Erythematous Oral Lesions: When to Treat, When to Leave Alone

ABSTRACT: Erythroplakia requires biopsy followed by wide local excision, since about 50% of these lesions represent invasive carcinomas. Geographic tongue and erythema migrans are largely benign; treatment is symptomatic if patients complain of pain. Red lesions caused by hypersensitivity to drugs, foods or, most commonly, dental materials (eg, denture adhesives, toothpastes, and mouth rinses) can arise anywhere in the oral cavity. Treatment consists of discontinuing the offending substance; up to 40 mg/d of prednisone can promote healing. Biopsy is not necessary for most vascular erythematous oral lesions, except Kaposi’s sarcoma. If vascular lesions are traumatized, surgery or embolization may be needed to control bleeding. Because pyogenic granuloma and peripheral giant cell granuloma can resemble amelanotic melanoma, they require biopsy. Treatment is excision.

Key words: erythroplasia, erythroplakia, stomatitis migrans, geographic tongue, erythema migrans, candidiasis, contact stomatitis, plasma cell gingivitis, pityriasis rosea, hemangioma, Kaposi’s sarcoma, Osler-Weber-Rendu disease, blue rubber bleb nevus syndrome, mucocutaneous dysplasia syndrome, Fabry’s disease, Sturge-Weber syndrome, pyogenic granuloma, peripheral giant cell granuloma

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If you know what to look for, the appearance of a puzzling oral lesion can help you narrow the possible causes. In previous issues of CONSULTANT (April 2012, page 301, and May 2012, page 347), I provided tips for identifying and managing white and pigmented oral lesions, respectively. In this article, I consider erythematous oral lesions, the appearance of which reflects the increased vascularity of the local tissues.

In some cases, the increased vascularity results from denudation or inflammation of mucosal or gingival areas by such diverse causes as allergy; fungal infection; dermatologic, hematologic, metabolic, and immunologic disorders; and neoplasia. The lesions associated with these erythematous mucosal alterations are generally flat or atrophic; however, epithelial hyperplasia is seen with erythroplakia and psoriasis.

In other erythematous oral lesions, vascular hyperplasia occurs, such as in Sturge-Weber syndrome. This may also take the form of neoplastic proliferations (hemangioma and Kaposi’s sarcoma), vascular malformations, or ectatic vessels (hereditary hemorrhagic telangiectasia). Finally, hypervascularized masses may appear on the gingiva in response to local trauma or irrita-
Erythematous Oral Lesions: When to Treat, When to Leave Alone

The Table classifies the lesions in detail.

**MUCOSAL ALTERATIONS**

**Erythroplasia, erythroplakia.** Erythroplasia simply denotes a non-specific red patch. Although some authors employ the terms “erythroplasia” and “erythroplakia” interchangeably, others consider erythroplakia analogous to leukoplakia, a specific histologic entity with a distinct premalignant potential. In fact, erythroplakia is more ominous than leukoplakia, since histologic study shows that about 50% of erythroplakic lesions represent invasive carcinomas (Figure 1).

Erythroplakia generally appears as a solitary red patch of varying size, which may be slightly raised. Although the lesion derives its color from the loss of surface keratin, it is painless. The area involved may be homogeneous or mixed with small areas of leukoplakia (speckled form). It most commonly occurs on the floor of the mouth and the retromolar triangle; the gingiva is rarely involved.

**Stomatitis migrans.** Migratory stomatitis may be encountered in both lingual and nonlingual forms. **Geographic tongue.** Benign migratory glossitis, or geographic tongue (Figure 2), is seen primarily in young adults, especially women. There also seems to be a higher incidence among patients with psoriasis or type 1 diabetes mellitus. The lesions develop on the lateral borders and dorsum of the tongue, where depapillated areas appear as smooth, erythematous patches with a gray-white rim. The fungiform papillae become prominent because of the selective loss of filiform papillae.

