Chapter

Ulcerative Lesions of the Oral Cavity

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Abstract

Apart from dental and periodontal diseases, oral mucosal lesions are also frequently encountered by both general dentists and dental specialists in outpatient clinics. Although these soft tissue lesions may only reveal a localized issue, sometimes they may be the only sign of a more serious underlying systemic condition. Thus, oral ulcerations pose a unique diagnostic challenge for healthcare providers and should be cautiously handled when they last for more than two weeks, even after any possible traumatic etiologies are eliminated. There are many different classifications regarding oral ulcerations based on their etiologic or clinical features. In order to provide a logical and simple stepwise guidance to accurate diagnosis, this chapter will categorize and explain these lesions based on their clinical properties.

Keywords: oral ulcer, oral mucosa, oral disease, aphthous stomatitis

1. Introduction

Oral ulcerative lesions are defects in the oral epithelia, its underlying connective tissue or both. The oral mucosa is considered among one of the susceptible areas in the human body to painful ulceration [1, 2]. An oral ulcer is not a disease itself but rather a sign of a different underlying condition, therefore it is usually challenging to diagnose the accurate etiology [1]. It is important to identify the etiologic factor to provide a complete resolution to patients rather than constantly prescribing certain medicines to suppress the symptoms [3].

Regardless of the etiology of these lesions, oral ulcerative lesions may be categorized as minor, major or herpetiform ulcerations. Minor ulcerations are usually less than 1 cm in diameter, and they most commonly present on the labial or buccal mucosa or the ventral surface of the tongue. Less common locations include the dorsum of the tongue, hard palate or the gingiva [4, 5].

Ulcerations that measure more than 1 cm in diameter are referred to as major oral ulcerations and have a lower prevalence than minor ones. Among these three types, the least common type is the herpetiform ulceration, which unlike what its name suggests, is irrelevant to herpetic stomatitis since no vesicle formation is observed in advance [5]. These type of ulcerations are multiple and usually are much smaller in diameter (1–3 mm) [4].

Another helpful classification is based on the duration of these lesions, which may aid clinicians establish a more logical stepwise progression towards an accurate

diagnosis. Accordingly, an oral ulcerative lesion is diagnosed as acute if it lasts for less than two weeks, chronic if it persists for more than two weeks or recurrent if it presents with a history ulcerative episode with intermittent periods of healing [1].

2. Acute ulcerative lesions

A short-lived oral ulcerative lesion which resolves in less than two weeks is considered as an acute oral ulcer and is commonly referred to as an "aphtha" [1, 2]. This word itself is attributed to Hippocrates which was used to describe disorders of the mouth in general back in his time (460–370 BC) [3]. In order to accurately diagnose and evaluate patients with acute ulcerative lesions, it is crucial that the physician is aware of the broad spectrum of possibilities that may cause these lesions. It is recommended to assess the history of the lesions first, meaning to question the patient regarding any periodic episodes, in order to exclude conditions which are characterized with recurrent oral ulcerations [2].

Clinically acute oral ulcers usually have an oval shape with an erythematous periphery due to the dilation of the blood vessels. Although commonly these are painful lesions, the pain is relatively weaker when the ulcer bed is layered with a yellowish fibro-membrane [2].

Most common acute oral ulcerations may be related to trauma (i.e., traumatic ulcers), chemotherapy (i.e. chemotherapy induced ulcers), necrotizing sialometaplasia, primary herpetic gingivostomatitis, herpes zoster infection, herpangina, hand-foot mouth disease, erythema multiforme, necrotizing ulcerative gingivitis, oral hypersensitivity reactions or plasma cell stomatitis [1, 6, 7].

Traumatic ulcerations are one of the most common oral ulcerative lesions [8]. If a traumatic ulceration is due to the mucosal irritation of natal or neonatal teeth at the ventral surface of the tongue, then it is called "Riga-Fede disease". Ulcerations due to thermal and electrical injuries most commonly occur in children and affect the lip and commissure areas. On the contrary, malformed or fractured teeth, ill-fitting dentures or overheated food are usually encountered in adults (**Figure 1**) [1, 9]. Traumatic ulcerations tend to heal within ten days once the etiologic factor is discarded [8].

