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Eosinophilic Ulcer

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Updated: May 18, 2007

Introduction

Background

Ulcerations of the oral mucosa are relatively common clinical findings. Oral ulcers may be related to the following:

- Trauma (eg, physical, chemical, thermal)
- Aphthous stomatitis
- Infectious agents (eg, viral, bacterial, fungal, mycobacterial)
- Contact or systemic allergy (eg, allergy to medication)
- Neoplastic disease
- Systemic diseases (eg, hematologic and autoimmune disorders, vasculitides)

Traumatic oral ulcers tend to have a sudden onset and usually heal within a few days or weeks, often without clinical intervention. Occasionally, ulcers may persist for an extended time. Eosinophilic ulcers (EUs) are included in this group of nonhealing traumatic ulcers. These lesions are microscopically characterized by a diffuse, pseudoinvasive, mixed inflammatory reaction that includes large mononuclear cells, numerous eosinophils, and T cells. The cellular infiltrate often extends deep into the submucosa to involve the underlying skeletal muscle.

Riga-Fede disease is a form of EU that develops in infants and usually occurs on the anterior ventral side of the tongue.¹ The distinctive, self-limiting ulcerations develop as a result of chronic mucosal trauma from adjacent anterior primary teeth and usually occur in association with breastfeeding.

Pathophysiology

In most patients with EUs, trauma is the etiologic factor, and the apparent source of irritation is easily identified. This mechanism is further supported by findings in rats in which microscopically similar lesions were experimentally induced by chronic mechanical injury.² However, in a number of studies, patients with multiple synchronous or metachronous lesions at different mucosal sites were identified. The source of the chronic irritation also is not evident in a number of patients; therefore, factors other than trauma may be involved in the pathogenesis of these ulcers. EU has also been reported to occur in association with medication use; therefore, EU also may represent an unusual manifestation of a drug reaction.

Several investigators have proposed that EUs develop as a result of a T-cell-mediated immune response. In certain predisposed individuals, recurrent trauma may lead to the alteration of tissue antigens or ingress of unknown factors (eg, viral particles, toxic microbial products), which result in a hypersensitivity or allergic reaction. However, neither virally altered cells nor viral DNA is identified in biopsy specimens of typical EU.

Tissue eosinophilia is not uncommonly associated with T-cell-mediated immune reactions. Activated T lymphocytes produce a variety of lymphokines that are involved in eosinophilic maturation and act as eosinophil-chemotactic factors. Damage and degeneration of mucosal tissues may be due to a proliferation of cytotoxic T cells or toxic products released by degranulating eosinophils. Constituents of eosinophil secretory granules include a number of highly cytotoxic proteins, including eosinophil cationic protein, major basic protein, and eosinophil-derived neurotoxin.

One study demonstrated that, in most EU, the synthesis of transforming growth factor-alpha and transforming growth factor-beta is not increased in infiltrating eosinophils.³ This observation is in contrast to that of the animal wound-healing model, in which eosinophils that express transforming growth factor are typically recruited to healing tissue sites. These findings may help explain the delayed healing that is characteristic of EU.

EU, tumorlike eosinophilic granuloma of the skin, and transient eosinophilic nodulomatosis have been suggested to represent a mucocutaneous reaction pattern⁴; thus, all may share a common pathogenesis.

Frequency

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Traumatic oral ulcers tend to have a sudden onset and usually heal within a few days or weeks, often without clinical intervention. Occasionally, ulcers may persist for an extended time. Eosinophilic ulcers (EUs) are included in this group of nonhealing traumatic ulcers. These lesions are microscopically characterized by a diffuse, pseudoinvasive, mixed inflammatory reaction that includes large mononuclear cells, numerous eosinophils, and T cells. The cellular infiltrate often extends deep into the submucosa to involve the underlying skeletal muscle.

Riga-Fede disease is a form of EU that develops in infants and usually occurs on the anterior ventral side of the tongue.¹ The distinctive, self-limiting ulcerations develop as a result of chronic mucosal trauma from adjacent anterior primary teeth and usually occur in association with breastfeeding.

Pathophysiology

In most patients with EUs, trauma is the etiologic factor, and the apparent source of irritation is easily identified. This mechanism is further supported by findings in rats in which microscopically similar lesions were experimentally induced by chronic mechanical injury.² However, in a number of studies, patients with multiple synchronous or metachronous lesions at different mucosal sites were identified. The source of the chronic irritation also is not evident in a number of patients; therefore, factors other than trauma may be involved in the pathogenesis of these ulcers. EU has also been reported to occur in association with medication use; therefore, EU also may represent an unusual manifestation of a drug reaction.

