

Available Online at http://www.journalajst.com

ASIAN JOURNAL OF SCIENCE AND TECHNOLOGY

Asian Journal of Science and Technology Vol. 07, Issue, 09, pp.3507-3517, September, 2016

RESEARCH ARTICLE

ORAL CAVITY AS A DIAGNOSITIC TOOL FOR SYSTEMIC DISORDERS

Dr. K. Saraswathi Gopal and *Dr. M. Shanmuga Sundaram

Department of Oral Medicine & Radiology, Meenakshi Ammal Dental College, Chennai

ARTICLE INFO	ABSTRACT
Article History: Received 08 th June 2016	Oral cavity and the lesions associated with oral cavity sometimes plays a key role in diagnosis of systemic disorders or act as an important examination site for early lesion that precedes due to any

Received 08th June, 2016 Received in revised form 24th July, 2016 Accepted 26th August, 2016 Published online 30th September, 2016

Key words:

Oral lesions, Systemic disorders, Nutritional deficiency, GIT disorders, Metaolic disorders, Hematological diseases, Dermatological diseases, Rheumatological disorders, Autoimmune disorders, Renal diseases, Diagnostic tool. Oral cavity and the lesions associated with oral cavity sometimes plays a key role in diagnosis of systemic disorders or act as an important examination site for early lesion that precedes due to any systemic disorders. Oral manifestations due to nutritional deficiency, GIT disorders, metabolic disorders, haematological disorders, rheumatological disorders, dermatological diseases, renal diseases and autoimmune disorders are common. Hence examination of oral cavity with through knowledge to diagnose lesions caused by systemic disorders can aid in early detection of the disease and prevention of major complications.

Copyright©2016, Saraswathi Gopal and Shanmuga Sundaram. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

The relation between systemic disorders and oral cavity is an interesting topic for the discussion since many systemic disorders have oral manifestations. In some cases oral manifestations precede the systemic one, which gives the clue to diagnosis in an early stages of the disease which helps us in treating the disease in a better way. The oral lesions can occur at any site and can involve any structures such as buccal mucosa, gingiva, teeth, salivary gland, tongue and periodontium. In this article we highlight the oral manifestations that is caused by Nutrtional deficiency, GIT disorders, metabolic disorders, Hematological diseases, renal diseases, dermatological diseases and autoimmune disorders.

Nutritional deficiency

Nutrition is the science that interprets the interaction of nutrients and other substances in food. Nutrients are components in food that an organism uses to survive and grow. Nutritional deficiency can cause many disorders. Some of these disorders can also cause oral manifestations.

*Corresponding author: Dr. M. Shanmuga Sundaram,

Oral manifestations and the vitamin and other nutritional deficiency causing are listed.

Vitamin A Deficiency

It is common in poorer countries but rarely seen in more developed countries. Approximately 250,000 to 500,000 malnourished children in the developing world go blind each year from a deficiency of vitamin A. Highest prevalence is seen in Southeast Asia and Africa. The prevalence of night blindness due to Vitamin A Deficiency is also high among pregnant women in many developing countries. Vitamin A Deficiency also contributes to maternal mortality and other poor outcomes in pregnancy and lactation.^{1,2}

Oral manifestations

Eruption rate of the teeth is retarded, retarded alveolar bone formation, hyperplasticgingival epithelium followed by keratinization.³

Treatment

Treatment of Vitamin A deficiency can be undertaken with both oral and injectable forms. As an oral form, the supplementation of vitamin A is effective for lowering the risk

Department of Oral Medicine & Radiology, Meenakshi Ammal Dental College, Chennai

of morbidity, especially from severe diarrhea, and reducing mortality from measles and all-cause mortality. Studies have shown that vitamin A supplementation of children under five who are at risk of Vitamin ADeficiency can reduce all-cause mortality by 23 per cent.⁴

Vitamin D deficiency

Vitamin D refers to a group of fat-soluble, secosteroids responsible for increasing intestinal absorption of calcium, iron, magnesium, phosphate, and zinc. In humans, the most important compounds in this group are vitamin D3 (also known as cholecalciferol) and vitamin D2 (ergocalciferol).⁵ Cholecalciferol and ergocalciferol can be ingested from the diet and from supplements.⁶A diet deficient in vitamin D in conjunction with inadequate sun exposure causes osteomalacia (or rickets when it occurs in children), which is a softening of the bones. In the developed world, this is a rare disease. However, vitamin D deficiency has become a worldwide issue in the elderly and remains common in children and adults. Low blood calcidiol (25-hydroxy-vitamin D) can result from avoiding the sun.⁷

Oral manifestations

Developmental anomalies of dentin and enamel, delayed eruption, and misalignment of the teeth in the jaws.³

Treatment

Vitamin D deficiency is a common condition requiring longterm management.⁸ For infants oral dosage of 200-800 IU/kg/day for 1 month is given depending upon severity. Children below 1 year can be given 1000 IU/kg/day for 3 months. In patient with age less than 18 can be given 2000-4000 IU/kg/day for 6 months.

Vitamin K deficiency

Vitamin K is a group of structurally similar to fat-soluble vitamins. The human body requires vitamin k for complete synthesis of certain proteins that are prerequisites for blood coagulation that the body needs for controlling binding of calcium in bones and other tissues.⁹ Vitamin K deficiency causes symptoms such as bruising, petechiae, hematomas, oozing of blood at surgical or puncture sites, stomach pains, risk of massive uncontrolled bleeding, cartilage calcification, and severe malformation of developing bones or deposition of insoluble calcium salts in the walls of arteries. In infants, it can cause some birth defects such as underdeveloped face, nose, bones, and fingers.¹⁰

Oral manifestations

Most common oral manifestation is gingival bleeding. Usually gingival bleeding occur after tooth brushing in the moderate cases and spontaneous gingival bleeding occur in severe cases. It can also cause petechiae or ecchymosis in oral mucosa.³

Treatment

Weitzel et al¹¹ reported that administration of a large dose of vitamin K was the first choice of treatment; if a patient had no

life-threatening bleeding, plasma or blood products should be reduced. If a patient has bleeding in vital organs such as intracranial bleeding or has unstable hemodynamics, fresh plasma or prothrombin complex plus vitamin K should be administered to increase the levels of blood coagulation factors or correct coagulation disorder.