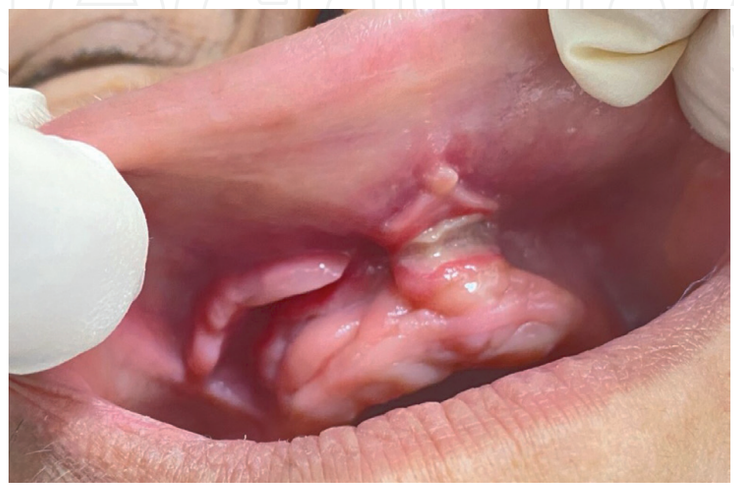

Figure 1.
Irritation fibroma of the right vestibular sulcus and an acute traumatic ulceration of the maxillary frenulum due to ill-fitting dentures.

Chemotherapy induced ulcers are commonly observed in oral mucositis, which is one of the most frequent complications of chemotherapy in oncologic patients [10]. These erythematous and painful ulcerative lesions are due to the detrimental effects of chemotherapy on oral mucosal epithelial cells. Patients receiving chemotherapy for a malignancy have a 24.8–67% incidence rate for oral ulcerations [11]. This rate increases to almost 90% in patients with head and neck cancer, who receive both chemotherapy and radiotherapy for their oncologic condition. Cisplatin, 5-fluoruracil, docetaxel, paclitaxel, everolimus, tenserolimus, ridaforolimus, cetuximab, panitunumab, erlotinib, gefinitib, afatinib, lapatinib and dacomitinib are among the most common chemotherapeutic agents associated with chemotherapy induced oral ulcers [12–15]. The risk to develop mucositis rises when a patient receives both chemotherapy and radiotherapy. The incidence and the severity of oral ulcerative lesions vary in patients with different agents and therapeutic regimen [15]. Besides the overall clinical manifestations such as mucosal congestion, edema, and severe pain, co-infection may affect these patients' oral intake and disturb the smooth progress of chemotherapy. Co-infection may progress into a more severe systemic infection and cumulatively threaten the lives of the patients [11]. Treatments using granulocyte colony-stimulating factor, keratinocyte growth factor, honey intake or low-level laser therapy have been proposed as preventive measures for chemotherapy induced ulcers however a consensus regarding the most effective preventive option is still not established [10]. Among these preventive options, the only drug approved both by Food and Drug Agency (FDA) and European Medical Agency (EMA) is palifermin, and it is a keratinocyte growth factor. It is advised to administer to patients undergoing high doses chemotherapy and radiotherapy prior to their oncologic treatment. Once oral ulcerations develop, it is important to prevent serious nutritional deficiencies due to inadequate food intake and consider parenteral nutrition options [15]. Current guidelines suggest morphine to provide analgesia for pain in these patients [16]. Moreover "magic" mouthwashes have also been formulated containing anesthetics, antacids and diphenhydramine. Formulations with steroids and anti-mycotics are also available [17].

Necrotizing sialometaplasia is a solitary benign condition due to an inflammatory reaction of salivary glands. The true etiology is still unknown however local infarction due to ischemia of the salivary tissue is blamed. Mostly these lesions occur on the posterior palate but may rarely observed on the lower lip, retromolar pad, sublingual region, tongue and the larynx. Clinically necrotizing sialometaplasia manifests as a crater like ulcer with indurated borders. Although it is a self-limiting condition, complete healing may take up to 7 weeks [1]. During this period, patients may aid supportive treatments focused on pain control. Necrotizing sialometaplasia may mimic salivary gland tumors, thus physicians should always question the evolution time since in most cases salivary gland tumors do not present such short evolution times like necrotizing sialometaplasia [18].

Primary herpetic gingivostomatitis is a viral condition due to Herpes Simplex Virus (HSV). It usually occurs in children younger than five years. Oral ulcerative lesions associated with primary herpetic gingivostomatitis develop as multiple pin-headed vesicles which rupture. These small lesions may merge and manifest as larger ulcerations. Systemic symptoms such as fever, nausea, anorexia, submandibular lymphadenopathy, halitosis and dysphagia are also noted [1]. Bed rest, fluids, soft diet and antipyretics are suggested for the systemic manifestations of primary herpetic gingivostomatitis. In order to reduce the spread of infection to other sites, patients must be discouraged from touching the ulcerative areas. Systemic antiviral therapies may be considered in severe cases or for immunocompromised patients [19].

