

REVIEW ARTICLE

**ORAL CAVITY- A SIGN OF SYSTEMIC
DISEASES**

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ABSTRACT

The oral cavity is a unique site, due to the company of hard and soft tissues in close approximation. It has various functions like respiration, speech, mastication and digestion. It is a chief entrance point for many pathogens in the body. The oral cavity might well be thought as porthole to the body because oral manifestations escort many systemic diseases. In a lot of instances, oral involvement precedes the appearance of other symptoms or lesions at other locations. These oral manifestations must be properly predicted if the patient is to receive proper diagnosis and referral for treatment. A dentist thus can regularly be exposed to such conditions and play a key role in the diagnostic process of various systemic diseases. Apt knowledge of these oral manifestations is essential for early diagnosis, treatment and referral of cases. This article is proposed as a general overview of conditions that have oral manifestations but also involve other organ systems.

INTRODUCTION

The mouth is a reflection of health or disease, a guard or early caution system. As the entryway to the body, a regular stream of invaders like bacteria, viruses, parasites, and fungi challenges the mouth. Various systemic diseases include oral manifestations. These lesions extend on the oral mucosa, tongue, gingiva, dentition, periodontium, salivary glands, facial skeleton, extra oral skin and other related structures. These oral finding must be properly acknowledged if the patient is to receive proper diagnosis and referral for treatment [1]. In a large number of cases, the oral symptoms or findings are the primary and sometimes even the only evidence of a particular disease like Koplik's spots occurring in the buccal mucosa which precede the cutaneous eruption of measles. In few cases, the oral symptoms or signs may analogous the complaints and clues somewhere else in the body. So the immediate development of an erosive lesion on the buccal mucosa near the angle of lips along with a butterfly rash on the face is diagnostic finding in lupus erythematosus. Lastly in other some cases the oral manifestations follow the occurrence of symptoms or sign in other parts of the body, like in pemphigus, where the bullae may

erupt on the skin days, before the oral ulcers occurs [2]. Therefore oral cavity is considered as an significant diagnostic area not just for the reason that it contains derivatives of all of the primary germinal layers but also it includes tissues not demonstrable wherever else in the body, so it is helpful in in diagnosing a number of systemic diseases just because of their oral manifestations[2,3]. This review article describes in detail about the oral manifestations of nutritional, hematologic, gastrointestinal, renal, cardiovascular, endocrine, metabolic and dermatologic disorders and their manifestation in the body.

Nutritional Deficiencies

Nutritional diseases are well thought-out to be the most common diseases, and also the most common diseases to go ignored. Due to rapid cell turnover of the oral mucosa, nutritional deficiencies may present earliest with oral manifestations the changes may occur in the color of the oral mucosa and also the papillae of the dorsum of the tongue in various nutritional deficiencies [4].

Table 1: Vitamin and other nutritional deficiencies and their oral manifestations.⁴

Vitamin & other nutritional deficiencies	Oral Manifestations
Vitamin A	Eruption rate is retarded, retarded alveolar bone formation, hyperplastic gingival epithelium followed by keratinization.
Vitamin D	Developmental anomalies of dentin and enamel, delayed eruption, and misalignment of the teeth in the jaws.
Vitamin D resistant rickets	There is often periapical involvement of grossly normal appearing deciduous or permanent teeth, followed by the development of multiple gingival fistulas. Radiographically there is abnormal alveolar bone pattern, cementum, and lamina dura around the teeth is absent or poorly defined.
Hypophosphatasia	There is loosening and premature loss of deciduous teeth, chiefly the incisors.
Vitamin K	Most common oral manifestation is gingival bleeding. Prothrombin levels below 35% result in bleeding after tooth brushing; and when below 20% result in spontaneous gingival hemorrhages.
Vitamin C deficiency (Scurvy)	There is inflammation of the interdental and marginal gingiva followed by bleeding, ulceration, foul breaths due to fusospirochetal stomatitis. Hemorrhages into and swelling of the periodontal membranes occur, followed by loss of bone and loosening of the teeth, which eventually exfoliate.
Riboflavin deficiency	Initially glossitis involving the tip and/or the lateral margins of the tongue, followed later by complete atrophy of all papillae. The tongue has a magenta color. Pallor, involving oral mucosa followed by cheilosis, maceration and fissuring at the angles of the mouth.
Niacin deficiency	Oral mucosa becomes fiery red and painful. Glossitis, pain, redness and ulceration begin at the interdental papillae and spread rapidly.

