Acute Onset Painful Oral Ulcerations

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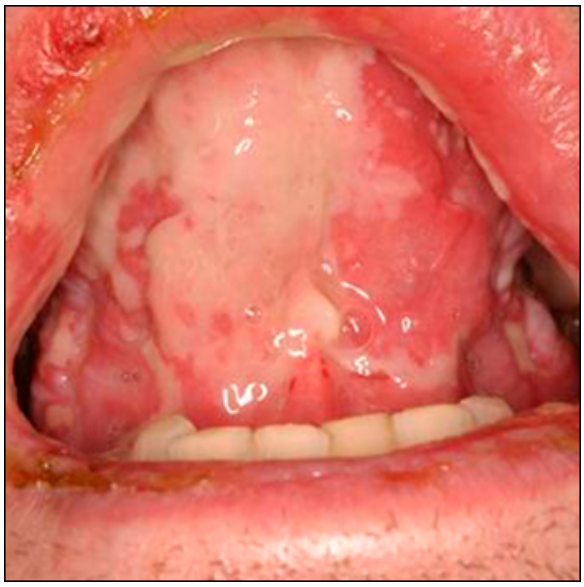
Online Case: *www.dentalcare.com/en-us/professional-education/case-challenges/case-challenge-067*



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

Len is 54-year-old white male who presents with painful mouth ulcers.

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

Diagnostic Information

History of Present Illness

Len is a 54-year-old white male who reports to your office in great distress. For the past 4 days he has been suffering from painful, widespread ulcerations affecting his mouth. He states is unable to eat and has been drinking nutritional protein shakes to get by. He woke up with mouth sores 4 days ago. He denies any constitutional signs and symptoms such as fever, malaise or fatigue. He denies having any rashes or ulcers affecting his skin or any other mucosal sites such as his eyes and genitalia. He does note a recent medication change for his osteoarthritis management from ibuprofen to naproxen about 2 weeks ago.

Medical History

- Adverse drug effects: none
- Medications: aripiprazole 5 mg qd, duloxetine 60 g qd, naproxen 500 mg bid, hydrochlorathiazide 25 mg qd
- Pertinent medical history: depression x 10 years, hypertension x 15 years, osteoarthritis x 20 years
- Pertinent family history: paternal - depression, non-fatal MI age 61; maternal - DM type 2; siblings - 2 healthy younger sisters
- Social history: denies tobacco use, 2-3 mixed drinks on weekends x 35 years, marijuana use while in college

Clinical Findings

Extraoral examination reveals normal TMJ function, no facial muscle tenderness, and no cervical lymphadenopathy. The labial mucosa exhibits a serohemorrhagic weep with crusting (Figures 1-2). Intraoral examination reveals wide-spread areas of bullae with mucosal sloughing affecting virtually all nonkeratinized tissues and palate (Figures 2-6). An incisional biopsy was performed on the right commissural area and the specimen was submitted for histologic assessment.function. An incisional biopsy was performed and the specimen was submitted for histologic assessment.

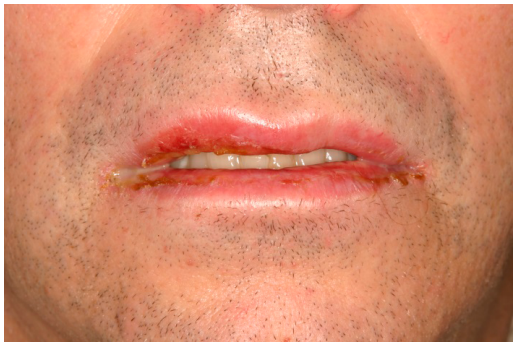


Figure 1. Weeping and crusting on the lip commissures.

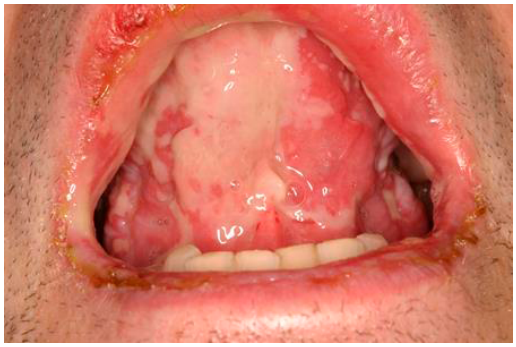


Figure 2. Bullae ventral aspect of the tongue and weeping and crusting on the upper and lower lip vermilion.