Herpes zoster infection is a secondary viral condition due to Varicella Zoster Virus (VZV). Clinically it is a painful condition with vesicular eruptions both on the skin and the mucosa. Symptoms are unilateral with extreme pain along the course of the nerve [20]. The involvement of the trigeminal nerve is rare but painful, with clustered ulcers of less than 5 mm in diameter. Depending on the involvement of specific nerves, these ulcers may appear on the hard palate, buccal gingivae or tongue in a characteristic unilateral pattern. Antiviral medicine may be required to manage the herpes zoster infection whereas the oral ulcerations are self-limiting and usually heal within two weeks [1].

Herpangina and hand-foot-mouth disease are both self-limiting and mild viral conditions caused by coxsackievirus commonly affecting children. Herpangina clinically manifests with sore throat, fever, blisters and ulcers involving the palate, oropharynx and tonsillar pillars [1, 8]. Posterior involvement of the oral cavity may help alarm the physicians in diagnosing herpangina. Hand-foot-mouth disease differs from other lesions since it simultaneously involves the extremities and oral cavity [8]. Ulcerative lesions related to hand-foot-mouth disease usually involve the tongue, hard and soft palate, and the buccal mucosa. Both diseases are similarly managed targeting analgesia and fever control. Currently, there are no available medical treatments against coxsackievirus infections [1].

Erythema multiforme is an autoimmune mucocutaneous condition with varying etiologic factors. Although oral ulcerative lesions are not the only oral symptoms, several oral manifestations such as macules and bullae are observed in almost 70% of patients with erythema multiforme [1, 21]. Similar to viral infections, erythema multiforme also presents with generalized symptoms like fever, lymphadenopathy, headache, malaise, cough, and sore throat. Oral ulcerative lesions associated with erythema multiforme are usually large, multiple and confluent. Management depends on the severity of the condition. Mild forms usually heal within 10–20 days. Liquid diet is suggested, analgesics or antipyretics are prescribed, and local wound care is applied if necessary [1].

Acute necrotizing ulcerative gingivitis (ANUG) is a bacterial opportunistic infection. The most common etiological factors are *Fusobacterium* and *Prevotella* species [22]. It is a painful and destructive gingival condition that specifically affects the interdental gum tissue. Clinically three essential findings help physicians in an accurate diagnosis which are (a) halitosis, (b) rapid onset, and (c) ulceration and necrosis of the interdental papillae that look like punched out, crater-like lesions. ANUG is often associated with poor oral hygiene, low immune system, nutritional deficiency, smoking or psychological stress [23]. Proper ANUG treatment should focus on the management of the acute symptoms and the prevention of further tissue destruction. Debridement of superficial gingival plaques and calculi at the necrotic lesions along with a prescription for 0.12% chlorhexidine gluconate mouth rinse twice daily should be considered initially. Signs of systemic involvement are fever, malaise or lymphadenopathy [22]. Due to its anaerobic activity, the first drug choice is metronidazole 250 mg, three times daily; however, penicillin, tetracyclines, clindamycin, amoxicillin, and amoxicillin with clavulanate also show acceptable results and may be considered. On the contrary, topical antimicrobials are not recommended [23]. Simultaneous antifungal agents should be considered in immunosuppressed patients along with the antibiotic therapy. Once the acute phase is managed, scaling and root planning along with proper oral hygiene maintenance should be established. Management of any predisposing factors should not be disregarded. Additional periodontal surgical procedures such as gingivectomy or gingivoplasty may be considered on a case-by-case basis [22].

Oral hypersensitivity reactions may be associated with a range of allergens including food, medications, mouthwashes, gums, toothpastes, restorative or cosmetic materials. Clinically these reactions may manifest as mucosal ulcerations or lichenoid reactions (**Figure 2**). Ulcerations usually have irregular borders and a red halo. Other oral symptoms may include erythema and edema of the oral structures or white patches and plaques [24]. Itching of the oral and pharyngeal tissues may or may not be present [1]. Clinical data recording is crucial in these patients. In order to accurately identify the allergens, the patch test is considered the gold standard. It is recommended to order a patch test for all patients when a hypersensitivity reaction is suspected to spot the true etiological factor [25]. Once the etiology is revealed, elimination of this causative agent often results in the resolution of the symptoms usually within two weeks [24]. Patients may aid from topical corticosteroids either as an ointment or mouthwash during this period especially if they present with severe symptoms [26].

