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Oral Manifestations of Dermatological Disorders.

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ABSTRACT

Dermatological diseases, besides involving the skin and its appendages may also involve the oral cavity. The lesions of oral cavity in dermatological disorders deserve special attention, considering that they may be the presenting clinical feature or the only sign of these disorders. Moreover, oral mucosal lesions in skin diseases can be life-threatening and also affect the quality of life in terms of pain, discomfort, social and functional limitations. Various dermatological disorders of diverse etiologies like infections and genodermatosis are associated with oral lesions but pemphigus vulgaris, lichen planus and candidiasis are the most common ones. Oral mucosal lesions may present to a dermatologist as well as a dental surgeon, thus improving the knowledge about them in both the settings will strengthen and enhance interdisciplinary and multisectoral approach and lead to better management of such patients.

INTRODUCTION

Oral cavity encompasses a diverse group of anatomical structures, including teeth and oral mucous membranes. An oral mucosal lesion (OML) is defined as any abnormal change or any swelling on the oral mucosal surface [1]. It may be a result of local pathology or secondary to other systemic disease, including those of skin. In oral medicine, dermatological diseases have significance as OML may be primary clinical feature or the only sign of these disorders. A prevalence of 35% of OML in patients affected with dermatological conditions has been observed. Various groups of dermatological diseases associated with OML are as follows:

- Infections
- Vesicobullous disorders
- Lichen planus and other lichenoid disorders
- Collagen vascular diseases
- Vasculitic
- Genodermatosis
- Miscellaneous

Pemphigus vulgaris, lichen planus, candidiasis and recurrent aphthous ulcers were the most frequently diagnosed conditions [2,3].

Infections

Herpes simplex

Herpes simplex is caused by the herpes simplex virus (HSV). There are two major antigenic types, of which type 1, is classically associated with oral mucosal lesions. Primary infection is often subclinical [4]. When clinical lesions develop, herpetic gingivostomatitis is the most common clinical manifestation. Most cases occur in children and begin with fever, malaise and excessive dribbling. The gums are swollen and bleed easily. Vesicles presenting as white plaques and ulcers with a yellowish pseudomembrane are seen throughout oral mucosa [5].

Recurrences occur in 30–50% of cases of oral herpes and do not affect the buccal mucosa, but labial lesions are common [4].

Varicella zoster virus

The varicella zoster virus (VZV) is the cause of both varicella and zoster.

Varicella

After an incubation period of 14–17 days, fever and malaise, is followed by the development of papules in crops which very rapidly become clear, unilocular vesicles. In 2–4 days a dry crust forms, soon separates and heals without scarring. Similar vesicles are common in the mouth, especially on the palate, and are occasionally seen on other mucous membranes [6].

Zoster

The first manifestation of zoster is usually pain, followed by onset of eruption comprising of closely grouped red papules, rapidly becoming vesicular, in a dermatome. Mucous membranes within the affected dermatomes are also involved. Zoster of the maxillary division of the trigeminal nerve produces vesicles on the uvula and tonsillar area, whilst with involvement of the mandibular division; the vesicles appear on the anterior part of the tongue, the floor of the mouth and the buccal mucous membrane. In orofacial zoster, toothache may be the presenting symptom [7].

Herpangina

Herpangina is a specific infection, caused by group A coxsackieviruses of types 2, 3, 4, 5, 6, 8 and 10 and group B type 3, mainly affecting children. Fever of sudden onset, is followed, by sore throat and dysphagia. Up to 15 or 20 tiny vesicles, 1–2 mm in diameter, with a vivid red areola, develop on the pharynx, tonsils, the pillars of the fauces, the uvula and soft palate. They erode to leave ulcers, which heal in 4 or 5 days.

Hand, foot and mouth disease

The characteristic syndrome, seen in children, has usually been associated with coxsackie A16, but outbreaks have been caused by A5, A10 and human enterovirus 71. The disease usually presents as painful stomatitis. The oral vesicles are large, irregularly distributed over the palate, buccal mucous membrane, gums and tongue and ulcerate rapidly. Characteristic skin lesions are small, pearly grey vesicles with a red areola, most commonly occurring on the sides or backs of fingers and toes [8].