Vitamin C deficiency

Vitamin C or L-ascorbic acid, or simply ascorbate (the anion of ascorbic acid), is an essential nutrient for humans. Deficiency cause the most severe symptoms of scurvy.Typical symptoms of scurvy are initially fatigue, followed by formation of spots on the skin, spongy gums, and bleeding from the mucous membranes.¹²

Oral manifestations

There is inflammation of the interdental and marginal gingiva followed by bleeding, ulceration, foul breaths due to fusospirochetal stomatitis. Hemorrhage and swelling of the periodontal membranes occur, followed by loss of bone and loosening of the teeth, which eventually exfoliate. In severe vitamin C deficiency the gingivae become swollen, purplish or maroon coloured and spongy (spongy gums),tending to cover the teeth and bleed easily; there is also delay in wound healing ³

Treatment

Vitamin C rich diet. Increased intake of vitamin C also enhances the absorption of iron.¹³

Riboflavin deficiency

Riboflavin (vitamin B2) is part of the vitamin B group. It helps in activation of other vitamins. Symptoms of neurode generation and peripheral neuropathy have been documented in several studies of riboflavin deficiency.¹⁴

Oral manifestations

Initially glossitis involving the tip and/or the lateral margins of the tongue, followed by complete atrophy of all papillae. The tongue becomes magenta color. Oral mucosa appears pale, cheloisis maceration and fissuring at the angles of the mouth.³

Treatment

Treatment involves a diet which includes an adequate amount of riboflavin containing food. Multi-vitamin and mineral dietary supplements often contain 100 mg of riboflavin for 2 weeks.^{15,16}

Niacin deficiency

Niacin also known as vitamin B3 and nicotinic acid, is an organic compound. At present niacin deficiency is sometimes seen in developed countries, and it is usually apparent in conditions of poverty, malnutrition, and chronic alcoholism. Severe deficiency of niacin in the diet causes the disease pellagra, which is characterized by diarrhea, dermatitis, and dementia, as well as Casal's necklace lesions on

the lower neck, hyperpigmentation, thickening of the skin, inflammation of the mouth and tongue, digestive disturbances, amnesia, delirium, and eventually death if left untreated.¹⁷

Oral manifestations

Oral mucosa becomes fiery red and painful.Ulceration begin at the interdental papillae and spread rapidly.³

Treatment

Nicotinic acid can be given 500mg for 12 weeks. Niacin is found in variety of foods, including liver, chicken, beef, fish, cereal, peanuts, and legumes, and is also synthesized from tryptophan which is an essential amino acid found in most forms of protein.¹⁸

Gastrointestinal Tract (GIT) disorder GERD

Gastroesophageal reflux disease (GERD) also known as gastro-oesophageal reflux disease (GORD) and acid reflux is a chronic condition of mucosal damage caused by stomach acid coming up from the stomach into the esophagus. The common signs are heartburn, regurgitation and pain while swallowing.¹⁹

Oral manifestations

Oral manifestations include halitosis and in severe cases it can cause erosion of the teeth.

Treatment

Treatment is typically via lifestyle changes and medications such as proton pump inhibitors, H2 receptor blockers or antacids. 20,21

Crohn's disease

Crohn's disease, also known as crohn's syndrome and regional enteritis. Crohn's disease is a type of inflammatory bowel disease (IBD) that may affect any part of the gastrointestinal tract from mouth to anus. Signs and symptoms often include abdominal pain, diarrhea, fever, and weight loss.²²Crohn's disease affects about 3.2 per 1,000 people in Europe and North America. It is less common in Asia and Africa. Males and females are equally affected. Usual onset between 15 and 30 years. In some conditions oral manifestations may be the first indicator for this disease.²²

Etiology

Due to genetic, immunological factors, microbes and environmental factors. $^{\rm 23}$

Oral manifestations

Usually the oral lesions are multifocal. Nodular, linear, polypoid or diffuse mucosal thicknings with common sites such as buccal mucosa, labial mucosa and mucobuccal folds.²⁴

Investigations

Blood test, endoscopy, radiological examination and endoscopic biopsy.

Treatment

Life style changes, medication such as corticosteroids are given to decrease the inflammation, surgery, alternative medicine. 25

Ulcerative Colitis

Ulcerative colitis (UC) is a chronic relapsing form of inflammatory bowel disease (IBD) that causes inflammation and ulcers in the colon. Peak incidence between 15 and 25 years. Symptoms can range from mild to severe with disease onset usually occurring in young adults. Its course is unpredictable but with a strong likelihood of life-long disease.²⁶ Ulcerative colitis newly occurs in 1 to 20 people per 100,000 per year, and about 8 to 246 per 100,000 individuals are affected. The disease is more common in northern regions of the world.²⁷

Etiology

Gentic factors, environmental factors, and autoimmune disease.²⁷

Investigations

Endoscopy, histological examination.

Oral manifestations

Oral lesions are rare sometimes preceds the GI lesions. Oral lesions of ulcerative colitis are termed as pyostomatitis vegetans characterized by scattered, clumped or linearly oriented with pustules on the erythematous mucosa that can occur any site. Males are most commonly affected at any age.²⁸

Treatment

Medication such as corticosteroid can also be used due to their immunosuppressing and short-term healing properties, but because their risks outweigh their benefits, they are not used long-term in treatment. Surgery, leukocytes apheresis, bacterial recolonization and alternative medicine.²⁹

Metabolic and endocrine

Hormonal imbalance can cause various oral lesions. The most common oral manifestation of hormonal imbalance is due to diabetic mellitus since its commonly seen in India. Parathyroid disorder are less often seen when compared to diabetes however these also have oral manifestations which helps in early detection of the disorder.