Plasma cell stomatitis or *plasma cell mucositis* is a rare benign condition. Although its true etiology is still debatable, several theories consider this entity also as a hypersensitivity reaction but with polyclonal plasma cell infiltration [27]. Clinically epithelial sloughing, desquamation and swelling may be observed besides ulcerations (**Figure 3**). It may affect anywhere on the oral mucosa but the gingivae is the most affected site [1]. Chewing gums, cinnamon, qat (a native plant in eastern Africa and Arabia), toothpaste or flavored mints have been suggested as possible etiologic factors but a specific causative agent is seldom identified [27–29]. Plasma cell

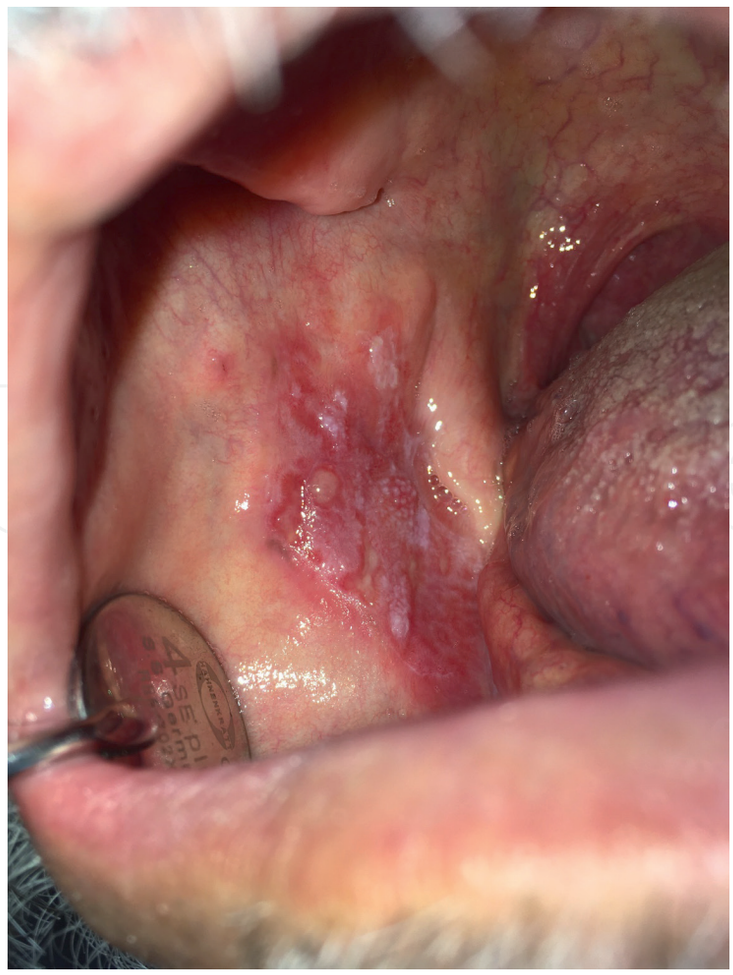

Figure 2.
Oral hypersensitivity reaction, three days after switching to a new brand of toothpaste.

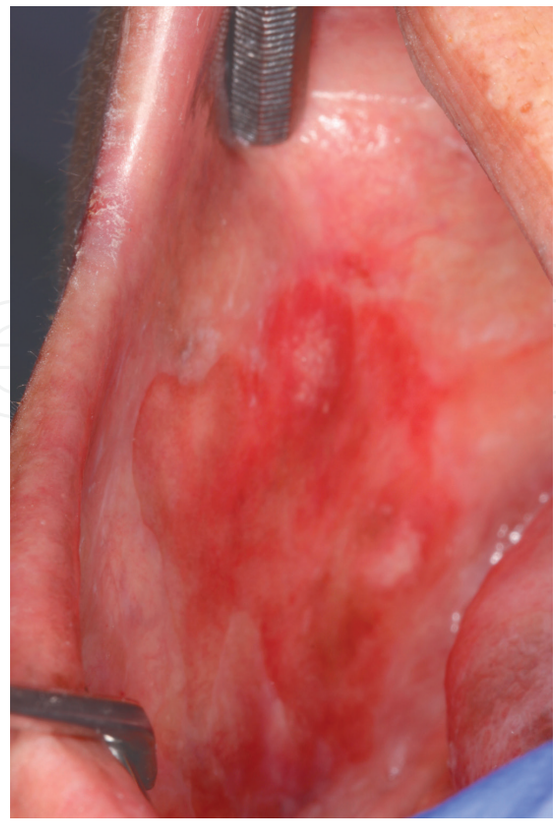

Figure 3.
Severe epithelial sloughing and erythema on a patient with plasma cell stomatitis.

stomatitis is managed with corticosteroids, either topical, intralesional or systemic, with additional antimicrobial medications depending on the systemic symptoms of the patients. Although complete regression is rare, most patients experience disease stabilization. Plasma cell stomatitis is a rare condition however clinically it may easily be confused more common benign and neoplastic conditions of oral cavity.