Oral hairy leukoplakia

This is an AIDS-associated lesion presenting as white plaques on the sides of the tongue occurring as a consequence of an opportunistic infection with EBV. It is also reported to occur in patients receiving immunosuppressive therapy and occasionally in immunocompetent individuals [9]. It presents as a white patch, usually seen on the parakeratinized mucosa of the tongue, frequently bilaterally. The lesions are corrugated or have a shaggy or hairy appearance, mostly symptomless [10].

HIV Infection

Skin disease may provide the first suspicion of the diagnosis of HIV infection and is also a prognostic indicator of the development of AIDS and overall survival [11]. Acute primary HIV infection presents clinically as a viral exanthem like illness 1–6 weeks after exposure. Transient intraoral redness, xerostomia, erosions and ulcers, candidosis and salivary gland swelling are all described [12].

Dermatological manifestations of HIV infection are diverse consisting of infections, inflammatory disorders and malignancies. Oral symptoms and signs are also common in established HIV infection [13].

Oral candidosis is very common in HIV-positive individuals and almost universal in AIDS [14]. HSV infection is common in and around the mouth. Hairy leukoplakia has emerged during the HIV epidemic [13]. Just over 1% of HIV-infected individuals have oral HPV infection. Distressing mouth ulceration occurs frequently. *Candida*, *Pseudomonas* and *Staphylococci*, causes severely symptomatic perioral ulceration complicated by pain, bleeding and inability to feed [15]. A necrotizing ulcerative stomatitis has also been described²⁶ as has cancrum oris (noma) [27]. Severe periodontal disease is also not unusual [13]. Kaposi's sarcoma occurs frequently in the mouth, often the palate. It appears as red patches, plaques or nodules. Other problems that can affect the oral cavity include petechiae from thrombocytopenia, hyperpigmentation and oral labial melanotic macules [18], oropharyngeal cancer [19], lymphoma, and the side effects of radiotherapy and drugs. IFN, foscarnet and zalcitabine can cause mouth ulceration [20,21].

Oral candidosis

Candidosis is an infection caused by the yeasts of the genus *Candida*. Superficial infections of the mucous membranes and skin are most important. Mucocutaneous candidiasis has a wide spectrum of clinical presentations [22]

- Acute and chronic pseudomembranous candidosis (oral thrush;) [23] characteristically presents as a sharply defined patch of creamy, crumbly, curdlike white pseudomembrane, which, when removed, leaves an underlying erythematous base.
- Acute erythematous candidosis ('antibiotic sore tongue') [24] is characterized by marked soreness and denuded atrophic erythematous mucous membranes, particularly on the dorsum of the tongue.
- Chronic erythematous candidosis (denture stomatitis) [25] is seen in denture wearers and children wearing orthodontic appliances, in the form of soreness.
- Chronic hyperplastic candidiasis (*Candida* leukoplakia) [26] occurs in form of very persistent, firm, irregular white plaques.
- Chronic nodular candidosis is a rare form, with cobbled appearance of tongue.
- Angular cheilitis (angular stomatitis; perleche) [27] presents as soreness and cracking at the angles of the mouth.
- Median rhomboid glossitis [28] is characterized by a diamond-shaped area on the dorsum of the tongue with loss of papillae.

Syphilis

Is a chronic sexually transmitted infectious disease caused by *Treponema pallidum*. In primary syphilis besides the characteristic genital chancre and inguinal lymphadenopathy, extragenital indurated ulcers may be found on the lips, tongue and tonsils as a result of kissing, cunnilingus or fellatio.

The secondary stage of the disease is characterized by recurrent activity of the disease, with mucocutaneous as well as systemic manifestations. The most commonly observed clinical presentation (80%) is a generalized, non-pruritic papulosquamous eruption. Mucosal lesions range from small, superficial ulcers that resemble painless aphthae to large gray plaques or oval mucous patches, which coalesce to form 'snail-track' ulcers. Sharply defined, round or oval lesions devoid of papillae on tongue and split papules at the oral commissures are also seen.

Late syphilis has variable range of manifestations. Approximately one-half of patients with tertiary syphilis have "benign" late syphilis with the development of gummas. Gummata attack the palate, with tissue destruction that may lead to loss of tissue and scarring. They may also cause diffuse interstitial glossitis, with fissuring and necrosis.