Diabetic

Diabetes mellitus (DM) commonly referred to as diabetes, is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period. Symptoms of high blood sugar include frequent urination, increased thirst, and increased hunger. If left untreated, diabetes can cause many complications.³⁰

Etiology

Diabetes is due to either the pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced.³¹

Types

- Type 1 DM results from the pancreas's failure to produce enough insulin. The cause is unknown.³²
- Type 2 DM begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses a lack of insulin may also develop. The primary cause is excessive body weight and not enough exercises.³²
- Gestational diabetes is the third main form and occurs when pregnant women without a previous history of diabetes develop high blood-sugar levels.³²

Oral manifestations

Oral lesion of diabetic include hyposalivation in 68% of patients, halitosis in 52% of patients, periodontal disease in 32% of patients, candidiasis in 28% of patients in a controlled diabetic mellitus. The oral manifestation of uncontrolled diabetic patients shows increase in percentage of occurrence.³³

Treatment

Prevention and treatment involve maintaining a healthy diet, regular physical exercise, and maintaining a normal body weight. Control of blood pressure and maintaining proper foot care are important for people with the disease. Type 1 DM must be managed with insulin injections.³⁴ Type 2 DM may be treated with medications with or without insulin.³⁵ Weight loss surgery in those with obesity is sometimes an effective measure in those with type 2 DM. Gestational diabetes usually resolves after the birth of the baby.³⁵

Hypoparathyroidism

Hypoparathyroidism is decreased function of the parathyroid glands with underproduction of parathyroid hormone. This can lead to low levels of calcium in the blood, often causing cramping and twitching of muscles or tetany (involuntary muscle contraction), and several other symptoms.

The condition can be inherited, but it is also encountered after thyroid or parathyroid gland surgery, and it can be caused by immune system-related damage as well as a number of other causes such as tumor.³⁶

Causes

Thyroidectomy, autoimmune, hemochromatosis.³⁶

Oral manifestations

Oral manifestations include enamel hypoplasia, delayed eruption and also cause multiple unerupted teeth. It can be associated with endocrine-candidiasis syndrome which have persistent oral candidiasis.^{37,38}

Investigations

Blood calcium and serum albumin, parathyroid hormone levels.

Treatment

Severe hypocalcaemia, a potentially life-threatening condition, is treated as soon as possible with intravenous calcium (e.g. as calcium gluconate).³⁹

Dental management

Candidiasis is treated with antifungal medications. Enamel hypoplasia is treated cosmetically.³⁹

Hyperparathyroidism

Hyperparathyroidism is inappropriate overactivity of the parathyroid glands resulting in parathyroid hormone (PTH) increase levels in the blood. Normal parathyroid glands measure the ionized calcium concentration in the blood plasma and secrete parathyroid hormone accordingly: if the ionized calcium rises above normal, the secretion of PTH is decreased.

Whereas when the Calcium level falls, parathyroid hormone secretion is increased. Goiter which refers to enlargement of the thyroid gland is also associated with hyperparathyroidism. This leads to nausea and vomiting, constipation, polyuria, polydipsia, cognitive impairment, kidney stones and osteoporosis.⁴⁰

Causes

Parathyroid adenoma, vitamin D deficiency and renal osteodystrophy.

Oral manifestations

Oral manifestations of the hyperparathyroidism includes browns tumor (can associate with swelling of jaw and pain), loosening of the teeth that may cause mobility, loss of bone density, constant vague pain in the jaw, tenderness of teeth due to the masticatory forces, soft tissue calcifications, delayed eruption of the teeth.⁴¹

Treatment

The treatment of hyperthyroidism depends on the cause and severity of the disease, as well as on the patient's age, goiter size, comorbid conditions, and treatment desires. Antithyroid drugs, radioactive iodine, and surgery are the main treatment options for persistent hyperthyroidism.⁴²

Dental treatment

The treatment of a Brown tumor is mainly pharmalogic by treating the underlying hyperparathyroidism however, surgical excision is sometimes necessary. Dental treatment such as extractions are avoided to prevent from iatrogenic bone fracture.

Hematalogical disorders

Anemias

It is a condition in which there is a deficiency of red cells or of haemoglobin in the blood, resulting in pallor and weakness. There are various oral manifestations of different types of anaemia.⁴³

Iron Deficiency Anemia

This anemia is mainly caused due to inadequate dietary intake of iron, faulty absorption of iron and increased requirement for iron. The Plummer Vinson syndrome is a severe form of anemia with iron deficiency. It is characterized by dysphagia, koilonychia and atrophic glossitis.⁵¹

Oral manifestations

In iron deficiency anemia cracks or fissure at the corners of mouth, a lemon tinted pallor of skin, smooth, red painful tongue with atrophy of filiform papilla and fungi form papilla & dysphagia. The mucous membrane appears pale; glossitis and angular stomatitis are encountered in these patients.⁵¹

Treatment

Oral Iron supplements 2-4mg/kg/day or intravenous iron is given for 3 months.⁵²

Pernicious Anaemia

It is due to deficiency of intrinsic factor namely mucoprotein in stomach. The intrinsic factor is necessary for absorption of vitamin B12 which is essential for erythropoiesis. The most common initial symptom is feeling tired. Other symptoms may include shortness of breath, pale skin, chest pain, numbness in the hands and feet, poor balance, a smooth red tongue, poor reflexes, and confusion.⁴⁴

Oral manifestations

Oral manifestations include pallor mucosa. The tongue is inflamed and beefy red in colour either entirely or partly. Small shallow ulcers like aphthous ulcers can be seen. The papilla undergoes atrophy with loss of papillae and becomes smooth or bald glossitis with glossopyrosis and glossodynia. This is also called Hunter glossitis or Moeller's glossitis.⁴³

Treatment

The standard treatment for Pernicious anemia has been intramuscular injections of cobalamin in the form of cyanocobalamin and hydroxocobalamin.⁴⁵

MegaloblasticAnemias

Megaloblastic anemias are a subgroup of macrocytic anemias, in which distinctive morphologic abnormalities occur in red cell precursors in bone marrow, namely megaloblastic erythropoiesis. Of the many causes of megaloblastic anemia, the most common are disorders resulting from cobalamin or folate deficiency. Usually occurs in older adults, the prevalence ranges from 1.5% to 4.6%. 50

Oral manifestations

The presence of oral signs and symptoms, including glossitis, angular cheilitis, recurrent oral ulcer, oral candidiasis, diffuse erythematous mucositis and pale oral mucosa.⁵⁰