3. Chronic ulcerative lesions

Chronic ulcerative lesions have a slower onset than acute ulcers and last for more than two weeks. Several vesiculobullous entities, lupus erythematosus, tuberculosis, some mycoses, eosinophilic ulcers and oral cancer are among the most common conditions associated with chronic oral ulcerative lesions [6].

Drug induced oral ulcers are associated with mycophenolate (immunosuppressant), tiotropium (anticholinergic bronchodilator), clopidogrel (platelet aggregation inhibitor), nicorandil (vasodilator), bisphosphonates, protease inhibitors, some antimicrobials and analgesics, antirheumatics and several antihypertensives such as labetalol, enalapril or captopril [30]. This type of ulcerations usually presents with single, isolated ulcers with an erythematous halo. Most commonly the lateral side of the tongue is affected. Once the drug is discontinued, the lesions tend to disappear however it is not always achievable. Drug induced ulcers are also resistant to usual treatments [6].

Erosive lichen planus is a subtype lichen planus, a chronic condition which affects both the skin and the mucosal tissues. It is associated with the attack of cytotoxic T-cells on basal keratinocytes, which results in the areas of atrophy, erosion or

ulcerations [6]. The World Health Organization considers lichen planus as a premalignant lesion with 1–5% chance of malignant transformation to oral squamous cell carcinoma. Erosive and atrophic forms are particularly considered at high-risk [31]. The most characteristic presentation of lichen planus is the Wickham's striae, which are white, lace-like keratotic mucosal configurations, commonly found bilaterally on the buccal mucosa (**Figure 4**) [32]. Several subtypes of lichen planus may simultaneously manifest in the oral cavity. Erosive lichen planus is one of the painful subtypes due to the ulcerations. These ulcerative lesions are usually covered with a pseudo-membrane and are erythematous (**Figure 5**) [1]. Once lichen planus is confirmed with a biopsy, corticosteroids are prescribed as an initial treatment. Drug resistance is common particularly in erosive lichen planus, thus topical immunosuppressant therapies, such as tacrolimus, aid in the management of this condition via inhibiting cytotoxic T-cell mediated response [6].

Pemphigus vulgaris is an autoimmune vesiculobullous mucocutaneous disease due to an IgG reaction against desmogleins which are specific proteins in desmosomes [6]. Almost 90% of the patients experience oral symptoms and in more than half of the cases these are the initial signs of the disease [8]. Clinically oral lesions in

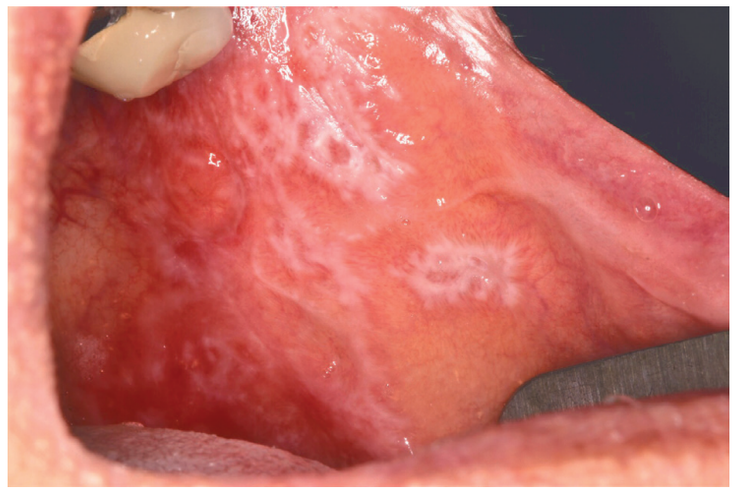

Figure 4.
Wickham's striae: The characteristic white, lace-like keratotic configurations seen in lichen planus.