Hematological Disorders

The oral cavity may be the site of the major signs of blood dyscrasias. The manifestations may include hemorrhage, infections, and cellular infiltration of tissues. The acute leukemia's tend to produce more evident oral manifestations mainly the diffuse gingival hypertrophy. Gingival bleeding or accumulation of blood in tissues may come about secondary to

thrombocytopenia. Pallor of the oral mucosa, loss of lingual papillae, pain and burning sensation may arise secondary to anemia [5].

Anemia

Iron deficiency anemia is the common familiar hematologic disorder with characteristic oral manifestations including atrophic glossitis, mucosal pallor, and angular cheilitis. The oral manifestation of Plummer Vinson syndrome also includes dysphagia due to pharyngoesophageal ulcerations [6]. Oral finding seen with sickle cell anemia include mandibular salmonella osteomyelitis that results in areas of osteoporosis and erosion followed by osteosclerosis. Anesthesia or paresthesia of the third branch of trigeminal nerve, and asymptomatic pulpal necrosis may also happen. Associated dentofacial deformities seen radiographically by areas of decreased densities and coarse trabecular pattern most simply seen between the root apices of the teeth and the inferior border of the mandible [7].

Leukemia

Oral manifestations of leukemia include gingival hypertrophy, petechiae, ecchymosis, and mucosal ulcers and hemorrhage [8]. Sometimes the patient complains of symptoms related to mental

nerve neuropathy, called “numb chin syndrome,” [9]. Palatal ulcerations and necrosis may be sign of mucormycosis affecting the nasal cavity and the paranasal sinuses [10]. Septicemia may occurs due to bacterial infections of the oral cavity. Treatment of leukemia with chemotherapeutic agents can result in oral microsites [1].

Multiple myeloma

It is a plasma cell dyscrasia .In these disease there is overproduction of specific immunoglobulins. When multiple myeloma occurs in the oral cavity, it shows late manifestations and mostly mandible is affected. It causes swelling of the jaws, pain, numbness, mobility of teeth and pathological fractures [11]. It has the characteristic radiological finding of punched out lesions of the skull and jaw [12]. As the disease causes immunosuppression it may cause oral hairy leukoplakia and candidiasis [13, 14] .Amyloid deposits when occurs in the tongue may lead to macroglossia [15].

Gastrointestinal Diseases

Crohn’s disease

There is no straight time correlation between intestinal and oral lesions .Oral lesions come first than the intestinal lesions by years and

in some cases is the only manifestation of the disease [1]. Clinically, these patients present with diffuse swelling of one or both lips with associated angular cheilitis, hyperplastic rigid mucosa and “cobble stoning” of the buccal mucosa [16].The other manifestations include painful linear ulcerations in the buccal vestibule, painless localized swellings within the lips or face, tissue tags attached to the buccal mucosa, fissuring on the midline of the lower lip, gingival inflammation and cervical lymphadenopathy [17].

Ulcerative colitis

Ulcerative colitis has been associated with destructive oral ulcerations resulting from immune-mediated vasculitis [18]. These are similar to aphthous ulcers, but appear less frequently than lesions of Crohn’s disease. Pyostomatitis vegetans characterized by multiple painless intraepithelial micro abscesses connecting in linear or serpentine tracks mostly on the labial mucosa, soft palate and ventral tongue may be seen. Pyostomatitis gangrenosum is the extreme variant with large, long-lasting and destructive ulcers, which cause significant tissue scarring [19].