Lasting changes in the shape of scars and defects caused by congenital infection called stigmata have diagnostic importance [29,30]. One of the most common and characteristic stigmata is deformity of the upper, central incisor teeth [31]. These so-called 'Hutchinson's teeth' are due to defective development of permanent teeth buds. The incisors are conical or barrel shaped, with a degree of notching at the free edge. Some are described as 'screwdriver teeth'.

Another deformity, not so characteristic, is the 'mulberry molar'—usually the first molar—which has a flat, occlusive surface with only poorly enamelled rudiments of the usual cusps.

Leprosy

Leprosy is a chronic infectious disease with prominent involvement of the skin and nerves that is caused by the bacillus *Mycobacterium leprae*. There is a wide spectrum of clinical findings in leprosy. Lesions of oral mucosa occur as papules on lips and nodules on palate (which may perforate), uvula, tongue and gums. The upper incisor teeth loosen or fall out [32].

Leishmaniasis

Leishmaniasis encompasses a spectrum of chronic infections caused by protozoans *Leishmania* and transmitted by sandflies from the genera *Phlebotomus* and *Lutzomyia*. Cutaneous leishmaniasis usually begins as a small, well-circumscribed papule at the inoculation site. This lesion may slowly enlarge over several weeks into an ulcerated or verrucous nodule or plaque. After a time period ranging from a few months to more than 20 years, some patients infected with *Leishmania* spp. (most commonly *L. braziliensis*; rarely *L. panamensis*, *L. guyanensis*) develop mucocutaneous disease. Oral mucosal lesions range from edema and infiltration of the lips to perforation of the palate. Similar involvement of nose is also seen. In some patients, there is extensive loss of tissue in both the mouth and nose, causing a characteristic "tapir face" known as espundia [33,34].

Vesico-bullous disorders

Pemphigus vulgaris

The term pemphigus describes a group of chronic autoimmune skin diseases characterised by the loss of cell-cell adhesion and widespread mucocutaneous blistering [35]. Essentially all patients with pemphigus vulgaris develop painful erosions of the oral mucosa. 50 to 70% of patients present with oral lesions and precede cutaneous lesions by months or may be the only manifestation of the disease. These painful erosions most commonly seen on buccal and palatine mucosa are of different sizes with an irregular ill-defined border and extend peripherally with shedding of the epithelium. The lesions may extend out onto the vermilion lip and lead to thick, fissured hemorrhagic crusts [36].

Paraneoplastic pemphigus

A distinctive form of pemphigus has been described in association with a variety of underlying neoplasms most commonly B-cell lymphoproliferative disorders but also thymoma, sarcomas and carcinomas³⁷ and with the use of fludarabine chemotherapy [38]. Patients have severe mucosal erosions and polymorphous cutaneous signs [37].

Mucous membrane pemphigoid

A chronic blistering disease of the mucosa that may involve the skin, and usually results in permanent scarring of the affected area, particularly the conjunctiva. Oral lesions occur in the majority of patients. In the mouth, vesicles or small blisters, which remain intact for some time, may be seen and when erosions form they are persistent and extensive. Desquamative gingivitis with eroded bleeding gums. Adhesions may develop between the buccal mucosa and the alveolar process and around the uvula and tonsillar fossae [39].

Epidermolysis bullosa

Inherited epidermolysis bullosa (EB), the prototypic mechanobullous disease, is characterized by the development of blisters following seemingly minor or insignificant trauma or traction to the skin [40]. Recurrent blisters, erosions, ulcers and scarring of mucous membranes including oral cavity is seen along

with ankyloglossia and microstomia. Dental enamel hypoplasia is associated with pitting of the surfaces of teeth. If untreated, these patients lose teeth during childhood due to excessive caries [41].

Connective tissue disorders

Systemic lupus erythematosus.

A systemic disease characterized by multisystem organ inflammation, most commonly the skin, joints and vasculature, and associated immunological abnormalities. Mucous membrane lesions occur in 26% of cases, usually on the palate (82%), buccal mucosa or gums, in active phases of the disease [42,43]. Lesions start as small erythematous or purpuric areas, which break down to form shallow and sometimes painful ulcers, with a dirty yellow base and surrounding reddish halo. Hyperkeratotic lichen planus-like plaques on the buccal mucosa and palate occur in 9%. The lips show slight thickening and roughness and redness, sometimes with superficial ulceration and crusting. Healing occurs with some scarring [42].

