#### **Medical History**

- Adverse drug effects: none
- Medications: flecainide, Pravachol, vitamin D, Centrum silver
- Pertinent medical history: paroxysmal supraventricular tachycardia, hypercholesterolemia, osteopenia
- Pertinent family history: mother and father deceased
- Social history: previous history of tobacco use
  discontinued 30 years ago; does not drink alcohol; denies recreational drug use

## **Clinical Findings**

Extraoral examination is within normal limits. No skin lesions are noted. Intraoral examination reveals multiple irregularly shaped ulcerations involving the left side of the lower labial mucosa, the left and right lateral tongue, and the ventral tongue (Figures 1-2). An incisional biopsy from the right lateral tongue is performed and the tissue submitted for histopathologic examination.



**Figure 1.** Irregular ulceration on left side of lower labial mucosa and an area of hemorrhage on the right side of the lower labial mucosa.



**Figure 2.** Multiple irregular ulcerations on the right lateral and ventral tongue.

#### **Histopathologic Findings**

An incisional biopsy reveals acantholysis in the lower levels of the epithelium. The basal epithelial cells are attached to the underlying connective tissue (Figure 3). Individual squamous epithelial cells (Tzanck cells) are noted in the intraepithelial blister (Figure 4). Direct immunofluorescence reveals the deposition of IgG and C3 in a netlike pattern around individual squamous epithelial cells.



**Figure 3.** High power histologic image of a mucosal soft tissue fragment consisting of stratified squamous surface epithelium exhibiting acantholysis. Basal epithelial cells are attached to the underlying connective tissue.



**Figure 4.** High power histologic image showing acantholysis and Tzanck cells.

# **Select Diagnosis**

### Can you make the diagnosis

A 68-year-old Hispanic female presents with numerous intraoral ulcerations involving the lower labial mucosa, right and left lateral tongue, and ventral tongue.





## Select the Correct Diagnosis

- A. Mucous membrane pemphigoid
- B. Pemphigus vulgaris
- C. Erythema multiforme
- D. Herpetiform aphthous ulcerations

## Mucous membrane pemphigoid

#### Choice A. Sorry, this is not the correct diagnosis.

Mucous membrane pemphigoid (MMP) is a chronic vesiculobullous disease that predominantly affects the mucous membranes. The disease represents a type II hypersensitivity reaction in which autoantibodies are made against antigens in the basement membrane. As a result of this antigen-antibody interaction, the entire surface mucosa separates from the underlying fibrous connective tissue leading to the formation of blisters followed by ulcerations. Most patients with MMP are adults and a marked female predilection is noted. Any mucosal surface may be affected. Oral mucosal involvement is common on the gingiva and is known clinically as desquamative gingivitis. Desquamative gingivitis is fiery red and painful; these same clinical features can be seen in erosive lichen planus and pemphigus vulgaris.<sup>1</sup> In addition to mucosal involvement, patients with MMP should be evaluated for ocular disease. The ocular mucosa may demonstrate fibrous adhesions between the conjunctiva (symblepharon), entropion, trichiasis, and corneal opacification leading to blindness.<sup>2</sup> Histopathologic examination reveals a subepithelial separation at the level of the basement membrane and an acute and chronic inflammatory infiltrate in the underlying connective tissue. Direct immunofluorescence (DIF) reveals the linear deposition of IgG and C3 at the level of the basement membrane. Indirect immunofluorescence is of limited diagnostic value since circulating antibodies levels in the serum are low. Treatment consists of topical and systemic corticosteroids.<sup>3</sup> For patients who cannot tolerate corticosteroids, tetracycline and niacinamide may be used.<sup>4</sup> Patients with desquamative gingivitis need to maintain meticulous oral hygiene for therapy to be successful. The prognosis is generally good. The histopathologic findings in this case do not support this diagnosis.

Please re-evaluate the information about this case.