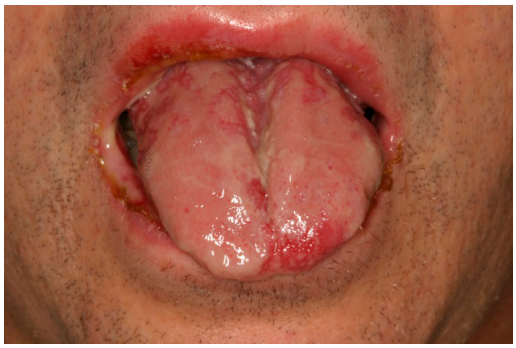


Figure 3. Bullae on the dorsal aspect of the tongue.

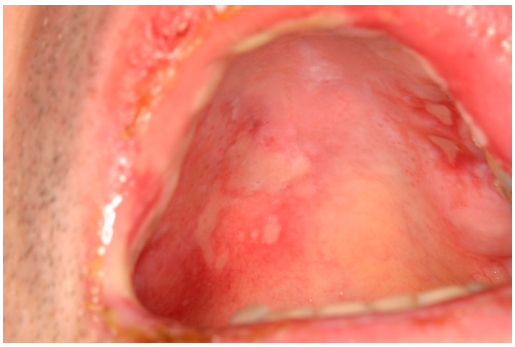


Figure 4. Multiple bullae affecting the hard palate.

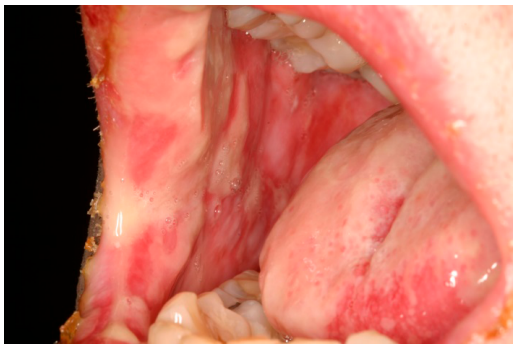


Figure 5. Bullous eruption on the right side commissure and buccal mucosa.

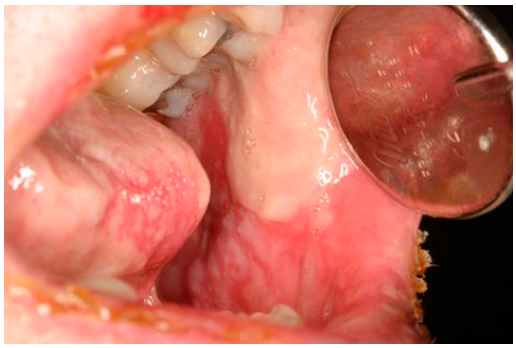


Figure 6. Bullous eruption on the left side commissure and buccal mucosa.

Histopathologic Findings

The biopsy shows inflamed oral mucosa consisting of reactive stratified squamous surface epithelium with subjacent fibrovascular connective tissue. The interface to perivascular inflammatory infiltrate consists predominantly of lymphocytes with admixed neutrophils and eosinophils. There is superficial stromal edema with areas of subepithelial and intraepithelial vesiculation. The basal portion of the epithelium displays scattered necrotic keratinocytes.

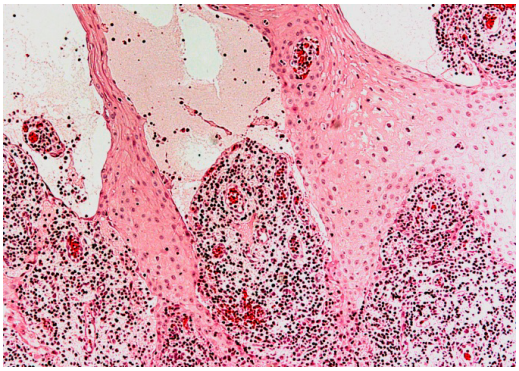


Figure 7. Low-power histologic image showing a dense superficial mixed interface inflammatory infiltrate with associated sub and intraepithelial vesicle formation.