Treatment

Treated with Folate 5 mg tablet and its over dose is not associated with adverse effects, 5 mg daily dosage for 3 months.⁵⁰

Polycythemia Vera

It is a neoplasm in which the bone marrow makes too many red blood cells. It may also result in the overproduction of white blood cells and platelets. Patients with polycythemia vera can be asymptomatic. A classic symptom of polycythemia vera is pruritus or itching, particularly after exposure to warm water (such as when taking a bath), which may be due to abnormal histamine release or prostaglandin production.⁵³

Oral Manifestations

A purplish red discoloration of the oral mucosa is visible on the tongue, cheeks, and lips. The gingiva is red and may bleed spontaneously. Petechiae and ecchymosis are observed in patients with platelet abnormalities. Varicosities in the ventral tongue a frequent normal finding, are exaggerated in cases of polycythemia.⁵⁴

Treatment

As the condition cannot be cured, treatment focuses on treating symptoms and reducing thrombotic complications by reducing the erythrocyte levels. Low levels of aspirin is given to reduce the symptoms. Phlebotomy is one form of treatment, which often may be combined with other therapies.Untreated, polycythemia vera can be fatal.⁵⁴

Aplastic Anemia

It is caused by lack of bone marrow activity, reduction of red blood cell count, white blood cell count and platelets which causes pancytopenia. Anemia may lead to malaise, pallor and associated symptoms such as palpitations. Low platelet counts (thrombocytopenia) if present is associated with an increased risk of hemorrhage, bruising and petechiae. Low white blood cell counts (leukocytopenia) if present leads to an increased risk of infections which can be severe.⁴⁶

Oral manifestations

Oral manifestations include pale & atrophic oral mucosa; smooth, bald and sore tongue, angular stomatitis, bleeding from the gingiva due to deficiency of platelets.⁴⁷

Treatment

Aplastic anemia is treated with bone marrow transplantation.⁴⁶

Cyclic Neutropenia

Cyclic neutropenia (or cyclical neutropenia) is a form of neutropenia, a white blood cell deficiency, that tends to occur every three weeks and lasts three to six days at a time due to changing rates of cell production by the bone marrow. Cyclic neutropenia is a disorder that causes frequent infections and other health problems in affected individuals.⁵⁵

Oral manifestations

Oral lesions are common in cyclic neutropenia and may be the major clinical manifestation of the disease.

The two most common oral manifestations are oral mucosal ulcers and periodontal diseases. The oral ulcers recur with each new bout of neutropenia and resemble large deep scarring ulcers seen in major aphthous stomatitis. The periodontal manifestations range from marginal gingivitis to rapidly advancing periodontal bone loss caused by bacterial infection of the dental supporting structures.⁵⁶

Treatment

Antibiotics are given to control infection and myeloid growth factor therapy for growth of neutrophils.⁵⁶

Leukemia

Leukemia represents several types of malignancies of hematopoietic stem cell derivation leading to production of abnormal white blood cells in the bone marrow and eventually overflows into the peripheral blood. White blood cells, which are involved in fighting pathogens, may be suppressed or dysfunctional. This could cause the patient's immune system to be unable to fight off a simple infection or to start attacking other body cells. Because leukemia prevents the immune system from working normally, some patients experience frequent infection, ranging from infected tonsils, sores in the mouth, or diarrhea to life-threatening pneumonia or opportunistic infections.⁵⁷

Oral manifestations

Oral findings include petechial hemorrhages of the posterior hard palate and the soft palate along with spontaneous gingival hemorrhage. Ulceration of oral mucosa is present as a result of impaired host immune capability to combat normal flora. Gingiva is usually the most affected due to the presence of abundant bacteria around the teeth. Ulcers are deep, punched out lesions with a gray-white necrotic base.

Oral candidiasis may be present and herpetic infections may involve any area of mucosa rather than just the keratinized mucosa as seen in immunocompetent individuals. Boggy swellings may be present and represent infiltrates of leukemic cells. This is seen in myelomonocytic leukemia and may cause diffuse gingival enlargement.⁵⁸

Treatment

Chemotherapy and consolidation theryapy.⁵⁸

Dental management

Dental treatment should be performed before starting the chemotherapy. Patients in long-term remission can undergo dental treatment, while patients with advanced or relapsed diseases with reserved prognosis should receive palliative or emergency treatment only.

Thalassemia

This is a type of anemia where the haemoglobin of RBC is affected and this is more of racial disease affecting Italian, Greek, Syrian and American in nature. This is hereditary disease – a congenital defect of globin synthesis resulting in formation of unstable haemoglobin. Extramedullary hemopoietic tissue sometimes grows beneath the periosteum, producing a scalloped cortex edge in hands, feet, tibiae, fibulae, knees, radii, and ulnae.⁴⁸

Oral manifestations

Oral manifestations include an unusual prominence of the premaxilla irregularly arranged maxillary teeth and pale oral mucosa color. In the skull, significant thickening of the cranium can take place, and overgrowth of the facial bones can impede pneumatization of sinuses.⁴⁹

Treatment

Bone marrow transplantation is the treatment of choice.

Renal disease

Renal disease include both acute and chronic renal failure. Oral health is the chief concern for dentist to treat the patients with renal diseases. Renal disease leads to fatigue, nausea, vomiting eventually dehydration. Statistics show that 90% of the patients suffering from chronic renal failure face oral health related problems because it affects the bone and soft tissue structures, and thus can effect periodontal tissues.⁵⁹

Oral manifestations

Bad odor/metallic taste due to increased concentration of urea in saliva and its transformation into ammonium. Xerostomia results from dry mouth and salivary gland alteration. Paleness of the mucosal members due to anemia. The four types of uremic stomatitis seen are pseudomembranous, ulcerative, hemorrhagic and hyperkeratotic that appears on the ventral surface of the tongue and on the anterior mucosal surfaces.