Several investigators have proposed that EUs develop as a result of a T-cell–mediated immune response. In certain predisposed individuals, recurrent trauma may lead to the alteration of tissue antigens or ingress of unknown factors (eg, viral particles, toxic microbial products), which result in a hypersensitivity or allergic reaction. However, neither virally altered cells nor viral DNA is identified in biopsy specimens of typical EU.

Tissue eosinophilia is not uncommonly associated with T-cell–mediated immune reactions. Activated T lymphocytes produce a variety of lymphokines that are involved in eosinophilic maturation and act as eosinophil-chemotactic factors. Damage and degeneration of mucosal tissues may be due to a proliferation of cytotoxic T cells or toxic products released by degranulating eosinophils. Constituents of eosinophil secretory granules include a number of highly cytotoxic proteins, including eosinophil cationic protein, major basic protein, and eosinophil-derived neurotoxin.

One study demonstrated that, in most EU, the synthesis of transforming growth factor-alpha and transforming growth factor-beta is not increased in infiltrating eosinophils.³ This observation is in contrast to that of the animal wound-healing model, in which eosinophils that express transforming growth factor are typically recruited to healing tissue sites. These findings may help explain the delayed healing that is characteristic of EU.

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Frequency

United States

EUs are not uncommon; however, they are infrequently reported in the literature. The frequency with which these lesions develop is unknown.

Mortality/Morbidity

- Although certain lesions may behave aggressively, overall, these ulcers do not cause significant morbidity.
- Occasionally, lesions may demonstrate atypical histologic features. They have been misdiagnosed as lymphoma, and unnecessary radical treatment can result.

Sex

- The sex prevalence varies from study to study; however, no overall sex predilection is apparent.

Age

- EUs develop in individuals of all ages, ranging from infants to those aged 92 years.
- The mean patient age at onset is 46 years.
- Riga-Fede disease typically is seen in children aged 1 week to 1 year.

Clinical

History

- The most common complaint is that of an asymptomatic or mildly tender, solitary, nonhealing ulcer of variable duration.
- The lesion may be present for as short as 1 week or 12 months or longer.
- Patients with early ulcers often report pain and severe discomfort.
- Patients may have a history of trauma to the affected area.
- Depending on the location of the ulcer, other signs and symptoms may include dysphagia, odynophagia, dysphonia, and dyspnea.
- Occasionally, patients may present with a history of recent weight loss.
- Infants with Riga-Fede disease often experience discomfort while breastfeeding, and they may fail to thrive in the postnatal period.

Physical

- Clinical appearance
 - EU typically presents as an irregular, solitary ulcer with a fibrinous membrane on the surface. A zone of erythema surrounds the ulcer.
 - The margins of the lesion are often raised and usually indurated.
 - Purulence emanating from the ulcer may be noted.
 - EUs may be a few millimeters to as large as 7-8 cm in greatest dimension.
 - In rare reports, multiple synchronous or metachronous lesions have been identified.
 - Occasional ulcers may be macular, whereas others may present as nonspecific erythroplakic or leukoplakic lesions.
 - In rare cases, an EU may present as an elevated, smooth mass that is free of ulceration; however, biopsy reveals the underlying, characteristic, invasive cellular proliferation. In some of these cases, the overlying epithelium may have regenerated without resolution of the underlying inflammation.
- Mucosal sites
 - Any mucosal surface can be affected; however, the tongue is the most common location, accounting for 60% of reported cases.
 - The lateral and dorsal surfaces are usually affected because these are the areas most often traumatized.
 - Lesions on the ventral surface of the tongue more commonly are observed in infants because of contact with the adjacent mandibular incisors during breastfeeding.
 - The dorsal surface of the tongue may also be affected in infants because of irritation associated with maxillary incisors.
 - The buccal mucosa and mucobuccal fold are also particularly susceptible to ulceration; lesions in these locations account for 24% of reported cases.
 - EUs have also been reported (in decreasing order of frequency) on the lips, gingiva, palate, floor of the mouth, and retromolar area.

- In extremely rare cases, cervical lymphadenopathy is reported.