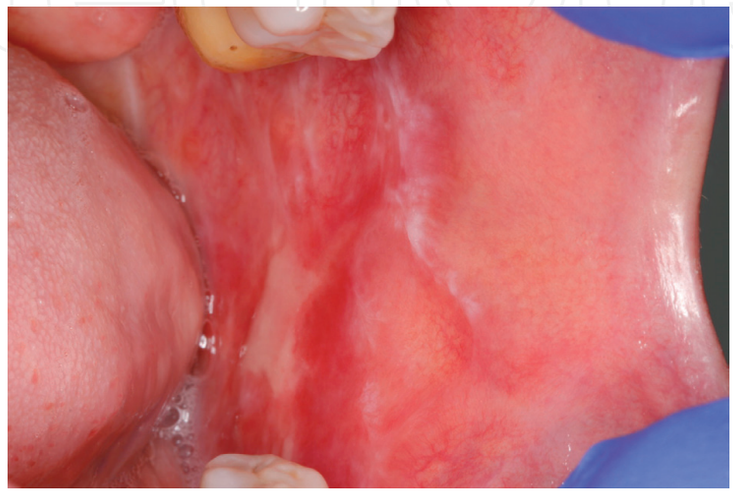

Figure 5.
Erosive lichen planus with an ulcerative area covered with a yellowish white pseudomembrane.

pemphigus vulgaris start as a bulla which quickly raptures in even a slight insult and results in a shallow irregular ulcerative lesion which endures for a long period of time and ultimately involves larger areas of the oral cavity [1, 8]. Ulcerative lesions of pemphigus vulgaris are painful and sometimes bleeding, and they heal with difficulty [8]. Buccal mucosa, palate and the gingival tissues are most commonly affected, and gingival involvement usually manifests as desquamative gingivitis [1]. Biopsy, and direct or indirect immunofluorescence studies confirm the diagnosis. Intraepithelial presence of Tzanck cells is a useful diagnostic sign for pemphigus vulvaris [6]. High dose systemic corticosteroids are used in the treatment of pemphigus vulgaris [1].

Mucous membrane pemphigoid or *cicatricial pemphigoid* is another autoimmune vesiculobullous disease that presents with subepithelial bullae which evolve spontaneously and rupture easily, resulting in painful ulcerative areas [6]. Bleeding into bullae results in blood blisters which are among the diagnostic features of mucous membrane pemphigoid [1]. Skin, ocular mucosa, esophagus, nasopharynx and larynx may also be involved besides the oral mucosa. Lesions of mucous membrane pemphigoid are chronic and persistent, thus often heal with a scar (cicatrix) which is particularly observed in lesions of the eye [33]. Contrary to pemphigus vulgaris, palatal mucosa is the most affected area within the oral cavity [6]. Buccal mucosa and the gingiva may also be affected. Gingival lesions in form of desquamative gingivitis may present as the only symptom of mucous membrane pemphigoid in some patients. Depending on the severity of the disease, mucous membrane pemphigoid is initially treated with either topical or systemic corticosteroids, and with dapsone in case of ocular involvement [1].

Lupus erythematosus is another autoimmune disorder of the connective tissue. Clinically oral lesions of lupus erythematosus may include areas of well-demarcated erythema, erosion or ulcerations, which tend to bleed. Whitish striae, similar to those seen in the oral manifestations of lichen planus, may also be present on the oral mucosa. Striae in lupus typically involves the hard palate, whereas in lichen planus these lesions are often bilaterally found on the buccal mucosa [6, 32]. Literature contains reports of oral lupus lesions transforming to oral squamous cell carcinoma, therefore it is crucial to regularly monitor and record the symptoms of these patients [34]. Therapeutic options for lupus erythematosus range from antimalarials to non-steroidal anti-inflammatory drugs and glucocorticoids, which may be combined with conventional immunosuppressive agents. Lately targeted therapies such as belimumab or rituximab are also gaining attention [35].

Linear IgA disease is also an autoimmune mucocutaneous condition that affects the sub-epithelium. Most patients with linear IgA disease are between 60 and 70 years old, but it may also affect the children. Oral lesions vary from vesicles to painful ulcerations or erosions mostly on the hard or soft palate. Topical or systemic corticosteroids or dapsone may be prescribed depending of the resistance and severity of the lesions [1].

Tuberculosis is a bacterial chronic granulomatous disease. Although rare, some tuberculosis patients may experience oral lesions which clinically manifest as solitary, deep, irregular and painful ulcers commonly on the lateral side of the tongue. These ulcers have a rounded rolled border. Final diagnosis is made via a tissue biopsy [1, 6].