Gingival bleeding, Gingival inflammation, Gingival hyperplasia: and Periodontal problems. Enamel hypoplasia, due to alterations in calcium and phosphorus metabolism. Erosions on the surface of the teeth because of acidic regurgitation and vomiting induced by uremia.⁶⁰

Management

Control of the risk factors, replacement of erythropoietin and calcitriol if required. Renal replacement therapy is usually required, in the form of either dialysis or a transplant.⁶⁰

Dermatological diseases

Lichen planus

It is a chronic, inflammatory disease that affects mucosal and cutaneous tissues. Oral lichen planus (OLP) occurs more frequently than the cutaneous form and tends to be more persistent and more resistant to treatment. It most commonly affect in 3^{rd} to 5^{th} decade of life.⁶¹

Etiology

Lichen planus is believed to result from an abnormal T-cellmediated immune response in which basal epithelial cells are recognized as foreign because of changes in the antigenicity of their cell surface.⁶²

Clinical features

The classic skin lesions of the cutaneous form of lichen planus can be described as purplish, polygonal, planar, pruritic papules and plaques. These skin lesions commonly involve the flexor surfaces of the legs and arms, especially the wrists.⁶²

Oral manifestations

Oral lichen planus may contain both red and white elements and provide, together with the different textures, the basis for the clinical classification of this disorder. The white and red components of the lesion can be a part of the following textures: Reticulum, Papules, Plaque-like, Bullous, Erythematous and Ulcerative. Burning sensation can occur most commonly in erythematous and ulcerative types.⁶³

Management

Topical and systemic corticosteroids depends on the severity and response of the lesion. Immuno modulators is also given in treatment. Symptomatic treatment and supportive care should be provided to the patients.⁶²

Pemphigus

Pemphigus is a potentially life-threatening disease that causes blisters and erosions of the skin and mucous membranes. These epithelial lesions are a result of autoantibodies that react with desmosomal glycoproteins that are present on the cell surface of the keratinocyte. There are 0.5 to 3.2 cases reported each year per 100,000 population, with the highest incidence occurring in the fifth and sixth decades of life.⁶⁴

Oral manifestations

Oral and ocular mucosal involvement rarely occurs. Occurrence of chronic painful ulcers in the mouth which hamper their daily oral functions. The bullae usually heal with post-inflammatory pigmentary changes and there is no scar formation. The vesicular form manifests as groups of small tense blisters, often on a erythematous base.⁶⁴

Management

Topical and systemic corticosteroids are effective for oral and skin lesions of the disease. Immunosuppresent, immunomodulators and supportive therapy is needed.⁶⁵

Pemphigoid

Pemphigoid is a group of rare autoimmune blistering skin disease. As its name indicates, pemphigoid is similar in general appearance to pemphigus. Pemphigoid is more common than pemphigus, and is slightly more common in women than in men. It is also more common in people over 60 years of age than it is in younger people.⁶⁶

Clinical features

The characteristic skin lesions is a blister on an inflame base that chiefly involves the scalp, arms, legs, axilla, and groin. Pruritis is a common feature of the skin lesions, which may initially present as macules and papules. The disease is self-limiting but can last for months to years without therapy.⁶⁷

Oral manifestations

The gingival lesions consist of generalized edema, inflammation, and desquamation with localized areas of discrete vesicle formation. The oral lesions are clinically and histologically indistinguishable from oral lesions of mucous membrane pemphigoid, but early remission is more common. Desquamative gingivitis is also commonly seen.⁶⁷

Management

Patients with localized oral lesions may be treated with highpotency topical steroids, such as clobetasol or betamethasone, whereas patients with more extensive disease require use of systemic corticosteroids combined alone or with immunosuppressive drugs such azathioprine, as cyclophosphamide, or mycophenolate. Patients with moderate levels of disease may avoid use of systemic steroids by use of dapsone or tetracycline, doxycycline, or minocycline, which may be combined with niacinamide.68

Autoimmune disorders

Systemic lupus erythematous

Systemic Lupus Erythematous (SLE) is a chronic, multisystemic disease of unknown etiology. It is characterized by the production of autoantibodies and immune complexes leading to protean systemic manifestations. Genetic, hormonal, racial and environmental factors all contribute to SLE. Common initial and chronic complaints include fever, malaise, joint pains, muscle pains, and fatigue.⁶⁹

Oral manifestations

Oral lesions of SLE develop in 5% to 25% of patients. The lesions usually affect the palate, buccal mucosa and gingiva. Sometimes they appear as lichenoid areas, but they may also look nonspecific or even somewhat granulomatous. Involvement of the vermilion zone of the lower lip (lupus cheilitis) is sometimes seen.

Varying degrees of ulceration, pain, erythema and hyperkeratosis may be present. Other oral complaints are xerostomia, stomatodynia, candidiasis, periodontal disease and dysgeusia.⁷⁰

Treatment

The general principle of management of SLE is analogous to that of other inflammatory disorders: suppression of inflammation in an attempt to prevent organ damage. The intensity of therapy is therefore dictated by the severity and site of organ involvement, and the overall prognosis isorgan specific involvement.⁷⁰

Sjogren's syndrome

Sjogren's syndrome (SS) is a chronic disease characterized by dry eyes and dry mouth resulting from immunologically mediated destruction of the lacrimal and salivary glands. The hallmark symptom of SS is a generalized dryness, typically including xerostomia and keratoconjunctivitis sicca. Sicca syndrome also incorporates vaginal dryness and chronic bronchitis.⁷¹

Oral manifestations

Oral manifestations of SS are grouped under subjective symptoms and objective symptoms. Subjective symptoms include dry mouth, termed xerostomia a dominant clinical oral symptom of SS. Severity of this dryness varies from patient to patient. Other manifestations include, chewing difficulty, particularly with dry foods, sensitivity to acids and voice alteration. Patients report burning and tingling sensations in the mouth with frequent voice hoarseness and a change in the sense of smell. Oral manifestations reduce self-esteem, affect work productivity and alter quality of life. Approximately 70% of patients exhibit dental caries and 85% manifest oral infections, particularly oral candidiasis. Patients also exhibit an inability to distinguish between normal, bitter and sweet tastes. The tongue may be dry, red, fissured. The lips may be cracked and have a tendency to peel.⁷¹

Treatment

Because there is no known cure for Sjögren syndrome, treatment focuses on relieving symptoms and preventing complications. Ocular treatment begins with topical tear replacement. Preservative-free artificial tears are tolerated better than solutions with preservatives. Treatment for xerostomia consists of good oral hygiene, salivary stimulation, use of saliva substitutes. Antifungal management may require for oral candidiasis.⁷²

Psoriasis

Psoriasis is a long-lasting autoimmune disease which is characterized by patches of abnormal skin. These skin patches are typically red, itchy, and scaly. They may vary in severity from small and localized to complete body coverage.