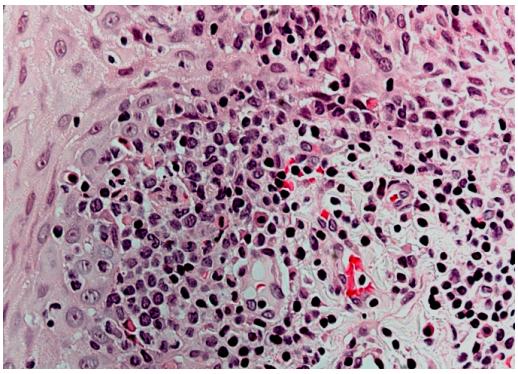
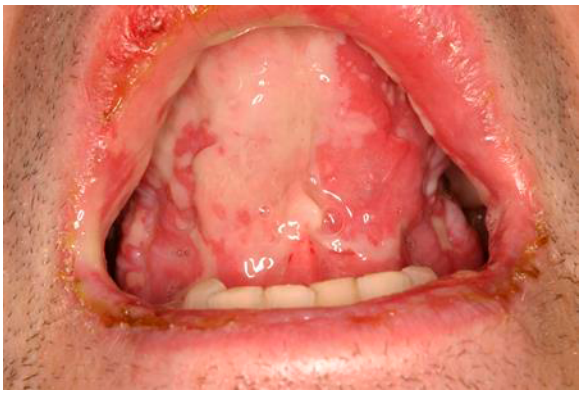


Figure 8. High-power histologic image showing an interface lymphocytic inflammatory infiltrate with basal epithelial disruption, exocytosis, and focal necrotic keratinocytes.

Select Diagnosis

Can you make the diagnosis

Len is 54-year-old white male who present with painful mouth ulcers.



Select the Correct Diagnosis

A. Pemphigus vulgaris
B. Herpetic gingivostomatitis
C. Erythema multiforme
D. Mucous membrane pemphigoid

Pemphigus vulgaris

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

Pemphigus vulgaris (PV) is a chronic vesiculobullous disease that affects the skin and mucous membranes. The disease predominantly occurs in adults and no sex predilection is noted. Like mucous membrane pemphigoid (MMP), PV represents a type II hypersensitivity reaction. Antibodies (usually IgG) are formed against the intercellular cement substance that holds individual squamous epithelial cells together. C3 is also activated and localized to intercellular areas. The subsequent separation of the individual squamous epithelial cells is known as acantholysis. Any oral mucosal surface may be affected. Because of the fragility of the oral mucosa, blisters are rarely seen. Patients usually present with painful erosions or ulcerations or desquamative gingivitis.[1,2] A positive Nikolsky sign (the ability to induce a blister with applied pressure is also seen) is also characteristic. Oral mucosal involvement typically precedes skin manifestations. Erosions and blisters may be seen on any cutaneous surface. Histopathologic examination reveals intraepithelial separation between individual squamous epithelial cells (acantholysis). The blisters that are created contain individual epithelial cells (Tzanck cells). The basal layer is attached to the underlying connective tissue which contains an acute and chronic inflammatory infiltrate. Direct immunofluorescence demonstrates the intercellular deposition of IgG, IgA, IgM, and/or C3 in a chicken-wire pattern. Indirect immunofluorescence utilizing the patient's serum will often contain circulating antibodies and is used to monitor disease progression. Treatment consists of systemic corticosteroids with or without immunosuppressive drugs. With appropriate therapy the prognosis is good but relapse is common.[2,3] The histopathologic findings in this case, along with the ocular findings, do not support this diagnosis.

Please re-evaluate the information about this case.

Herpetic gingivostomatitis

Choice B. Sorry, this is not the correct diagnosis.

Herpes simplex virus type 1 is a common infection usually transmitted during childhood via nonsexual contact, with peak prevalence between 2-3 years of age.[1,4] The vast majority of cases result in asymptomatic disease. Adult cases do occur and are more likely to develop clinical disease. Classical clinical disease is termed “herpetic gingivostomatitis” and is characterized by a prodrome of fever, pharyngitis, fever, and cervical lymphadenopathy, followed in a few days by an acute generalized oral eruption. The oral lesions initially present as multiple discrete vesicles which often coalesce to form larger shallow erosions and ulcerations. Painful gingival involvement is common and manifests as intense erythema and edema with pinpoint erosions or ulcerations.[1] Histologic findings include in intraepithelial acantholysis and epithelial ballooning degeneration, condensation of chromatin at the cellular periphery, and the formation of multinucleated epithelial cells from fusion.[1] Herpetic gingivostomatitis typically resolves within 2 weeks and management is focused on relieving pain (analgesics, topical soothing rinses), ensuring adequate nutrition / hydration (hydration, liquid dietary supplements), and preventing secondary infection. Antiviral therapy is only effective if provided within the first 3 days of symptom onset and generally reserved for patients with some form of immunocompromise.[4] The histopathologic findings in this case do not support this diagnosis.