Systemic sclerosis

Systemic sclerosis (SSc, scleroderma) is an autoimmune connective tissue disease of unknown etiology that affects the internal organs, blood vessels and skin in the form of widespread cutaneous induration. Stiffness of lips and tongue is seen. Dental changes [44] occur in the form of widening of the periodontal membrane because of fibrosis, in approximately 30% of cases. Usually the whole root is involved, and the lamina dura may or may not be abnormal. Osteolysis of the mandibular angle and coronoid process occurs with equal frequency, and these osteolytic areas may fracture [45].

Sjögren's syndrome

Sjögren's syndrome (SjS) is an autoimmune disorder that affects secretory glands, in particular the lacrimal and salivary glands. The saliva is thick, mucoid and decreased in volume. The tongue is red, smooth and dry, and in severe cases there may be difficulty in swallowing dry food. Parotid duct narrowing and web formation may develop. Dental caries is often severe and progressive. The lips are red, dry and scaly. There are frequently cracks at the corners of the mouth. Chronic oral candidiasis is frequent. Recurrent episodes of swelling of salivary glands is common [46].

Lichenoid dermatosis

Lichen planus

Lichen planus (LP) is an idiopathic inflammatory disease of the skin and mucous membranes characterized by pruritic, violaceous papules that favor the extremities [47]. Mucous membrane lesions are very common, occurring in 30 -70%. Lesions confined to the mouth or with minimal accompanying skin involvement, are not uncommon, accounting for about 15% of all cases and, may lead to great difficulty in diagnosis. They are often referred first to a dental surgeon.

The buccal mucosa and tongue are most often involved.

Oral LP can appear in at least seven forms: atrophic, bullous, erosive, papular, pigmented, plaquelike and reticular. The most common and characteristic form of oral LP is the reticular pattern. It is characterized by bilaterally symmetrical, asymptomatic, slightly raised whitish linear lines in a lace-like pattern or in rings with short radiating spines on buccal mucosa. Gingival involvement is common and typically presents as chronic desquamative gingivitis. On the tongue, the lesions are usually in the form of fixed, white plaques, often slightly depressed below the surrounding normal mucous membrane. Ulceration and pigmentation of oral cavity are also seen [48].

Contact Stomatitis/ Contact Lichenoid reaction

Contact Stomatitis and cheilitis occurs due to numerous foods, food additives, and materials used in dentistry. Lipsticks and lipsalves are also implicated [49]. The clinical features of contact stomatitis are localized to the buccal mucosa or lateral borders of the tongue and appears as shaggy white or erythematous keratotic areas with or without peripheral striae [50], and they can resemble oral lichen planus. Lipstick cheilitis may present as persistent irritation and scaling or a more acute reaction with oedema and vesiculation.

Lesions disappear within a week of discontinuing the offending product. When contact stomatitis secondary to amalgam is suspected, patch testing is recommended and appropriate alternative dental materials, can be used to replace it [51].

Vasculitis

Kawasaki disease

This disease also called mucocutaneous lymph node syndrome, predominantly affects young children [52]. The onset is acute, with a high fever followed by a widespread exanthem on the limbs and trunk, swollen erythematous hands and feet and subsequent desquamation. All the mucosa and conjunctiva are injected. In the mouth, the lips are dry and fissured, the tongue appears red with prominent papillae (strawberry tongue) [53].

Behçet's disease

Behçet's disease, is a multisystem disease that is defined by the presence of oral aphthosis with at least two of the following: recurrent genital aphthae, cutaneous lesions, eye lesions (uveitis) and a positive pathergy test [54]. Aphthous stomatitis, the major criterion, is frequently the first symptom of Behçet's disease (65–70% of patients). In some, recurrent, severe aphthous ulceration dominates the clinical picture with absence of other criteria; they may represent a *forme fruste* of the disorder. Oral ulcers begin as an erythematous papule, which develops a yellowish pseudomembrane and then forms a painful non-scarring ulcer [55]. Primary cutaneous lesions are acral and facial sterile vesicopustules as well as purpuric papules [56].

Wegener's granulomatosis

WG is classically described as a triad consisting of systemic small vessel vasculitis, necrotizing granulomatous inflammation of both the upper and lower respiratory tracts, and glomerulonephritis [57]. The most common cutaneous manifestation of WG is palpable purpura on dependent skin sites. Oral ulcers are the second most common mucocutaneous sign of WG [58].