Causes

- Common causes of oral trauma include the following:
 - Self-inflicted injury in which the patient accidentally or deliberately traumatizes the mucosa
 - Injury due to sharp-edged teeth or food
 - Injury due to neonatal or natal teeth (Riga-Fede disease)
 - Toothbrush abrasion
 - Injury due to ill-fitting dentures
 - Injury due to orthodontic or occlusal appliances
 - Iatrogenic injuries (eg, those that occur during dental procedures, such as anesthetic necrosis that occurs during intubation for surgery)
 - Injuries due to accidents
- Certain patients may be inherently predisposed to the development of EUs, although this factor remains controversial.
- The role of drug reactions, if any, is unclear.
- Medical conditions or therapeutic regimens that predispose an individual to immune suppression may also delay healing.

Differential Diagnoses

Angiolymphoid Hyperplasia with Eosinophilia
 Cancers of the Oral Mucosa
 Chronic Granulomatous Disease
 Contact Dermatitis, Allergic
 Contact Dermatitis, Irritant
 Cutaneous Tuberculosis
 Kimura Disease
 Langerhans Cell Histiocytosis
 Metastatic Neoplasms to the Oral Cavity
 Necrotizing Sialometaplasia

Noncandidal Fungal Infections of the Mouth
 Oral Manifestations of Drug Reactions
 Oral Manifestations of Systemic Diseases
 Oral Pyogenic Granuloma
 Sarcoidosis
 Squamous Cell Carcinoma
 Syphilis
 Traumatic Ulcers
 Viral Infections of the Mouth
 Wegener Granulomatosis

Other Problems to Be Considered

Noma (necrotizing stomatitis)

Atypical herpes stomatitis (in patients who are immunocompromised)

Workup

Procedures

- The clinical presentation and history often suggest the cause and nature of EUs; however, many cases can resemble ulcerative squamous cell carcinoma. However, if the origin of the lesion is not obvious or if EU does not respond to conservative therapy, biopsy under local anesthesia is indicated.
- For small lesions, excisional biopsy may be performed; however, incisional biopsy is recommended for larger ulcers.
- In general, a biopsy specimen of an eroded or ulcerated area should include a portion of the adjacent intact epithelium.

Histologic Findings

Microscopic sections typically show ulcerated stratified squamous epithelium with underlying granulation tissue characterized by an invasive, dense, mixed cellular infiltrate composed mainly of sheets of large mononuclear cells with pale nuclei and numerous eosinophils. The eosinophils, including many cells that show evidence of degranulation, usually infiltrate deep into the subjacent skeletal muscle, dissecting through and separating the muscle fibers. Degenerating muscle, interfascicular fibrosis, and regenerative myocytes may be identified.

The adjacent surface epithelium may be normal or hyperplastic and occasionally hyperkeratotic. Numerous capillaries, often lined by plump endothelial cells, are usually seen deep to the ulcer. This vascular hyperplasia may lead to surface elevation, which gives the lesion a clinically raised appearance.

Immunohistochemical studies have demonstrated that the large mononuclear cells include 2 phenotypically distinct cell types: CD68-positive histiocytes and factor-XIIIa–positive submucosal dendrocytes in varying ratios. Longer-standing lesions may have more dendrocytes than histiocytes; however, this finding is controversial.

Typically, small T lymphocytes are scattered throughout the connective tissue, and a minority of these cells are of the CD4 phenotype. Usually, B cells are scarce. Neutrophils are often clustered within and near the base of the ulcer; mast cells, occasional plasma cells, and focally scattered S-100–positive histiocytes also are seen. An increased number of dendritic Langerhans cells may be identified in the epithelium immediately adjacent to the ulcer.

Smooth muscle actin and muscle-specific actin tests usually fail to highlight any of the cells in the connective tissue (except endothelial cells). This finding suggests that myofibroblasts are not an integral component of the cellular proliferation.

Although cellular atypia or mitoses are not typical findings, in rare cases, large atypical cells and mitotic figures may be scattered throughout the cellular infiltrate, creating a pseudolymphomatous pattern. These lesions are termed atypical histiocytic granulomas.

Immunohistochemical studies are often necessary to rule out lymphoma. In some cases, these atypical lesions recur and are subsequently determined to be CD30-positive T-cell non-Hodgkin lymphoma.⁵

The histologic differential diagnosis may include lymphoma, Langerhans cell disease, angiolymphoid hyperplasia with eosinophilia, and Kimura disease. Immunohistochemical studies may be necessary to confirm the diagnosis.