Celiac disease

This is a chronic intestinal disease caused by intolerance to gluten associated with poor

digestion and absorption of the majority of nutrients and vitamins, which may affect both developing dentition and oral mucosa [20]. Enamel hypoplasia is the most common manifestation in untreated celiac children and adolescents [21]. Incisors and permanent first molars are the most affected teeth, perhaps because the ontogenesis phase coincides with the active phase of the disease [22]. Hypocalcaemia during enamel formation and other systemic factors such as malnutrition and vitamin D and A deficiency may result in enamel hypoplasia[23].The main oral signs associated with celiac disease are angular cheilitis, glossitis, depapillated tongue and dry mouth[20]. Ulcers are the most common type of oral lesions presenting in a popular or erosive form, generally with an erythematous margin [24].

Psychiatric Disorders

Anorexia & bulimia nervosa

The dentists and dental hygienists may be the first health care providers to assess the physical and oral effects of anorexia nervosa and bulimia nervosa. The oral manifestations include dental erosion, traumatized oral mucosal membranes and pharynx, dry mouth, dental caries, periodontal disease, and soft tissue lesions [25]. More specifically, dental erosion

involves lingual erosion on the palatal surfaces of the maxillary teeth with a smooth, glossy appearance and increased tooth sensitivity. Also known as perimyolysis, this erosion is characterized by loss of enamel with rounded margins, a notched appearance of the incisal surfaces of the anterior teeth, amalgam restorations that appear as raised islands, and loss of contours on unrestored teeth. Self-induced vomiting may cause trauma to the soft palate and pharynx. Soft tissue lesions such as angular cheilitis, candidosis, glossitis, and oral mucosal ulceration may also occur, stemming from nutritional deficiencies [26].

Renal Disease

Uremic stomatitis has become relatively rare, seen mostly in cases of undiagnosed and untreated chronic renal failure. Painful plaques and crusts are distributed predominantly on the buccal mucosa, dorsum of the tongue, and floor of the mouth. This occurs when the intraoral concentration of urea exceeds 30 mmol/L.

Hemorrhagic diathesis from inhibited platelet aggregation may also play a role due to local hemorrhage, resulting in decreased vitality and viability of the affected tissues, thus allowing bacterial infection. There are two predominant types of uremic stomatitis. In Type I, there is a generalized or localized

erythema of the oral mucosa and a thick gray pseudomembranous exudate, which does not leave a bleeding or ulcerated base when removed. Additional findings may include pain, burning, xerostomia, halitosis, gingival bleeding, dyspepsia, or candida infection. Type II leaves ulceration if the pseudomembranous film is removed. This type may indicate a more severe form of stomatitis, secondary infections, anemia or underlying systemic hematologic disturbances caused by renal failure [27].

Cardiovascular Disorders

Medications used for management of hypertension have various oral manifestations. Diuretics cause oral dryness, adrenergic inhibitors cause oral dryness and ulcerations, calcium antagonists give rise to gingival overgrowth while ACE inhibitors may cause loss of taste and lichenoid reactions of the oral mucosa [28].

Metabolic and Endocrine Disorders

Oral manifestations may result from abnormal hormonal regulation. Manifestations of diabetes frequently occur in the oral cavity. These may include dry mouth, burning mouth syndrome, increased reactivity to local irritation of bacteria plaque, acute gingival inflammation, multiple periodontal abscess, delayed healing and secondary infection may be

present following minor trauma and oral treatments. Sex hormone imbalance can result in marked reaction to local irritations of oral tissues. Changes resemble gingivitis and periodontitis, with marked inflammatory reaction to bacterial plaque present in the oral cavity. Also hyperplastic tissue responses are commonly seen, resulting in soft tissue growths on the gum tissue. Hypo function of the adrenal cortex, resulting in Addison's disease, may present in accumulation of brownish melanotic pigment in a general fashion, or as blotches in the oral soft tissue [3].