Oral manifestations

Oral manifestation of psoriasis is rare. Oral psoriasis has been seen to manifest in broadly four types of lesions: (1) well-defined yellowish-white lesions, round to oval in shape, which are independent of cutaneous psoriasis; (2) white, lacy, circinate, elevated lesions on the mucosa and tongue that are congruent with skin lesions; (3) erythema or redness of the entire oral mucosa associated with acute exacerbation of psoriasis; (4) geographic tongue, seen more frequently in patients with cutaneous psoriasis than in controls.⁷⁶

Treatment

Topical corticosteroid preparations are the most effective agents when used continuously for 8 weeks; retinoids and coal tar were found to be of limited benefit and may be no better than placebo.⁷⁶

Rheumatoid Arthritis

Rheumatoid Arthritis (RA) is a chronic systemic inflammatory disorder that may affect many tissues and organs like skin, blood vessels, heart, lungs and muscles. But principally attacks the joints, producing a nonsuppurative proliferative and inflammatory synovitis that often progresses to destruction of the articular cartilage and ankylosis of the joints. Although the cause is unknown, autoimmunity plays a role in its chronicity and progression.⁷³

Oral manifestations

The TMJ is affected to some degree in more than 40% of persons with rheumatoid arthritis. If TMJ is involved it is usually bilateral and occurs late in the disease. The signs and symptoms are less severe than in other joints and include stiffness, crepitation, pain or ache, tenderness and limitation of mouth opening. Pain of TMJ rheumatoid arthritis is not related to motion but rather to pressure on the joint. Clenching the teeth on one side produces pain of the contralateral joint. Subluxation or ankylosis is less frequent in the TMJ than in other joints, but gross destruction of the condylar heads may be so severe that mandibular micrognathia causes a receding chin and malocclusion may develop in children who are affected.⁷⁴

Treatment

RA was treated symptomatically with non-steroidal and steroidal anti-inflammatory drugs. These may provide symptomatic relief and slow the progression of the disease, but are associated with serious adverse effects and are relatively non-specific in their actions.⁷⁵

Conclusion

To conclude, oral manifestations of systemic diseases will play key role in early diagnosis of many systemic diseases. Since some of the oral manifestations are common in few diseases one should know to identify the underlying cause in order to avoid the mis-diagnosis. Dental physician are the only people, who are aware of all the oral manifestations which preceeds the systemic diseases and are capable of diagnosing underlying diseases by suitable investigations. Dental professional's opinion of this sepacality about the oral manifestations is important for the other dental speciality to diagnose the underlying cause and treat their patients accordingly to avoid further complications.

REFERENCES

1. Latham, Michael E. 1997. Human Nutrition in the Developing World (Fao Food and Nutrition Paper). Food

& Agriculture Organization of the United. ISBN 92-5-103818-X.

- Sommer, Alfred 1995. Vitamin a Deficiency and Its Consequences: A Field Guide to Detection and Control. Geneva: World Health Organization. ISBN 92-4-154478-3.
 Shearta the dual formula the dual time. Six dual time.
- 3. Shafers text book of oral pathology. Sixth edition.
- 4. Underwood, Barbara A. Vitamin A Deficiency Disorders: International Efforts to Control A Preventable "Pox." *J. Nutr.* 134: 231S–236S, 2004.
- Calvo MS, Whiting SJ, Barton CN; Whiting; Barton February 2005. "Vitamin D intake: a global perspective of current status". J. Nutr. 135 (2): 310–6. PMID 15671233
- 6. Wolf G June 2004. "The discovery of vitamin D: the contribution of Adolf Windaus". J Nutr 134 (6): 1299–302.
- 7. Wolf G June 2004. "The discovery of vitamin D: the contribution of Adolf Windaus". *J Nutr* 134 (6): 1299–302.
- 8. Ross AC, Taylor CL, Yaktine AL, Del Valle HB 2011. Dietary Reference Intakes for Calcium and Vitamin D. Washington, D.C: National Academies Press.
- Newman P., Shearer MJ; Newman, Paul 2008. "Metabolism and cell biology of vitamin K". Thrombosis and Haemostasis 100 (4): 530–547.
- Wallin R, Schurgers L, Wajih N 2008. "Effects of the blood coagulation vitamin K as an inhibitor of arterial calcification". Thromb. Res. 122 (3): 411–7.
- 11. Weitzel JN, Sadowski JA, Furie BC, Moroose R, Kim H, Mount ME, et al. Surreptitious ingestion of a long-acting vitamin K antagonist/rodenticide, brodifacoum: clinical and metabolic studies of three cases. Blood 1990; 76: 2555-2559.
- Padayatty SJ, Katz A, Wang Y, Eck P, Kwon O, Lee JH, Chen S, Corpe C, Dutta A, Dutta SK, Levine M (February 2003). "Vitamin C as an antioxidant: evaluation of its role in disease prevention". *J Am Coll Nutr* 22 (1): 18–35.
- 13. Boudrant J May 1990. "Microbial processes for ascorbic acid biosynthesis: a review". *Enzyme and Microbial Technology* 12 (5): 322–9.
- Riboflavin. IN: Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline. National Academy Press. 1998, PP.87-122.
- Maizels M, Blumenfeld A, Burchette R Oct 200). "A combination of riboflavin, magnesium, and feverfew for migraine prophylaxis: a randomized trial". Headache 44 (9): 885–890
- Ruane PH, Edrich R, Gampp D, Keil SD, Leonard RL, Goodrich RP Jun 2004. "Photochemical inactivation of selected viruses and bacteria in platelet concentrates using riboflavin and light". Transfusion 44 (6): 877–885.
- Cox, Michael; Lehninger, Albert L; Nelson, David R. 2000. Lehninger principles of biochemistry. New York: Worth Publishers. ISBN 1-57259-153-6.
- Hegyi, J.; Schwartz, R. A.; Hegyi, V. 2004. "Pellagra: Dermatitis, dementia, and diarrhea". *International Journal* of Dermatology 43 (1): 1–5.
- 19. Hershcovici T, Fass R April 2011. "Pharmacological management of GERD: where does it stand now?". Trends in pharmacological sciences 32 (4): 258–64.
- Kasasbeh A, Kasasbeh E, Krishnaswamy G. 2007. "Potential mechanisms connecting asthma, esophageal reflux, and obesity/sleep apnea complex—a hypothetical review". Sleep Med Rev 11 (1): 47–58.