**Table – Erythematous oral lesions**

<table>
<thead>
<tr>
<th>Mucosal alterations</th>
<th>Vascular lesions</th>
<th>Reactive lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythroplasia, erythroplakia</td>
<td>Vascular tumors (hemangioma, Kaposi’s sarcoma)</td>
<td>Pyogenic granuloma (pregnancy tumor)</td>
</tr>
<tr>
<td>Stomatitis migrans (geographic tongue, erythema migrans)</td>
<td>Arteriovenous malformations</td>
<td>Peripheral giant cell granuloma</td>
</tr>
<tr>
<td>Candidiasis</td>
<td>Genodermatoses (Osler-Weber-Rendu disease, blue rubber bleb nevus syndrome, mucopolysaccharide dysplasia syndrome, Fabry’s disease)</td>
<td></td>
</tr>
<tr>
<td>Allergy (contact stomatitis, plasma cell gingivitis)</td>
<td>Sturge-Weber syndrome</td>
<td></td>
</tr>
<tr>
<td>Denuded bullous lesions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermatologic disorders (psoriasis, pityriasis rosea)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin deficiencies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematologic disorders</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 2 – Irregular, erythematous areas that characterize geographic tongue, or benign migratory glossitis, result from the loss of filiform papillae. The patterns change at intervals that range from days to weeks or months.
The patterns in geographic tongue change at intervals ranging from days to weeks or months, and recurrences are the rule. If patients complain of burning (usually after they have eaten spicy or acidic foods), prescribe a bland diet and an antihistamine mouth rinse.

**Erythema migrans.** Although geographic tongue is commonly recognized as a migratory stomatitis, the nonlingual form, stomatitis areata migrans (erythema migrans), is not. The latter appears as multiple, flat, irregularly shaped, serpiginous red patches with raised keratotic rims that heal spontaneously and reappear in constantly changing patterns. The lesions usually occur on the buccal mucosa and the labial and oral vestibule, but the floor of the mouth, ventral tongue, soft palate, and gingiva may be also involved. Brooks and Balciunas found that geographic tongue and fissured tongue were frequently associated with this condition.

Erythema migrans is seen mainly in young adults. The condition is generally painless, despite the acute and chronic inflammatory infiltrates seen on microscopic examination. Its migratory character points to the diagnosis. If patients complain of associated pain, prescribe an antihistamine mouthwash and an oral antibiotic to forestall secondary bacterial infection.

**Candidiasis.** Oral candidiasis characteristically presents as a pseudomembranous lesion that mimics keratosis. Nevertheless, the condition may appear in several other variations. The erythematous form—atrophic candidiasis—is caused by the loss of surface epithelium, including filiform and fungiform papillae.

Involved areas appear as bright red patches without evidence of ulceration. Sites of predilection are the dorsum of the tongue and the palate. Denture stomatitis is a variant wherein *Candida albicans* colonizes desquamated mucosal areas beneath a dental prosthesis (Figure 3). Treat patients with clotrimazole troches (5 daily) or with nystatin oral suspension, 400,000 U bid for 7 to 10 days.

**Allergy.** Red lesions caused by hypersensitivity to a systemic or topical drug can arise anywhere in the oral cavity. Other substances or foods may also be culprits.

**Drugs and other agents.** Sulfonamides, barbiturates, and iodine preparations are traditionally associated with allergic stomatitis, although the occurrence is rare. More often, contact allergy develops from denture adhesives, toothpastes, mouth rinses, and dental materials. Patients generally experience local pain, burning, or itching.

Since the clinical appearance of the lesion is nonspecific, a thorough drug history—including oral and dental preparations—is required. Fisher provides a list of the active ingredients in dental mouthwashes and dentifrices. The topical allergic lesions have been broadly subdivided into two types, erythema multiforme and lichenoid, because of their resemblance to the lesions seen in erythema multiforme and lichen planus, respectively:

- **Erythema multiforme–type lesions** have been associated with a variety of antibiotics (eg, penicillin, clindamycin, sulfonamides, rifampin, and...
Erythematous Oral Lesions: When to Treat, When to Leave Alone

- Lichenoid lesions can be produced by NSAIDs, thiazides, penicillamine, systemic gold compounds, ß-blockers, methyldopa, and lithium.8

Plasma cell gingivitis. This entity, also known as atypical gingivostomatitis, was first recognized in 1968.9 As the name implies, it is characterized by an intense and diffuse gingival erythema that shows plasma cell infiltration on biopsy. Patients may also have lesions on the lips, buccal mucosa, and tongue (with loss of filiform papillae).