Treatment

Medical Care

- Dental-related trauma
 - The source of chronic irritation must be eliminated when an EU is due to obvious trauma.
 - Referral to a dentist is recommended if the lesion is related to a tooth, dental restoration, or appliance.
 - Although extraction of the anterior primary teeth is not recommended, this may resolve the ulcerations in Riga-Fede disease. However, if the teeth are stable, they should be retained. In these cases, breastfeeding should be discontinued, or a protective shield should be constructed to prevent any further trauma. These measures are usually sufficient to resolve the condition.
- Treatment modalities
 - Palliative care: Nonsteroidal anti-inflammatory drugs (NSAIDs) or topical anesthetics (eg, viscous lidocaine, benzocaine, dyclonine) may be used to provide temporary relief and comfort when the patient eats. A magic mouthwash may also provide symptomatic relief.
 - Therapeutic care: Some clinicians suggest that the use of corticosteroids may delay healing; however, a mixture of Orabase and a topical corticosteroid ointment (eg, clobetasol, fluocinonide, triamcinolone) is often effective. Dexamethasone elixir is also effective. Although unnecessary, systemic or intralesional corticosteroids may be used.

Surgical Care

- As a rule, if the lesion does not resolve or it continues to appear ominous after 2 weeks of treatment, biopsy is warranted.
- After biopsy, rapid healing of the ulcer is often typical, even with large EUs, and no further treatment is necessary.
- Occasionally, lesions may have to be surgically excised.

Consultations

- Consultation with a dentist may be indicated to evaluate and repair fractured teeth or restorations or to alter dentures.
- Consultation with an internist may be indicated for the evaluation of an underlying systemic condition in cases in which the ulcer persists, even after biopsy.

Diet

Advise patients to maintain hydration and nourishment.

- A soft diet is recommended for patients with painful ulcers and to avoid any further irritation.
- Nutritional supplements, such as Ensure or Boost, may be necessary.
- Advise patients to avoid eating acidic or spicy foods because they may cause additional discomfort.

Medication

NSAIDs or topical anesthetics (eg, viscous lidocaine, benzocaine, dyclonine) may be used to provide temporary pain relief and comfort while the patient eats.

Some clinicians suggest that the use of corticosteroids may delay healing; however, a mixture Orabase with a topical corticosteroid ointment (eg, clobetasol, fluocinonide, triamcinolone) often is effective.

Although unnecessary, treatment with systemic prednisone or intralesional injections of triamcinolone has been successful in some patients.

Dexamethasone elixir and magic mouthwash may also provide relief.

Topical anesthetics

These agents may provide temporary symptomatic relief of pain. They also may improve the patient's comfort while eating.

Viscous lidocaine 2% (Xylocaine)

Anesthetic liquid prescribed to treat painful lesions of the oral mucosa or lips. Inhibits neuronal membrane depolarization, blocking nerve impulses.

For small lesions, apply to ulcer with a cotton-tipped applicator. Generally not recommended for use in children because therapeutic doses usually approach potentially toxic levels. If necessary, use lowest effective dose and supervise children.

Dosing

Adult

15 mL (1 tbsp) topically or swish and spit q3h prn; not to exceed 8 doses/24h, 4.5 mg/kg, or 300 mg/d

Pediatric

<3 years: Not established

>3 years: Apply 3.75-5 mL topically or swish and spit q3h

Interactions

If significant systemic levels are reached (only theoretically with local or topical administration), systemic drug interactions may occur with medications metabolized by or affecting metabolism by CYP (P-450) 3A4 (eg, digitalis, disopyramide, ephedrine, isosorbide dinitrate, mexiletine, pentobarbital, phenytoin, propafenone, propanone, tocainide)

Contraindications

Documented hypersensitivity; avoid IV use in Adams-Stokes syndrome and Wolff-Parkinson-White syndrome

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

For external or mucous membrane use only; not for use in eyes; advise patients not to swallow because serious adverse effects can occur if too much is ingested

Benzocaine (Americaine, Benzocol, Cylex)

Inhibits neuronal membrane depolarization, blocking nerve impulses. In pediatric patients, this is a safe alternative to lidocaine.