Please re-evaluate the information about this case.

Erythema multiforme

Choice C. Congratulations! You are correct.

Erythema multiforme (EM) represents a clinical spectrum of immune mediated disorders that affect the skin and/or mucous membranes.[5] In increasing order of severity EM may be further categorized as: EM minor (EMm), EM major (EMM), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN). The etiopathogenesis remains complex with milder forms frequently associated with an infectious agent trigger (usually herpes simplex virus or Mycoplasma pneumoniae) and more severe presentations such as SJS and TEN being associated with a toxin or drug exposure.[5] As a consequence, many authorities consider the milder forms of EM to be separate entities from the major forms (SJS and TEN). Cutaneous involvement, when present, is variable and ranges from highly characteristic symmetric, "bull's-eye" target lesions to extensive sloughing. The histopathologic findings include subepithelial or intraepithelial vesiculation with basal keratinocyte necrosis and a mixed inflammatory infiltration, often in a perivascular pattern.[1] The histopathologic findings are nonspecific and the diagnosis of EM is one of exclusion, after ruling out other vesiculobullous conditions. Immediate therapy for EM is essentially supportive and may require hospitalization for severe disease. Long-term control of EM is centered on identifying potential triggers. The prognosis varies with a reported mortality rate up to 5% and 35% for SJS and TEN, respectively.[5] The current case was attributed to his recent switching to the NSAID naproxen and, upon discontinuation, the lesions cleared within two weeks.

Mucous membrane pemphigoid

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

Mucous membrane pemphigoid (MMP) is a chronic vesiculobullous disease that affects any mucous membrane. The disease occurs in adults and a female sex predilection is noted. Mucous membrane pemphigoid represents a type II hypersensitivity reaction and antibodies (usually IgG) are produced against components of the basement membrane causing the surface epithelium to detach from the underlying connective tissue. C3 is also activated and localized to the basement membrane area. Although any oral mucosal surface may be affected, MMP most commonly involves the attached gingiva where it presents as desquamative gingivitis. Desquamative gingivitis is characterized by erythematous, painful gingiva.[6] This clinical appearance may also be seen in erosive lichen planus and pemphigus. Other clinical manifestations include blisters, erosions, and ulcerations. A positive Nikolsky sign is noted - the ability to induce a blister with applied pressure. Eye involvement occurs in 25% of patients and is most commonly seen as symblepharon - fibrous adhesions between the bulbar and palpebral conjunctiva.[1,7] Histopathologic examination reveals a split at below the basement membrane between the surface epithelium and the underlying connective tissue. Direct immunofluorescence demonstrates the linear deposition of IgG, IgA, IgM, and/or C3 at the level of the basement membrane. Indirect immunofluorescence is not useful since circulating antibodies are rare.[1] Treatment consists of topical or systemic corticosteroids, or niacinamide and tetracycline.[8] Gingival involvement requires meticulous oral hygiene. All patients with MMP should be evaluated by an ophthalmologist on a yearly basis. The histopathologic findings in this case do not support this diagnosis.

Please re-evaluate the information about this case.

References

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Dr. Michaell A. Huber is a Professor of Oral Medicine, Department of Comprehensive Dentistry, the UTHSCSA School of Dentistry. He received his DDS from the UTHSCSA in 1980 and a Certificate in Oral Medicine from the National Naval Dental Center, Bethesda, Maryland in 1988. He is certified by the American Board of Oral Medicine. Dr. Huber served as Graduate Program Director in Oral Medicine at the National Naval Dental Center, Bethesda, Maryland. In addition he served as Specialty Leader for Oral Medicine to the Surgeon General of the United States Navy, Washington, DC; and Force Dental Officer, Naval Air Force Atlantic, Norfolk, Virginia.

Since joining the faculty in 2002, Dr. Huber has been teaching both pre-doctoral and graduate dental students at the UTHSCA School of Dentistry. In 2014, he was awarded the UTHSCSA Presidential Teaching Excellence Award. He is a Past President of the American Academy of Oral Medicine. Dr. Huber has spoken before many local, state, and national professional organizations. He has published over 70 journal articles, book chapters, and online postings.

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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 University of Texas Health Science Center at San Antonio. She is currently a Distinguished Teaching Professor in the Department of Pathology and is board certified by the American Board of Oral and Maxillofacial Pathology.

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