This condition represents an allergic reaction to an unknown antigen in some chewing gums and toothpastes.8 To treat plasma cell gingivitis, tell patients to discontinue use of the offending substance. Healing can be promoted with up to 40 mg/d of prednisone.9

Denuded bullous lesions. At first glance, many vesiculobullous oral disorders may appear to be erythematous lesions because the loss of the surface epithelium leaves an irregular, inflamed base. This is especially true of such conditions as systemic lupus erythematosus (Figure 4), erythema multiforme, pemphigus, and pemphigoid. Accordingly, search for residual mucosal fragments that point to the true nature of the disease. Moreover, the bullous disorders tend to have widespread oral involvement, often with cutaneous lesions.

Dermatologic disorders. A relatively common inflammatory skin disorder, psoriasis vulgaris is characterized by erythematous scaling plaques. In severe cases, the plaques may extend from the facial skin onto the lips. Less frequently, similar irregularly shaped, scaling lesions may appear on the buccal mucosa, tongue, and palate.10 However, geographic tongue and its ectopic buccal mucosal form occur in as many as 10% of patients with psoriasis. An increased incidence of fissured tongue has also been reported.11

The presence of typical chronic skin lesions (principally involving the elbows, knees, scalp, and nails) helps to establish the diagnosis. Prescribe emollient mouthwashes for patients with oral lesions.

Pityriasis rosea is a common, self-limited skin disorder that presents with an oval erythematous plaque (typically on the trunk), which is termed the “herald patch.” This is followed by a generalized body eruption 3 to 14 days later. The characteristic clinical presentation is diagnostic. Intraorally, erythematous patches may occur with punctate areas of hemorrhage on the buccal mucosa, especially in children.12 No treatment is necessary.

Vitamin deficiencies. Vitamin B deficiency produces loss of the filiform papillae, resulting in an atrophic and red tongue. With riboflavin (B2) deficiency, the dorsum of the tongue becomes intensely colored (magenta tongue); this is often accompanied by fissuring of the commissures of the lips, or angular chei-
loss (Figure 5). With niacin deficiency, atrophy and reddening of the tongue also occur; however, painful ulcerations develop on the tongue and on all the oral mucous membranes, gingiva, and lips. Pyridoxine (B6) deficiency produces glossitis and angular cheilosis. Vitamin C deficiency is characterized by painful hemorrhagic gingivitis.

Diagnosis relies on a careful nutritional history, which is confirmed by serum vitamin assays. Treatment consists of dietary correction and vitamin supplementation.

Hematologic disorders. Anemia is commonly associated with pallor of the mucous membranes; however, the loss of filiform and fungiform papillae on the dorsum of the tongue results in denuded areas, which are atrophic and erythematous. The process of depapillation begins along the lateral borders of the tongue and may involve the entire tongue in severe cases. This finding is nonspecific; it occurs in both microcytic anemia (iron deficiency) and macrocytic anemia (pernicious anemia), as well as after acute viral infections.

Conversely, excessive red blood cell formation, as seen in polycythemia vera, produces a deep red coloration of the mucous membranes, which diffusely involves the oral cavity and lips. Thrombocytopenia produces discoloration of the oral cavity by the development of mucosal ecchymoses and petechiae.

The diagnosis is made by a complete blood cell count. The appearance of the oral tissues normalizes when the blood disorder is corrected.

VASCULAR LESIONS

Vascular tumors. Hemangiomas are produced by the disordered formation of blood vessels and may arise anywhere in the deep or superficial structures of the head and neck. When close to the surface of the oral cavity, they appear as red to blue, slightly elevated to exophytic, smooth to lobulated masses that range widely in size. Their vascular nature can be confirmed by blanching on compression. Sites of predilection are the tongue, buccal mucosa, and lips. Hemangiomas are classified microscopically as capillary or cavernous based on the size of the endothelium-lined blood vessels; these vessels are larger in the cavernous type (Figure 6). Treatment, which depends on the extent and location of the lesion, includes embolization, injection of sclerosing solution, cryosurgery, laser therapy, and surgical excision.