# **Pemphigus vulgaris**

#### Choice B. Congratulations! You are correct.

Pemphigus vulgaris (PV) is a chronic vesiculobullous disease that affects the skin and mucous membranes. Similar to mucous membrane pemphigoid, PV represents a type II hypersensitivity reaction. However, in PV autoantibodies are formed against the intercellular cement substance (desmoglein 1 and 3) that holds individual squamous epithelial cells together. Involvement of the oral mucosa often occurs before skin lesions arise. Pemphigus vulgaris is typically diagnosed in adults and no significant sex predilection is noted. Due to the superficial nature of the intraepithelial separation, the blisters formed in PV are extremely fragile and quickly evolve into ulcerations. Oral examination reveals multiple areas of painful ulcerations surrounded by erythema.<sup>1,3,5</sup> Involvement of the gingiva leads to desquamative gingivitis.<sup>6</sup> Histopathologic examination reveals intraepithelial separation (acantholysis) and the formation of individual squamous epithelial cells (Tzanck cells) floating in the blister fluid. An acute and chronic inflammatory infiltrate in seen in the underlying connective tissue. Direct immunofluorescence (DIF) reveals a chicken-wire pattern of deposition of IgG and C3 around individual squamous epithelial cells. Indirect immunofluorescence is useful for monitoring treatment effectiveness since circulating autoantibodies are commonly seen in the serum. Pemphigus vulgaris is treated with systemic corticosteroids and immunosuppressive drugs.<sup>3</sup> The disease tends to require long-term therapy since recurrence is common.

# **Erythema multiforme**

#### Choice C. Sorry, this is not the correct diagnosis.

Erythema multiforme (EM) is blistering disease of acute onset that affects the skin and mucous membranes. The exact etiology is unknown but the disease appears to be a hypersensitivity reaction triggered by an infectious disease or exposure to certain drugs. Most cases arise in young adults and a female sex predilection is noted. Depending upon severity, three clinical patterns are noted: EM minor, EM major (Stevens-Johnson syndrome), and toxic epidermal necrolysis (TEN). Cutaneous manifestations include macules, papules, or vesicles. Larger bullae may be seen. Classic "target" lesions are noted in which a red macule or papule is seen with a pale eroded or vesicular center. Oral lesions consist of erosions and ulcerations with surrounding erythema. Hemorrhagic crusting of the lips is common. In SJS and TEN, involvement of the ocular and genital mucosa also occurs. Histopathologic findings are nonspecific and include intraepithelial or subepithelial vesicle formation, necrosis of basal keratinocytes, and a perivascular inflammatory infiltrate in the underlying connective tissue. Treatment consists of identifying and removing the causative factor along with topical and systemic corticosteroids. Erythema multiforme minor is self-limiting and typically resolves in several weeks. If not diagnosed quickly and treated appropriately, SJS and TEN may be life threatening.<sup>3,7</sup> The clinical features and histopathologic findings in this case do not support this diagnosis.

Please re-evaluate the information about this case.

# Herpetiform aphthous ulcerations

#### Choice D. Sorry, this is not the correct diagnosis.

Herpetiform aphthous ulcerations are an uncommon but unique variant of aphthous ulceration. These ulcerations are the least common type of aphthous ulceration. The cause of aphthous ulcerations is unknown but the disease is thought to represent a T-cell mediated immunologic abnormality. Precipitating factors include trauma, stress, hormonal changes, and certain systemic diseases. Herpetiform aphthous ulcerations present as numerous tiny (1-2 mm) ulcerations. Unlike minor and major aphthous ulcerations, the herpetiform variant may occur on keratinized or non-keratinized mucosa and tends to resemble the ulcerations seen in primary herpetic gingivostomatitis. However, unlike primary herpetic gingivostomatitis, patients with herpetiform aphthous ulcerations do not demonstrate systemic symptoms of infection. A diagnosis is typically made based on the characteristic clinical findings combined with a lack of systemic symptoms.<sup>8</sup> Histopathologic examination reveals a non-specific ulceration and a mixed inflammatory infiltrate in the underlying connective tissue. Treatment consists of topical corticosteroids and the prognosis is good although recurrences occur.<sup>3</sup> The clinical features and histopathologic findings in this case do not support this diagnosis.

Please re-evaluate the information about this case.

## References

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Anne Cale Jones graduated from the University of Alabama in 1981 with the Bachelor of Science degree (Magna Cum Laude) in Natural Sciences. She received a Doctor of Dental Surgery degree (Magna Cum Laude) from the Medical College of Virginia, Virginia Commonwealth University in 1986. Following a three-year residency program in Oral and Maxillofacial Pathology at Booth Memorial Medical Center in Queens, New York, Dr. Jones joined the faculty at the University of Florida, College of Dentistry. In 1998, she became a faculty member at The

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