Mycosis-related ulcerative lesions generally affect immunocompromised or uncontrolled diabetes patients, and present secondary to other infections. Clinical manifestations of different kinds of fungi may vary from painless or painful ulcers with indurated borders, areas of erythema, nodules, granuloma formation or areas of necrosis [1, 6, 36]. It is important to make a histologic evaluation via biopsy with

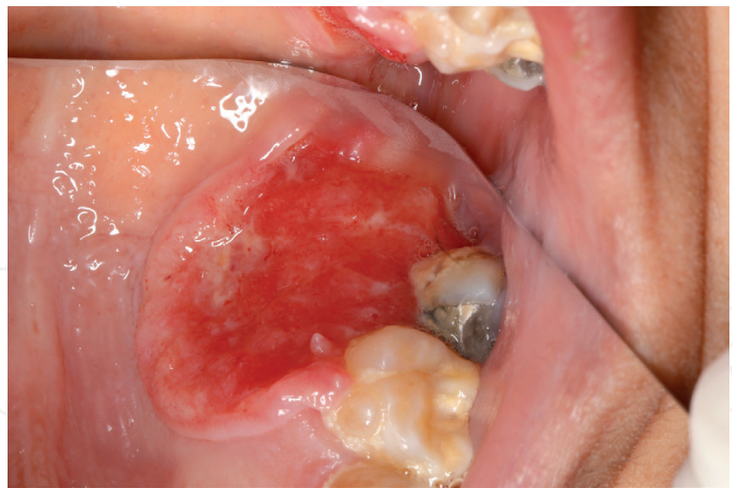

Figure 6.
Typical "crater like lesion with rolled borders"-look on a malignant ulcerative lesion of the hard palate.

specific stains to accurately diagnose mycoses because the oral symptoms of fungal infections may easily be confused with malignancies. The choice of treatment depends on the type of mycosis and may include antifungal medications with or without surgical intervention [36].

Eosinophilic ulcer or *traumatic ulcerative granuloma with stromal eosinophilia* is a benign, solitary ulcer which usually affects patients between fourth and sixth decades of life [1]. Its etiology is not well determined but it is associated with trauma in nearly half of the patients [6]. Viral and toxic agents, eosinophilic cytokines or chemotactic factors, mast cells or other cell-mediated immunity-related factors have also been suggested in the literature. Clinically an eosinophilic ulcer develops rapidly and has elevated borders with a white-yellow fundus [37]. Although it is a self-limiting condition, it heals very slowly and may easily mimic malignancies clinically. Eosinophil-rich inflammatory cell infiltrate also consisting of lymphocytes and mast cells help exclude the possibility of a malignancy [6, 37]. These solitary lesions usually respond to surgical excision with a rare recurrence rate. Other treatment modalities include intralesional or oral corticosteroids, topical antibiotics or cryotherapy [1].

Malignant ulcers may include epithelial neoplasms, solid tumors like lymphomas or minor salivary gland malignancies. Oral squamous cell carcinoma is the most common malignancy in the oral cavity [8]. It may present as a red white, exophytic, endophytic or ulcerative lesion [6]. Ulcerative lesions are usually asymptomatic and progressive, with a crater-like appearance and rolled, indurated borders (**Figure 6**) [1]. Biopsy is the only reliable method of diagnosis, and the treatment options vary depending on the severity of the disease. Smoking is one of the main risk factors for oral squamous cell carcinoma, therefore these patients must be educated properly and monitored closely for any suspicious lesion [6].

4. Recurrent ulcerative lesions

Recurrent aphthous stomatitis (RAS) is painful condition of the non-keratinized mucosa of the oral cavity. It is the most common inflammatory disease of the oral mucosa [1]. RAS has three forms: minor, major and herpetiform. Minor type consists of ulcers with less than 1 cm diameter, whereas the ulcers are larger than 1 cm, long-lasting and they heal with scarring in the major type. Herpetiform type consists

of ulcers with less than 2 mm diameter, but the lesions are numerous and extremely painful [1, 3]. Clinically, round and shallow ulcerations occur repeatedly. These ulcers may be solitary or multiple, covered by fibrin and with an erythematous border [1, 8]. Although the true etiology is still unclear, it has been associated with stress, hormonal imbalances, several systemic diseases, certain vitamin or mineral deficiencies [3]. In order to provide a cause-based treatment rather than palliative and temporary management options, it is essential to determine the true cause of RAS. Among the most common causes, iron, zinc, vitamin B12 and folic acid deficiencies, immune disturbances such as either HIV or non-HIV immunodeficiencies, gastrointestinal diseases such as celiac, gluten-sensitive enteropathies, Crohn's or ulcerative colitis, or periodic fever-aphthae-pharyngitis-adenitis syndrome should be questioned, and medical tests should be ordered accordingly. Pain management may be achieved using topical, intralesional or systemic corticosteroids, immunosuppressants or pentoxifylline [3].