Kaposi’s sarcoma is a vascular neoplasm that occurs in several clinical forms:
- Classic (a racial genetic lesion found predominantly in elderly, Mediterranean men).
- Endemic (among African children and adults).
- Associated with a non-AIDS immunocompromised state (among patients who are receiving immunosuppressive therapy, especially those with a renal transplant).
- Associated with AIDS.

While various viruses have been implicated in the pathogenesis of Kaposi’s sarcoma, its cause remains unclear. Involvement of the oral cavity is most common in AIDS patients, especially among homosexual men. In these patients, the oral cavity is often the initial site of occurrence and may even be the only site. Tumors may develop anywhere in the mouth; however, the palate is the predominant site (over 90%), followed by the gingiva (about 20% to 30%).

The purple-red lesions progress from multiple macules to a nodular mass (Figure 7). Larger lesions arise in severely immunosuppressed patients. They may be confused with other pigmented (melanoma), vascular (hemangioma), or infectious (bacillary angiomatosis) lesions; biopsy is necessary for definitive diagnosis. Microscopic examination reveals spindle cells that line irregular vascular spaces.

Pain occurs in about one quarter of patients; bleeding is uncommon. Treatment options include systemic interferon alfa-2b, intralesional injection with vinblastine, injection of
sclerosing solution, radiation therapy, surgical excision, laser therapy, and systemic chemotherapy.

**Arteriovenous malformations.** In these congenital lesions, vascular shunting occurs through vessels that may be predominantly arteries, veins, arteriovenous channels, or capillaries. The signs and symptoms are related to the size, site, and degree of shunting within the mass. Physiologically, the lesions may be classified as high-flow, high-shunting or low-flow, low-shunting. The latter resemble hemangiomas. The former are pulsatile—often with a bruit—and may produce local soft-tissue discoloration, deformity, and gigantism. Ulceration of the overlying skin may cause life-threatening hemorrhage. The principal sites of involvement in the oral cavity are the buccal mucosa and the floor of the mouth and tongue.

Multidisciplinary management involves angiography and embolization and radical surgery. Partial management results in regrowth with bleeding or airway obstruction.

**Genodermatoses.** In these hereditary syndromes, a variety of lesions can involve the skin, mucous membranes, and other ectodermal tissues, as well as mesodermally and endodermally derived structures. Syndromes that produce erythematous lesions in the mouth are vascular except for mucoepithelial dysplasia, which can also be classified as a mucosal alteration.

**Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu disease).** In this autosomal dominant hereditary disease, telangiectasis occurs in the skin and mucous membranes, and angiodysplasia is present in the viscera and the CNS. In the oral cavity, the lesions appear as multiple, small (1- to 5-mm), red macules and papules on the lips and anterior tongue (Figure 8). They are produced by a defect in the wall of small venules.

If the lesions are traumatized, bleeding can be controlled by electrocautery or laser therapy. However, the arteriovenous malformations that can occur in the lungs and liver—as well as other angiodysplastic lesions in the CNS, gastrointestinal (GI) tract, and other viscera—may produce serious hemorrhage. Epistaxis from nasal mucosal lesions is a common presentation.

**Blue rubber bleb nevus syndrome.** In this autosomal dominant disorder that presents at birth or during early childhood, multiple, soft, compressible, blue nodules appear on the skin. The lesions are often associ-
ated with pain and sweating. Venous malformations also develop in the GI tract (especially the small intestine), heart, lungs, and other viscera; these malformations may bleed and cause chronic anemia. In the oral cavity, cavernous hemangiomas typically develop on the tongue. Traumatized lesions may produce bleeding that requires surgical control.