Dosing

Adult

Apply 2-3 gtt topically or swish and spit q4-6h prn; not to exceed 5 g/d

Pediatric

Administer as in adults

Interactions

None reported

Contraindications

Documented hypersensitivity to ester-type anesthetics and PABA

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Potent sensitizer and more likely to induce allergy if applied to broken or fissured/dermatitic skin; methemoglobinemia may occur; not intended for use when infection is present

Dyclonine (Dyclone)

Ketone local anesthetic agent administered topically. Affects cell membrane permeability and blocks impulses at peripheral nerve endings in mucosa.

Dosing

Adult

Mouth sores: Apply 5-10 mL of 0.5-1% topically to oral mucosa q2-3h prn or swish and spit tid/qid prn; not to exceed 200 mg, 40 mL of 0.5% solution, or 20 mL of 1% solution

Pediatric

Administer as in adults

Interactions

None reported

Contraindications

Documented hypersensitivity; not for use around conjunctiva

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

May increase risk of aspiration (impairs swallowing); caution in shock or heart block; caution in presence of severely traumatized mucosa because rapid absorption possible

Analgesics

Analgesics are used for the relief of mild to moderate pain.

Ibuprofen (Motrin, Advil, Pediaprofen)

DOC for patients with mild to moderate pain. Inhibits inflammatory reactions and pain by decreasing prostaglandin synthesis.

Dosing

Adult

200-400 mg PO q4-6h while symptoms persist; not to exceed 3.2 g/d

Pediatric

<6 months: Not established

6 months to 12 years: 4-10 mg/kg/dose PO tid/qid

>12 years: Administer as in adults

Interactions

Coadministration with aspirin increases risk of serious NSAID-related adverse effects; probenecid may increase concentrations and, possibly, toxicity of NSAIDs; may decrease effect of hydralazine, captopril, and beta-blockers; may increase risk of prerenal azotemia in patients taking an ACE inhibitor; may decrease diuretic effects of furosemide and thiazides; monitor PT closely (instruct patients to watch for signs of bleeding), increases risk of hemorrhage if used with other anticoagulants, thrombolytic agents, or alcohol; may increase risk of methotrexate toxicity; phenytoin and lithium levels may be increased when administered concurrently

Contraindications

Documented hypersensitivity (including aspirin); peptic ulcer disease; recent GI tract bleeding or perforation; renal insufficiency; high risk of bleeding

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Category D in third trimester of pregnancy; not recommended if patient is breastfeeding; caution in congestive heart failure, hypertension, and decreased renal or hepatic function; caution in anticoagulation abnormalities or during anticoagulant therapy; Pediaprofen susp and Motrin susp contain sucrose (caution in DM); Motrin chewable tab contains aspartame (caution if PKU)

Acetaminophen (Tylenol, Tempra, FeverAll, Aspirin-Free Anacin)

DOC for pain relief in patients with documented hypersensitivity to aspirin or NSAIDs, those with upper GI tract disease, or those who are taking oral anticoagulants.

Dosing

Adult

325-650 mg PO q4-6h prn or 1000 mg tid/qid; not to exceed 4 g/d

Pediatric

<12 years: 10-15 mg/kg/dose PO q4-6h prn; not to exceed 2.6 g/d

>12 years: 325-650 mg PO q4h; not to exceed 5 doses/24 h

Interactions

Rifampin can reduce analgesic effects; coadministration with barbiturates, carbamazepine, hydantoins, and isoniazid may increase hepatotoxicity; may potentiate oral anticoagulants (eg, warfarin); monitor chloramphenicol concentrations and adjust dosage of chloramphenicol as necessary; concomitant diflunisal results in a 50% increase in plasma concentrations of acetaminophen; coadministration with zidovudine may result in neutropenia or hepatotoxicity

Contraindications

Documented hypersensitivity (including sulfites); known G-6-PD deficiency

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Hepatotoxicity possible in long-term alcoholism with various dose levels; severe or recurrent pain or high or continued fever may indicate a serious illness; many OTC products contain acetaminophen (combined use with these products may result in cumulative doses exceeding recommended maximum dose); caution with formulations that contain aspartame in patients with PKU; caution in patients with history of anemia, cardiac, pulmonary, renal, or hepatic disease; patients that have taken therapeutic doses of acetaminophen may have falsely elevated serum uric acid levels using the chemical phosphotungstic acid method

Dental aids and preparations

These are topical corticosteroids that share anti-inflammatory, antipruritic, and vasoconstrictive properties. However, they should be mixed with a carrier such as Orabase to ensure adherence of the drug to the mucosal surface. Otherwise, saliva quickly washes away the medication.