Genodermatosis

Tuberous sclerosis complex

Tuberous sclerosis complex (TSC) represents a genetic disorder of hamartoma formation in many organs [59]. The characteristic features of the syndrome are skin lesions in form of angiofibromas, periungual fibromas (Koenen's tumours), the shagreen patch and ash-leaf-shaped macules, mental retardation and epilepsy [60].

Fibromatous tumours are occasionally present on the gums and palate and rarely are found on the tongue, larynx and pharynx [61]. Small pits commonly occur in the tooth enamel in adult patients; although less obvious in the deciduous teeth, these pits have been used as an early diagnostic sign in children with TSC [62].

Ectodermal dysplasias

These are a group of inherited disorders that share in common developmental abnormalities of two or more of the following: hair, teeth, nails, sweat glands and other ectodermal structures. Hypohidrotic ectodermal dysplasia is the most common of the ectodermal dysplasias and is characterized by hypotrichosis, hypohidrosis, hypodontia, and distinctive facial features with relative frontal bossing and concave midface [63]. Skin is fine, smooth and dry with periorbital hyperpigmentation. A wide range of dental abnormalities may be associated, ranging from complete absence of teeth (anodontia) to sparse, abnormally shaped teeth. Dentition is delayed and the erupted teeth tend to be small, widely spaced and frequently conical or peg-shaped. The alveolar ridges are hypoplastic, which gives rise to full, everted lips [64].

Miscellaneous

Erythema multiforme, Stevens–johnson syndrome and Toxic epidermal necrolysis

Erythema multiforme presenting with characteristic targetoid lesions are related to infections (especially herpesvirus) and perhaps on occasion to drug reactions. In contrast, Stevens–Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) presenting as extensive bullous lesions and peeling of skin, are more closely linked to drug sensitivities, and may be regarded as severe variants of a single disease [65,66].

In erythema multiforme, lesions may involve the oral and genital mucous membranes in the minor form but more extensive mucous membrane involvement in the form of vesicles and erosions is seen in the major form [67]. SJS and TEN are severe illness of usually sudden onset, associated with marked constitutional symptoms and extensive involvement of skin in the form of targetoid, purpuric and bullous lesions and denudation covering less than 10% and more than 30% body surface area, respectively. There is significant involvement of mucous membranes. The oral mucous membrane shows extensive bulla formation followed by erosions and a greyish white membrane and the mouth and lips show characteristic haemorrhagic crusting [68,69].

Angio-oedema

This is a variant of urticaria characterized by swellings of the subcutaneous tissue. Almost any part of the body may be involved, but the commonest sites are the lips, eyelids and genitalia [70]. Itching is often absent. The lesions last for a few hours, or occasionally persist for 2–3 day. The angio-oedema especially mucosal lesions require quick management on the lines of anaphylaxis [71,72].

Sarcoidosis

A systemic granulomatous disorder of unknown origin that most commonly involves the lungs. Up to a third of patients develop skin lesions, most commonly as flat topped papules and plaques, varying in colour from yellow–brown to erythematous to violaceous [73]. Buccal lesions or tongue involvement are occasionally found. Nodules with a hyperpigmented halo, diffuse pale yellow plaques or ulceration may be found on the buccal mucosa, palate, larynx or tongue. Parotid gland enlargement may occur as a part of Heerfordt's syndrome [74].

Langerhans' cell histiocytosis (LCH)

LCH is a reactive condition in which a clonal population of cells of the Langerhans' cell accumulate in various tissues and cause damage. LCH can affect many different organs but the most characteristic presentation is with scalp involvement, being erythematous with greasy scales, and yellow-brown, scaly papules on trunk. The commonest presentation in the mouth is with periodontal involvement, affecting particularly the lower molar areas [75]. There may be destruction of the alveolar ridge with infiltration of the gums with LCH cells resulting in the teeth floating free from their sockets. Premature eruption of the teeth may be a presenting sign [76].

SUMMARY

To summarize, certain amount of skin lesions are strongly associated with oral lesions and could be neglected or misdiagnosed by dentists due to lack of information. Therefore, improving the knowledge about oral lesions both at the dermatology and the dental clinic will improve the management of such patients by strengthening interdisciplinary and multisectoral approach. Moreover, oral manifestations of skin diseases deserve special attention because they can be life-threatening and also affect quality of life in terms of pain, discomfort, social and functional limitations.

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