- van der Pol RJ, Smits MJ, van Wijk MP, Omari TI, Tabbers MM, Benninga MA May 2011. "Efficacy of proton-pump inhibitors in children with gastroesophageal reflux disease: a systematic review". *Pediatrics*, 127 (5): 925–35.
- Dessein R, Chamaillard M, Danese S 2008. "Innate Immunity in Crohn's Disease". *Journal of Clinical Gastroenterology* 42: S144–7.
- Stefanelli T, Malesci A, Repici A, Vetrano S, Danese S 2008. "New Insights into Inflammatory Bowel Disease Pathophysiology: Paving the Way for Novel Therapeutic Targets". Current Drug Targets 9 (5): 413–8.
- 24. Kumar V, Fausto N, Abbas A. Robbins and Cotran's Pathologic Basisof Disease, 7th edn. Philadelphia: Elsevier Saunders, 2005.
- Bernstein M, Irwin S, Greenberg GR 2005. "Maintenance Infliximab Treatment is Associated with Improved Bone Mineral Density in Crohn's Disease". The American *Journal of Gastroenterology* 100 (9): 2031–5.
- 26. Wanderås, Magnus Hofrenning; Moum, Bjørn A; Høivik, Marte Lie; Hovde, Øistein 2016-05-06. "Predictive factors for a severe clinical course in ulcerative colitis: Results from population-based studies". World Journal of Gastrointestinal Pharmacology and Therapeutics 7 (2): 235–241.
- 27. Danese, S. & Fiocci, C. 2011. "Ulcerative colitis". The *New England Journal of Medicine*, 365:1713–1725.
- Ruiz-Roca JA, Berini-Aytes L, Gay-Escoda C. Pyostomatitis vegetans. Report of two cases and review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2005;99:447–54.
- Summers RW, Elliott DE, Urban JF, Thompson RA, Weinstock JV 2005. "Trichuris suis therapy for active ulcerative colitis: A randomized controlled trial". Gastroenterology 128 (4): 825–832.
- Kitabchi, AE; Umpierrez, GE; Miles, JM; Fisher, JN. Jul 2009."Hyperglycemic crises in adult patients with diabetes.". Diabetes Care 32 (7): 1335–43.
- Shoback, edited by David G. Gardner, Dolores 2011. "Chapter 17". Greenspan's basic & clinical endocrinology (9th ed.). New York: McGraw-Hill Medical. ISBN 0-07-162243-8.
- Kitabchi, AE; Umpierrez, GE; Miles, JM; Fisher, JN. Jul 2009."Hyperglycemic crises in adult patients with diabetes.". Diabetes Care 32 (7): 1335–43.
- RSSDI textbook of diabetes mellitus. (Rev. 2nd ed.). New Delhi: Jaypee Brothers Medical Publishers. 2012. p. 235.
- Rippe, edited by Richard S. Irwin, James M. 2010. Manual of intensive care medicine (5th ed.). Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins. p. 549.
- 35. Picot, J; Jones, J; Colquitt, JL; Gospodarevskaya, E; Loveman, E; Baxter, L; Clegg, AJ. September 2009. "The clinical effectiveness and cost-effectiveness of bariatric (weight loss) surgery for obesity: a systematic review and economic evaluation". Health Technology Assessment (Winchester, England) 13 (41): 1–190, 215–357, iii–iv.
- 36. Bilezikian JP, Khan A, Potts JT, et al. October 2011. "Hypoparathyroidism in the adult: epidemiology, diagnosis, pathophysiology, target-organ involvement, treatment, and challenges for future research". J. Bone Miner. Res. 26 (10): 2317–37.
- 37. Sanjeev Mittal, Deepak Gupta1, Sahil Sekhri, Shivali Goyal Oral manifestations of Parathyroid Disorders and Its

Dental Management. *Journal of Dental and Allied Sciences*, Jan-Jun 2014, Volume 3, Issue 1.