Clobetasol 0.05% dental paste (Temovate in Orabase)

Class I superpotent topical steroid; suppresses mitosis and increases synthesis of proteins that decrease inflammation and cause vasoconstriction. Ointment is recommended for intraoral use. Most pharmacists mix 15 g of clobetasol with 15 g of Orabase; this should be indicated on the prescription.

Dosing

Adult

Apply thin film tid for as long as 2 wk; do not rub in

Pediatric

<12 years: Not recommended

>12 years: Administer as in adults

Interactions

None reported

Contraindications

Documented hypersensitivity; herpes simplex infection; fungal, viral, or tubercular mucosal lesions

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Prolonged therapy may suppress adrenal function; with prolonged use of intraoral corticosteroids, superimposed candidal infection may develop; in predisposed patients (eg, those with HIV/AIDS or diabetes), a topical antifungal medication (eg, clotrimazole, nystatin) should also be prescribed

Fluocinonide 0.05% dental paste (Lidex in Orabase)

Class II high-potency topical corticosteroid that inhibits cell proliferation; immunosuppressive and anti-inflammatory. Ointment is recommended for intraoral use. Most pharmacists mix 15 g of fluocinonide with 15 g of Orabase; this should be indicated on the prescription.

Dosing

Adult

Apply thin film tid for as long as 2 wk; do not rub in

Pediatric

<12 years: Not recommended

>12 years: Administer as in adults

Interactions

None reported

Contraindications

Documented hypersensitivity; herpes simplex infection; fungal, viral, or tubercular mucosal lesions

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

May cause adverse systemic effects if used over large areas, denuded areas, on occlusive dressings, or for prolonged periods; with prolonged use of intraoral corticosteroids, superimposed candidal infection may develop; in predisposed patients (eg, those with HIV/AIDS or diabetes), a topical antifungal medication (eg, clotrimazole, nystatin) should also be prescribed

Triamcinolone acetonide 0.1% dental paste (Kenalog in Orabase)

Group III, intermediate potency. Used to treat inflammatory mucosal lesions that are responsive to steroids. Decreases inflammation by suppressing the migration of polymorphonuclear leukocytes and reversing capillary permeability. Ointment is recommended for intraoral use. Most pharmacists mix 15 g of triamcinolone with 15 g of Orabase; this should be indicated on the prescription.

Dosing

Adult

Apply thin film tid/qid until favorable response obtained

Pediatric

<12 years: Not recommended

>12 years: Administer as in adults

Interactions

None reported

Contraindications

Documented hypersensitivity; fungal, viral, and mycobacterial mucosal infections

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Not for use in decreased skin circulation; prolonged use, application over large areas, and use of potent steroids and occlusive dressings may result in systemic absorption; systemic absorption can cause Cushing syndrome, reversible HPA-axis suppression, hyperglycemia, or glycosuria

Corticosteroids

These agents have anti-inflammatory properties and cause profound and varied metabolic effects. They modify the body's immune response to diverse stimuli.

Dexamethasone (Decadron, Dexone, Hexadrol, Methasone)

Elixir for various allergic and inflammatory diseases. Decreases inflammation by suppressing migration of polymorphonuclear leukocytes and reducing capillary permeability. Supervise pediatric patients during administration.

Dosing

Adult

Saturate 2 X 2 gauze with medication and hold in mouth over affected area as long as possible and spit out qid

Pediatric

Administer as in adults

Interactions

Effects decrease with coadministration of barbiturates, phenytoin, and rifampin; decreases effect of salicylates and vaccines used for immunization

Contraindications

Documented hypersensitivity; active bacterial or fungal infection

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Use only externally (ingestion of excess medication may increase risk of multiple complications, including severe infections)

Prednisone (Orasone, Deltasone, Meticorten)

May decrease inflammation by reversing increased capillary permeability and suppressing PMN activity. In most cases, systemic corticosteroids are unnecessary in the management of EUs. Dividing dose may increase efficacy, but also increase risk of adrenal suppression/adverse effects.

