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Review Article

Oral ulcerations due to drug medications

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Summary Ulcers are common symptoms observed in the oral cavity and some ulcerations are induced by drug medications. When ulcers show typical clinical findings differential diagnosis may be easy, but the exact diagnosis is often difficult. We reviewed differential diagnosis of oral ulcerative diseases, clinical characteristics of drug-induced oral ulcerations and drugs inducing oral ulcerations. Many kinds of drugs have been reported to cause oral ulcerations. Among them, non-steroidal anti-inflammatory drugs are popular and well-known. However, several recent reports have described oral ulceration associated with relatively new drugs for the treatment of chronic disorders such as, diabetes, angina pectoris, rheumatoid arthritis, and osteoporosis. We reviewed these new drugs and also reported typical cases of drug-induced oral ulcerations.

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1. Introduction

Many kinds of adverse reactions induced by drug medications in the oral cavity are now well recognized [1—3]. Among these, the most frequent are dry mouth (hyposalivation), dysgeusia, and stomatitis. Stomatitis is a general term for disturbance of oral epithelial cells and covers several types of oral mucosal symptoms. Oral mucosal symptoms caused by drugs can be further divided as follows: (1) lichenoid reaction/lichen planus; (2) ulcers; (3) erythema multiforme; (4) pigmentation; (5) autoimmune vesiculo-bullous disease; (6) infections; (7) tumors (fibrovascular hyperplasia); (8) swellings (angioedema); and (9) keratosis [1]. This paper focuses on ulcers and/or erosions in the oral cavity induced by pharmacotherapy, with an emphasis on new drugs for the treatment of chronic diseases such as diabetes, angina pectoris, rheumatoid arthritis and osteoporosis.

2. Oral ulcers

Oral ulcers are common symptoms observed in the oral cavity and include traumatic, infective, aphthous, ulceration related to dermatoses, drug-induced, ulceration as a manifestation of systemic disease, and ulceration due to malignancy (Table 1) [4—6]. When ulcers show typical clinical findings, differential diagnosis may be easy; however, the exact diagnosis is difficult in most cases, and histopathological diagnosis may be needed.

3. Differential diagnosis

Careful examination of the oral mucosa is the most important factor for determining a provisional diagnosis. Patients are often confused by the term stomatitis, and the precise nature of the complaint should be confirmed. The age, sex, and dental and medical histories of the patient may provide useful information, and the number, shape, size, and location of lesions must also be carefully observed [7,8].

Traumatic ulceration is caused by mechanical, thermal, or chemical irritants. The most frequent causes are ill-fitting dentures, sharp-edged crowns or bridges, and tooth decay. The ulcer floor is usually clear and ulcer margins do not typically show induration on palpation, but sometimes show bleeding, granular appearance, or induration resembling malignant tumor.

Viral infection is generally associated with multiple small aphthous ulcerations. The initial presentation is fluid-filled vesicles, but these rapidly break down to form small, round, painful ulcers with ragged margins that often fuse to form large, irregular ulcers. Viral infections in the oral cavity are most commonly due to herpes simplex virus (HSV)-1, varicella-zoster virus (VZV), coxsackie virus and cytomegalovirus. Acute herpes zoster causes eruption of multiple small, painful vesicles that rapidly rupture to form punctate or confluent ulcers in a portion of the trigeminal nerve distribution [7].

Aphthous ulceration is the most common type of oral ulceration and improves within 10—14 days. The lesions usually occur in non-keratinizing epithelium and form small,

Table 1 Chronic oral ulcers.

Diagnosis	Clinical features
Drug-induced ulcers	Single, isolated ulcers, located on the side of the tongue, surrounded by an erythematous halo and resistant to usual treatments
Erosive lichen planus	Areas of atrophy, erosions or painful ulcers, generally resistant to conventional treatments
Pemphigus vulgaris	Bullae appear in oral cavity (posterior region), forming painful ulcers with necrotic fundus and erythematous halo
Mucous membrane pemphigoid	Spontaneous onset of bullae that readily rupture, giving rise to a highly painful ulcerated area (most common areas are palate and gingiva)
Lupus erythematosus	Erythema and oral ulcers, without induration and accompanied by whitish striae and a tendency to bleeding
Reiter's syndrome	Arthritis, urethritis, conjunctivitis and oral ulcers similar to those of recurrent aphtous stomatitis
Tuberculosis	Primary tuberculosis: deep, irregular, persistent and painful ulcer on the tongue, with rolled border and granulation tissue in the fundus Secondary tuberculosis: chronic ulcer, painful and indurated
Mycosis	Mycoses give rise to chronic ulcers on the oral mucosa, most commonly in immunocompromised patients
Other bacterial and parasitic diseases	Klebsiella and Leishmania spp. can produce chronic oral ulcers in HIV-infected patients
Eosinophilic ulcer	Large ulcer, generally in the tongue, with raised, indurated borders and white-yellowish fundus that may resemble a malignant lesion. Persists for weeks or months
Oral squamous cell carcinoma	Can produce ulcers (exophytic, endophytic or mixed). Metastatic lesion can appear as ulcers in the oral cavity

Munoz-Corcuera et al. [5].
HIV, human immunodeficiency virus.