Recurrent herpetic stomatitis is an oral infection caused by herpes simplex virus and may either manifest as *recurrent herpes labialis*, which affects the lips, or *recurrent intraoral herpes*, which is confined mainly to the keratinized mucosa, especially the hard palate [38]. Low immunity, stress, ultraviolet light, cold weather, hormonal fluctuations or trauma may trigger these lesions [1]. Recurrent intraoral herpes starts as vesicles on the oral mucosa which often rupture and lead to ulcerative lesions. Patient history and clinical examination are important to achieve a correct diagnosis. Once the diagnosis is made, patients should be educated on the contagious nature of the disease. Palliative treatments include ice or lanolin applications, topical or systemic antiviral medications. Prophylactic use of sunscreen with sun protection factor (SPF) 15 or higher may be considered for patients suffering from recurrent herpes labialis [38].

Herpes-associated erythema multiforme is a challenging diagnosis which requires a through patient history and clinical evaluation. Erythema multiforme (EM) is a reactive mucocutaneous disorder usually due to hypersensitivity to drugs or other allergens [39]. It may also be induced by other infectious agents like the herpes simplex virus [1, 40]. Herpes-associated erythema multiforme makes up almost the quarter of patients with EM. Herpes-associated EM may proceed simultaneously with or within several weeks after herpes simplex infection [41]. Hemorrhagic crusts on the lips and target lesions on the skin are pathognomonic signs that help make a diagnosis of erythema multiforme [39]. Oral lesions present with macules, blisters or ulcerations. Bleeding and the involvement of the non-keratinized mucosae are common [40]. EM, with mild symptoms, is managed by local wound care, topical anesthetic or analgesic agents, whereas patients with more severe symptoms require oral antihistaminic medications and topical corticosteroids. Herpes-associated EM may successfully be managed with systemic antivirals, if prescribed early. Recurrences are seen in almost 20–25% of patients with a rate of 2–24 recurrences per year [41].

Cyclic neutropenia is a lethal condition due to defects in neutrophil maturation which lead to a periodic decrease in neutrophil counts. Gene mutations have been blamed in the etiology of cyclic neutropenia [8, 42]. Recurrent cycles of neutropenia may range from 14 to 35 days and the duration of symptoms also vary between patients [42]. Fever, sore throat, cervical lymphadenopathy, gingivitis, oral ulcerations, tonsillitis, fatigue, otitis media or skin infections are among the most common manifestations of cyclic neutropenia. Ulcers in cyclic neutropenia may either be solitary or multiple, and they heal with scarring [8, 42].

Behçet's disease is a systemic immune-mediated vasculitis. The classic triad of Behçet's disease includes oral and genital ulcers, ocular lesions such as uveitis or

retinal vasculitis, and skin lesions mostly consisting of folliculitis-like rashes, ulcers or erythema nodosum [1, 43]. Recurrences occur at least three times a year. Oral ulcers are present in more than 90% of patients and may sometimes precede other symptoms. The ulcers may be shallow or deep, with slightly raised erythematous borders. They may appear anywhere within the oral cavity and heal spontaneously [44]. Proper management of Behçet's disease should focus on improving the quality of life and maintain the remission of lesions. In case of oral ulcers, pain relief and anti-inflammatory applications are aimed. Although there is no gold standard treatment or management method for oral ulcers in Behçet's disease, antimicrobial mouthwashes, laser treatments, topical corticosteroids, or systemic treatment options including colchicine, azathioprine or thalidomide may be considered [45].

5. Conclusions

Cause-based treatment options are more beneficial than palliative management options. Therefore it is crucial for physicians to make a sound clinical examination and take a through patient history [3]. Biopsy should be considered if an ulcerative lesion with an unknown etiology shows no signs of healing after two weeks, or if the lesions is not responsive to a treatment aimed at a probable known etiology. Ulcers of less than 5 mm diameter are advised to undergo an excisional biopsy, whereas for larger ones an incisional biopsy is suggested [6].

Conflict of interest

The author declares no conflict of interest.

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