Dosing

Adult

10-40 mg/d PO qd or divided bid/qid; taper over 2 wk as symptoms resolve

Pediatric

2 mg/kg/d PO qd or divided bid/qid; taper over 2 wk as symptoms resolve

Interactions

Coadministration with estrogens may decrease clearance; concurrent use with digoxin may cause digitalis toxicity secondary to hypokalemia; phenobarbital, phenytoin, and rifampin may increase metabolism of glucocorticoids (consider increasing maintenance dose); monitor for hypokalemia with coadministration of diuretics

Contraindications

Documented hypersensitivity; connective tissue and viral infections; peptic ulcer disease; hepatic dysfunction; fungal or tubercular mucosal infections; GI tract disease

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Abrupt discontinuation of glucocorticoids may cause adrenal crisis; hyperglycemia, edema, osteonecrosis, myopathy, peptic ulcer disease, hypokalemia, osteoporosis, euphoria, psychosis, myasthenia gravis, growth suppression, and infections may occur with glucocorticoid use; a superimposed candidal infection may develop with prolonged use of corticosteroids; in predisposed patients (eg, those with HIV/AIDS or diabetes), a topical antifungal medication (eg, clotrimazole, nystatin) should also be prescribed

Palliative agents

These agents provide temporary symptomatic relief and may improve the patient's comfort while eating.

Diphenhydramine, aluminum hydroxide, magnesium carbonate (Magic Mouthwash)

Provides symptomatic relief of stomatitis. Variations of this formulation may be available through a pharmacy or may be personally specified.

Standard recipe may include 30 mL diphenhydramine (Benadryl) elixir, 60 mL calcium carbonate and magnesium hydroxide (Mylanta), and 4 g sucralfate (Carafate). Preparations may also include tetracycline (avoid tetracycline if <9 y), attapulgite (Kaopectate), lidocaine, cherry syrup (for children), or hydrocortisone.

Dosing

Adult

5 mL swish and spit or swish and swallow tid ac and prn

Pediatric

Apply small amounts to lesion ac and prn

Interactions

Diphenhydramine potentiates effect of CNS depressants; aluminum and magnesium reduce efficacy of fluoroquinolones, corticosteroids, benzodiazepines, and phenothiazines

Aluminum and magnesium potentiate effects of valproic acid, sulfonyleureas, quinidine, and levodopa

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Diphenhydramine may exacerbate angle-closure glaucoma, hyperthyroidism, peptic ulcer, and urinary tract obstruction; xerostomia may occur
With magnesium hydroxide, caution in severe renal impairment; use aluminum-containing antacids with caution in patients with recent massive upper GI hemorrhage

Follow-up

Further Outpatient Care

- Once treatment is initiated, advise patients to return in 2 weeks for re-evaluation.
- Biopsy is warranted if the lesion does not appear to be resolving with either topical steroid use or removal of the traumatic irritant.

Deterrence/Prevention

- Patients should eliminate the source of the chronic irritation to prevent recurrence (see Causes).

Complications

- If the ulcer does not resolve, even after biopsy, the patient may have an underlying systemic condition that prevents the lesion from healing. The patient should be referred for a medical workup.
- Clinicians should remember that deliberate self-mutilation may be a symptom of an underlying emotional disturbance.
 - In cases of self-mutilation, patients may inflict injury to themselves to seek attention and sympathy or to obtain prescription medications.
 - Psychiatric or psychological counseling is often necessary for these patients.

Prognosis

- The prognosis is excellent, even with conservative treatment.
- Recurrence is rare; however, the source of the chronic irritation should be eliminated to ensure that the ulcer does not recur.

Miscellaneous

Medicolegal Pitfalls

- Occasionally, lesions may demonstrate atypical histologic features. These lesions have been misdiagnosed as lymphoma and unnecessary radical treatment can result.
- Conversely, CD30-positive anaplastic lymphomas have been misdiagnosed as EUs; therefore, immunohistochemical studies may be needed to confirm the diagnosis.⁵

Multimedia



Media file 1: A 47-year-old African American woman with an eosinophilic ulcer on the lateral surface of the tongue. The anterior border of the lesion is raised. Courtesy of Dr Paul D. Freedman.