**Mucoepithelial dysplasia syndrome.** This autosomal dominant disease first appears in infancy and is characterized by severe erythema of the mucous membranes of the mouth, nose, genitourinary tract, and anus. In the oral cavity, the gingivae are intensely red. The skin is rough with follicular keratoses. Noncutaneous manifestations involve the hair (alopecia), eyes (cataracts), and lungs (bullous lung disease). Microscopic examination reveals a lack of epithelial cohesion, dyskeratosis, and cytoplasmic inclusions. There is no tendency to malignant transformation.

**Fabry’s disease.** This X-linked recessive disorder of glycosphingolipid metabolism presents in children as a diffuse rash over the lower trunk. It is formed by small angiofibromas that appear as small red-blue macules and papules—hence, the name angiofibromatosis corporis diffusum. Severe burning pain develops before the skin lesions appear. In the oral cavity, angiokeratotic lesions appear on the lips and buccal and palatal mucosa. This lipid storage disorder also involves the kidney, heart, GI tract, eyes, CNS, and other organs. Renal or cardiac failure often causes death in midlife.

**Encephalotrigeminal angiomatosis (Sturge-Weber syndrome).** In this neurocutaneous disorder, a port-wine stain (nevus flammeus) occurs along the distribution of the trigeminal nerve, and meningeal angiomas and calcifications are present along the cerebral convolutions. Many patients also have seizures, glaucoma, and mental retardation. When the second and third divisions of the trigeminal nerve are involved, increased vascularity and vascular hyperplasia may develop in the oral cavity, especially the buccal mucosa, gingiva, and lips (Figure 9). Uncommonly, the increased regional blood flow may result in gigantism of the gingiva or underlying bone. If the oral lesions bleed, they may be treated with cryosurgery or selective embolization of regional blood vessels.

**REACTIVE LESIONS**

**Pyogenic granuloma.** This lesion arises as a reaction to local trauma. It appears as a small (0.5- to 1.5-cm), exophytic, red, friable mass with a predilection for the gingiva (especially of the anterior maxilla) of young adults, but it may also occur on the buccal mucosa, tongue, or lips. Microscopic examination reveals a mass of capillaries in a loose connective tissue stroma with interspersed chronic inflammatory cells. With continued trauma, the surface ulcerates and granulation tissue forms. Biopsy is necessary, since amelanotic melanoma may have an identical appearance. Treatment is excision.

A variant of this lesion is the pregnancy tumor, which arises on the gingiva of gravid women in response to hormonal stimulation (Figure 10). These lesions are histologically identical to pyogenic granulomas. If troublesome, they may be removed in the second trimester or postpartum.

**Peripheral giant cell granuloma.** This lesion also arises on the gingiva in response to local trauma (eg, dental restorations or calcul-
Erythematous Oral Lesions: When to Treat, When to Leave Alone

CLINICAL HIGHLIGHTS

- Although oral candidiasis usually presents as a pseudomembranous lesion, it may appear in an erythematous form that results from the loss of surface epithelium, including filiform and fungiform papillae. Denture stomatitis is a variant that consists of desquamated mucosal areas beneath a dental prosthesis.

- At first glance, many vesiculobullous oral disorders may appear to be erythematous lesions because the loss of the surface epithelium leaves an irregular, inflamed base; residual mucosal fragments point to the true nature of the disease.

- Vitamin B deficiency produces loss of the filiform papillae, resulting in an atrophic and red tongue, while vitamin C deficiency is characterized by painful hemorrhagic gingivitis. Diagnosis is based on a careful nutritional history, which is confirmed by serum vitamin assays.

- Anemia is commonly associated with pallor of the mucous membranes; however, the loss of filiform and fungiform papillae on the dorsum of the tongue results in atrophic, erythematous, denuded areas. Excessive red blood cell formation, as seen in polycythemia vera, produces a deep red coloration of the mucous membranes, which diffusely involves the oral cavity and lips.

- Peripheral giant cell granulomas are clinically indistinguishable from pyogenic granulomas; however, on microscopic examination, the presence of multinucleated giant cells within the granulation tissue is diagnostic.

REFERENCES:


Figure 10 – This exophytic, intensely erythematous lesion occurs on the maxillary gingiva of a gravid woman. Pregnancy tumors arise in response to hormonal stimulation.