Diabetes mellitus

There are many oral manifestations of diabetes mellitus, some having been described as early as 1862. About a third of diabetic patients complain of xerostomia, which may be due to an overall diminished flow of saliva and an increased salivary glucose level. Concomitant diffuse, nontender, bilateral enlargement of the parotid glands, called diabetic sialadenoses, may be seen in these patients. Xerostomia, results in increase susceptibility to opportunistic infections like *Candida albicans*. Other oral manifestation includes Erythematous candidiasis presenting as Central papillary atrophy of the dorsal tongue papillae, mucormycosis, benign

migratory glossitis, altered taste and burning mouth syndrome [29]. The increased glucose levels in the saliva and crevicular fluid in poorly controlled diabetes result in high incidence of dental caries. Poor healing, xerostomia with subsequent increased accumulation of plaque and food debris, higher susceptibility to infections, and pronounced hyperplasia of attached gingiva all contribute to the increased incidence of periodontal disease in diabetics [30].

Hypoparathyroidism

If the hyperparathyroidism develops early in life, during odontogenesis or tooth development, a pitting enamel hypoplasia and failure of tooth eruption may occur. The presence of persistent oral candidiasis in a young patient may be a signal for the onset of endocrinecandidiasis syndrome [31, 32].

Hyperparathyroidism

Radiographically loss of the lamina dura surrounding the roots of the teeth is an early manifestation of hyperparathyroidism, with alterations in the jaw trabecular pattern characteristically developing next. There is also a decrease in trabecular density, and blurring of the normal pattern resulting in a “ground glass” appearance on the radiograph. With persistent disease, “brown

tumor” of hyperparathyroidism may develop. Radiographically, these lesions are unilocular or multilocular well-demarcated radiolucencies, which commonly affect the mandible, clavicle, ribs and pelvis. They may be solitary, but more often are multiple. The long-standing lesions may produce significant cortical expansion [33].

Hypocortisolism

The patient may present with a variable degree of facial hirsutism. Pathological fractures of the mandible, maxilla or alveolar bone may occur upon low impact trauma due to osteoporosis. Healing of fractures as well as healing of alveolar bone and soft tissues after dental extractions is also delayed [34].

Hypoadrenocorticism

Hypoadrenocorticism results from insufficient production of adrenal corticosteroid hormones caused by destruction of the adrenal cortex, a condition known as primary hypo adrenocorticism or Addison’s disease. Orofacial manifestations include “bronzing” or hyperpigmentation of skin, especially predominant in sun-exposed areas and over pressure points. These skin changes are often preceded by oral mucosal melanosis. The diffuse or patchy brown macular pigmentation most commonly

occurs on the buccal mucosa, but can also occur on the floor of the mouth, ventral tongue, and other areas of the oral mucosa [35].

Dermatologic Diseases

In number of dermatologic diseases oral manifestations appear alone or prior to the general skin changes. The environment of the oral cavity is subject to significant local irritation and thus may present the most significant signs and symptoms of the condition.

Lichen planus

The oral manifestations of lichen planus may occur weeks or months before the appearance of the skin lesions. The oral lesions are characterized by presence of striae of Wickham, and the clinical presentation may range from radiating white striae to vesiculobullous, atrophic, or erosive form [4].

Psoriasis

Characterized by angular cheilosis, fissured tongue and benign migratory glossitis. Lesions involve the lips, buccal mucosa, palate, gingiva and floor of the mouth and appear as gray or yellowish-white plaques; as silvery white, scaly lesions with an erythematous base; as multiple papular eruptions, which may be ulcerated; or as

small, papillary, elevated lesions with a scaly surface [4].

Erythema multiforme

Oral manifestations include hyperemic macules, papules or vesicles, which may become eroded or ulcerated and bleed freely. The tongue, palate, buccal mucosa and gingiva are commonly involved [4].

Stevens Johnson's syndrome

Oral lesions may be extremely severe and so painful that mastication is impossible. Mucosal vesicles or bullae occur which rupture and leaves surfaces covered with a thick white or yellow exudate. The lips may exhibit ulcerations with bloody crusting and are painful [4].

Acanthosis nigricans

The tongue and lips are most commonly involved. There are papillomatous growths involving the dorsum of tongue, lips and buccal mucosa. Gingival enlargement is also seen [4].