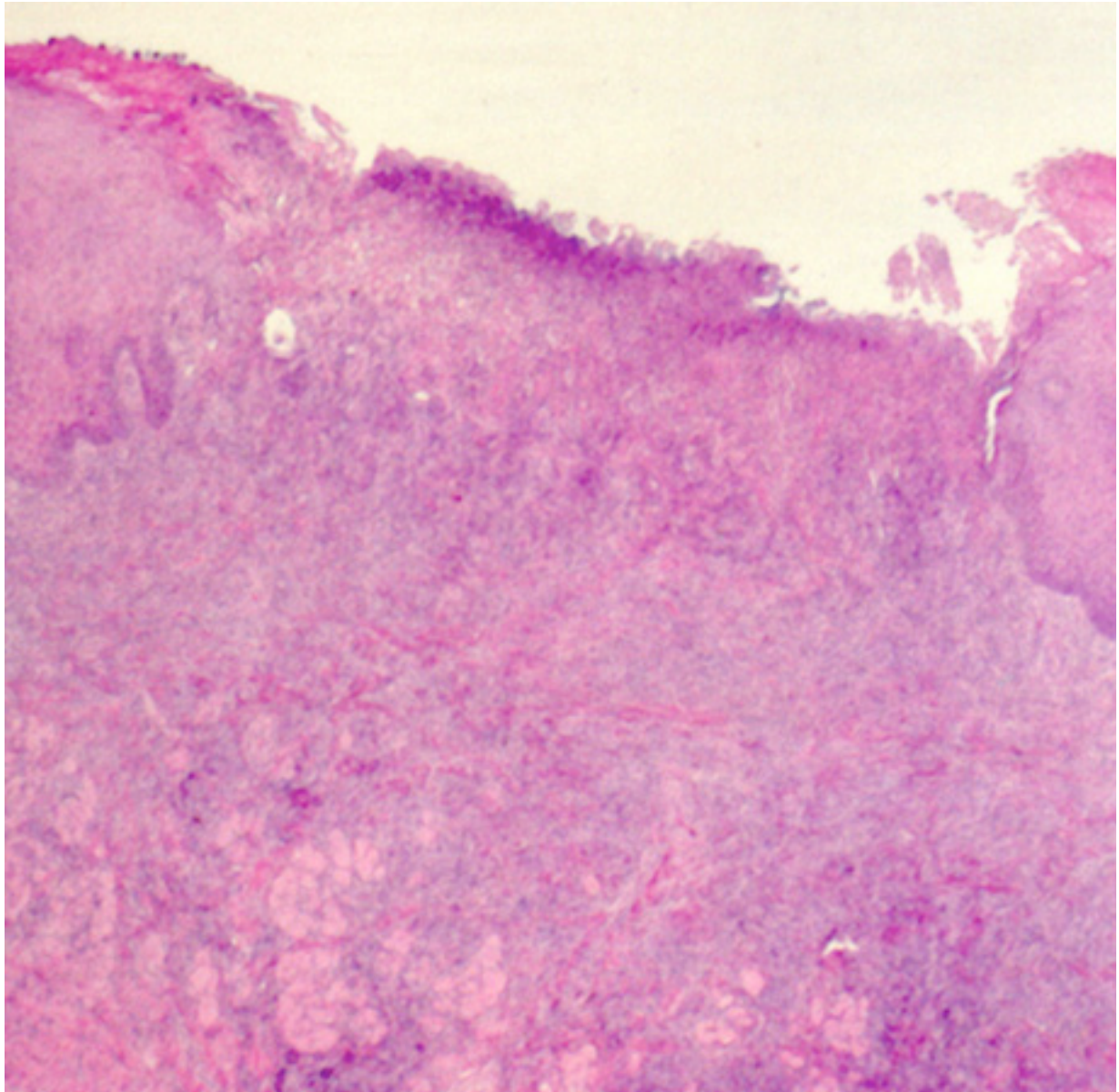
Media file 2: Raised, indurated, nonhealing ulcer on the lateral surface of the tongue. The lesion was related to an adjacent fractured tooth. Courtesy of Dr Paul D. Freedman.



Media file 3: Ulcer on the ventrolateral surface of the tongue. The differential diagnosis should include squamous cell carcinoma or an infectious etiology. Courtesy of Dr Paul D. Freedman.



Media file 4: Lesion on the lateral surface of the tongue. Courtesy of Dr Paul D. Freedman.



Media file 5: Low-power view showing an ulcerated surface epithelium with a dense cellular inflammatory infiltrate underlying the mucosal surface (original magnification X40). Courtesy of Dr Paul D. Freedman.