- 38. Vishal Mehrotra, Parvathi Devi, Thimmarasa Venkappa Bhovi, Bhuvan Jyoti MOUTH AS A MIRROR OF SYSTEMIC DISEASES Gomal *Journal of Medical Sciences* July-December 2010, Vol. 8, No. 2
- 39. Winer KK, Zhang B, Shrader J, et al. Synthetic human parathyroid hormone 1-34 replacement therapy: A randomized crossover trial comparing pump versus injections in the treatment of chronic hypoparathyroidism. *J Clin Endocrinol Metab*. Nov.2011.
- 40. Fraser WD July 2009. "Hyperparathyroidism". Lancet 374 (9684): 145–58
- 41. Marxy E Reynoso Rodríguez, María A Monter García Ignacio Sánchez FloresII Congenital hypothyrodism and its oral manifestations Revista Odontológica Mexicana Vol. 18, No. 2 April-June 2014 pp 133-138
- 42. Zink AR, Panzer S, Fesq-Martin M, Burger-Heinrich E, Wahl J, Nerlich AG 2001. "Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications.". Endocr Rev. 22 (4): 477–501.
- Lanza A, Heulfe I, Perillo L, Dell'Ermo A, Cirillo N. Oral Pigmentation as a Sign of Addison's disease, A Brief Reappraisal. *The Open Dermatology Journal*, 3, 2009, 3-6.
- Hvas AM, Nexo E November 2006. "Diagnosis and treatment of vitamin B12 deficiency—an update.". Haematologica 91 (11): 1506–12.
- 45. Carmel, R. 7 July 2008. "How I treat cobalamin (vitamin B12) deficiency". Blood 112 (6): 2214–2221.
- DeZern, Amy E; Brodsky, Robert A. 10 January 2014. "Clinical management of aplastic anemia". Expert Review of Hematology 4 (2): 221–230.
- 47. Loh FC, Ravindranathan N, Yeo JF. Amyloidosis with oral involvement. Case report. *Aust Dent J.* 35(1), 1990, 14-8.
- Cianciulli P October 2008. "Treatment of iron overload in thalassemia". Pediatr Endocrinol Rev 6 (Suppl 1): 208– 13. PMID 19337180
- 49. Lourenço SV, Hussein TP, Bologna SB, Sipahi AM, Nico MM. Oral manifestations of inflammatory bowel disease, a review based on the observation of six cases. *J Eur Acad Dermatol Venereol*, 24(2), 2010, 204-7.
- 50. Dalal RJ, Udani PM, Parekh JG Megaloblastic anemia in infancy and childhood. Indian Pediatr 1969, 6:255-262.
- Looker AC, Dallman PR, Carroll MD, Gunter EW, Johnson CL. Prevalence of iron deficiency in the United States. JAMA. 1997;277(12):973–6.
- Akay OM, Akin E, Mutlu FS, Gulbas Z. Effect of iron therapy on platelet function among iron-deficient women with unexplained menorrhagia. Pathophysiol Haemost Thromb. 2008; 36(2):80–3.
- 53. Steinman H, Kobza-Black A, Lotti T, Brunetti L, Panconesi E, Greaves M 1987. "Polycythaemia rubra vera and water-induced pruritus: blood histamine levels and cutaneous fibrinolytic activity before and after water challenge". *Br J Dermatol* 116 (3): 329–33.
- 54. Fjellner B, Hägermark O 1979. "Pruritus in polycythemia vera: treatment with aspirin and possibility of platelet involvement". Acta Derm Venereol 59 (6): 505–12.
- 55. Sera Y, Kawaguchi H, Nakamura K, et al. 2005. "A comparison of the defective granulopoiesis in childhood cyclic neutropenia and in severe congenital neutropenia". Haematologica 90 (8): 1032–41.

- 56. Scully C, MacFadyen E, Campbell A. Oral manifestations in cyclic neutropenia. Br J Oral Surg. 1982;20:96-101.
- 57. Else, M., Ruchlemer, R., Osuji, N. 2005. "Long remissions in hairy cell leukemia with purine analogs: a report of 219 patients with a median follow-up of 12.5 years". Cancer 104 (11): 2442–8.
- 58. Franch AM, Esteve CG, Perez, GS. Oral manifestations and dental management of patient with leukocyte alterations. J Clin Exp Dent. 2011; 3(1):e53-59
- Bayraktar G, Kurtulus I, Duraduryan A, Cintan S, Kazancioglu R, Yildiz A, et al. Dental and periodontal findings in hemodialysis patients. Oral Dis. 2007; 13(4): 393-7.
- Jover Cerveró A, Bagán JV, Jiménez Soriano Y, Poveda Roda R. Dental management in renal failure: patients on dialysis. Med Oral Patol Oral Cir Bucal. 2008;13:419-26.
- 61. Burkits textbook of oral medicine 11th edition.
- Mollaoglu N. Oral lichen planus: a review. Brit J Oral Maxillofacial Surg 2000; 38(4):370-7
- Gal Jungell P. Oral lichen planus: a review. Int J Oral Maxillofac Surg 1991; 20(3):129-35
- 64. Shivashankar S, Shamina MP, Varghese, V, S Thorakakkal S. Pemphigus Vulgaris in oral cavity. Clinical analysis of 71 cases Med Oral Petol Oral Cr Buccal 2008; vol 13 (10),622-6.
- 65. Bilani C,Miloglu O, Mustefa G, Saadetin D .Oral Pemphigus Vulgaris a case report with review of literature.Journal Of Oral Science2008; 50 ,(3),359-62.
- Sansaricq F, Stein SL, Petronic-Rosic V (2012) Autoimmune bullous diseases in childhood. Clin Dermatol 30: 114-127.
- 67. Stanley JR 1995. Autoantibodies against adhesion molecules and structures in blistering skin diseases. J Exp Med 181: 1-4.
- 68. Kuenzli S, Grimaître M, Krischer J, Saurat JH, Calza AM, et al. 2004. Childhood bullous pemphigoid: report of a case with life-threatening course during homeopathy treatment. Pediatr Dermatol 21: 160-163.
- 69. Manson JJ, Rahman A. Systemic lupus erythematosus. Orphanet J Rare Dis. 2006, 1:6.
- Gladman D, Urowitz M. American College of Rheumatology Ad Hoc Committee on Systemic Lupus Erythematosus Guidelines. Guidelines for referral and management of systemic lupus erythematosus in adults. Arthritis Rheumtol.1999; 42(9):1785-1796.
- 71. Constantopoulous SH, Papadimitrioce CS, Moutsopoulos HM. Respiratory manifestations in primary Sjogren's syndrome: A clinical, functional and histological study. Chest 1985; 88: 226-9.
- Fairfax A, Haslam P, Pavia D et al. Pulmonary disorders associated with Sjogren's syndrome. Q J Med 1981; 50: 279.
- Mazzucchelli R, Yebra M, Barbadillo C, Berrocal E, Gea JC, Andreu-Sanchez JL. Double disease in rheumatology: coexistence of rheumatoid arthritis and psoriatic arthritis. Clin Exp Rheumatol. 1992 Jan–Feb;10(1):83–5.
- 74. Kary S, Worm M, Audring H, Huscher D, Renelt M, Sörensen H, et al. New onset or exacerbation of psoriatic skin lesions in patients with definite rheumatoid arthritis receiving tumour necrosis factor alpha antagonists. Ann Rheum Dis. 2006 Mar;65(3):405–7
- 75. Moon YM, Yoon BY, Her YM, Oh HJ, Lee JS, Kim KW, et al. IL-32 and IL-17 interact and have the potential to

aggravate osteoclastogenesis in rheumatoid arthritis. *Arthritis Res Ther.* 2012 Nov;14(6):R246

76. Yesudian PD, Chalmers RJ, Warren RB, Griffiths CE. In search of oral psoriasis. *Arch Dermatol Res*, 2012;304:125