Pemphigus

The bullae tend to rupture as soon as they form. The oral mucosa also exhibits Nikolsky's phenomenon and may be denuded by the peripheral enlargement of the erosions. Lesions are tender, bleed easily have ragged border and be covered by a white or blood tinged exudate. Extension

onto the lips with the production of crusting may occur. There may be profuse salivation, and the stench is overwhelming [4].

Cicatricial pemphigoid

It is vesiculo bullous lesions, showing relatively thick walled which may persist for 24 to 48 hours before rupturing and desquamating. When rupture they leave a raw, eroded, bleeding surface. The gingiva appears to be erythematous for weeks or even months after the original erosions have healed [4]. Ocular involvement is also a characteristic of Cicatricial Pemphigoid [28].

Epidermolysis bullosa dystrophica characterized by oral bullae which on rupturing result in pain and scar formation resulting in obliteration of sulci and restriction of the tongue. Dental defects consist of rudimentary teeth, congenitally absent teeth, hypoplastic teeth and crowns denuded of enamel [4].

Connective Tissue Diseases

Sjogren's syndrome

It is characterized by dry mouth (xerostomia), keratoconjunctivitis sicca, and other collagen diseases-often rheumatoid arthritis. Signs and symptoms include difficulty in chewing and mastication, altered taste sensation, difficulty with speech, mastication and denture use, an

increase in incidence of dental caries, especially around the cervical region of the teeth, and burning sensation of the oral mucosa. Xerostomia can be associated with fissured tongue, depapillation and redness of the tongue, cheilitis, and candidiasis. Bacterial parotitis, which is usually accompanied by fever and purulent discharge from the gland, may also occur [36].

Scleroderma

Scleroderma is a chronic disease characterized by diffuse sclerosis of the skin, gastrointestinal tract, heart muscles, lungs, and kidney. The lips of a patient with scleroderma may appear to be pursed due to constriction of the mouth aperture, thus making it difficult to open the mouth. The oral mucosa appears pale and feels rigid. The tongue can lose mobility and become smooth in appearance as the palatal rugae flatten [37]. Salivary hypo function can also be present, although usually to a lesser degree than in Sjogren's syndrome. Radio graphically, the periodontal ligament space is often thickened [1].

Lupus erythematosus

The oral lesions in the discoid form commence as erythematous areas, usually depressed, and typically with white spots or radiating white striae. Sporadically,

superficial, painful ulceration may arise with crusting or bleeding. The central healing may result in depressed scarring. These lesions are most frequent on the buccal mucosa, palate, and tongue and vermilion border of mostly the lower lip. There is severe fissuring and atrophy of lingual papilla [4]. The American Rheumatism Association Committee on Diagnostic and Therapeutic Criteria has defined the oral or nasopharyngeal ulceration as a major diagnostic manifestation of SLE [38]. These ulcerations are usually painless and often involve the palate. Purpuric lesions such as ecchymoses and petechiae may also occur. In up to 30% of patients with SLE, salivary gland involvement may occur concomitantly, leading to secondary Sjogren's syndrome and severe xerostomia [39].

Rheumatoid arthritis

The Temporomandibular joint (TMJ) is often involved in rheumatoid arthritis. This is usually characterized by erosions in the condyle leading to a decreased range of motion of the mandible with pain upon movement. Oral dryness and salivary gland swelling can also be found in patients with rheumatoid arthritis. These patients can also develop secondary Sjogren's syndrome. The limited jaw function may necessitate TMJ

reconstruction once the active disease is controlled [40].

CONCLUSION

The oral manifestations are the first sign or the most important sign of systemic disease. Dentists must acquire familiarity with systemic conditions that can affect the oral cavity, so that proper referral can be made. Physicians need to be aware of significance of oral complaints, their relationship to local causes, and potentially to systemic diseases. Thus mouth presents a window for easy inspection of signs and symptoms of various systemic diseases because of its easy accessibility for visual investigation, and examination. By palpation.

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