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RED BLOOD CELL DISORDERS- AN INSIGHT FOR ORAL PATHOLOGISTS

Dental Science

Sahanaz P Ahmed* MDS, Post Graduate Student,SRM Dental College, Bharathi Salai, Ramapuram, Chennai, Tamil Nadu 600089 *Corresponding Author

Priyadharsini Nataraj MDS, Reader, SRM Dental College, Bharathi Salai, Ramapuram, Chennai, Tamil Nadu 600089

Ashwini Ajay MDS, Post Graduate Student,SRM Dental College, Bharathi Salai, Ramapuram, Chennai, Tamil Nadu 600089

Arumugam Hemalatha MDS, Post Graduate Student,SRM Dental College, Bharathi Salai, Ramapuram, Chennai, Tamil Nadu 600089

ABSTRACT

This paper aims to review the literature of hematological diseases, with emphasis on the oral manifestations, signs and symptoms and their influence on the treatment plan of the dental health professional with particular reference to red blood disorders. An electronic literature exploration using MEDLINE was conducted for published articles on orofacial expressions of hematological diseases, with emphasis on red blood disorders or anemia. Mesh phrases used were: oral diseases AND anaemia; oral manifestations AND anaemia; orofacial lesions AND anaemia. The Boolean operator "AND" was used to combine and narrow the searches. Anemic disorders associated with orofacial signs and symptoms include iron deficiency anemia, Plummer–Vinson syndrome, megaloblastic anemia, sickle cell anemia and thalassaemia. Anemia is a global public health problem affecting both developing and developed countries with major consequences for human health as well as social and economic development. It occurs at all stages of the life cycle, but is more prevalent in pregnant women and young children. Of significance is the fact that India is among the countries with highest prevalence of anemia in the world. The manifestations include conjunctiva and facial pallor, atrophic glossitis, angular stomatitis, dysphagia, magenta tongue, midfacial overgrowth, osteoclerosis, osteomyelitis and paraesthesia/anesthesia of the mental nerve. An extensive range of anemic disorders stumble upon in internal medicine which has manifestations in the oral cavity and the facial region. Most of these manifestations are non-specific, but should alert the hematologist and the dental surgeon. Oral cavity is window to body and is often the area where systemic diseases present

KEYWORDS

Oral diseases, oral manifestations, red blood disorders, anemia, sickle cell, thalassaemia, megaloblastic anemia.

INTRODUCTION

Among the many conditions that may be encountered in the oral cavity, haematological disorders and their oral manifestations pose an inordinate challenge in terms of diagnosis and treatment planning. Dental work performed without a prior detailed analysis of the patient's general condition may lead to serious complications and sometimes even death. Clinical signs of various blood dyscrasias in the oral cavity are quite varied and sometimes very similar with other local or general conditions, this imposing to the dental practitioner thorough knowledge of the signs and symptoms specific to each condition reflected at this level, in order to be able to make an accurate positive and differential diagnosis. In fact the oral site in many instances could act as the forerunner of its manifestations before the systemic signs and symptoms. The importance of understanding the orofacial manifestations of these disorders also lies in the fact that orofacial signs and symptoms may be the first clinical presentation that alerts the dentist/hematologist to an underlying hematological disorder.(1) This review is to present the common oral manifestations, and the treatment plans of some commonly encountered red blood dyscrasias.

A computerized literature search using MEDLINE was conducted for published articles on orofacial manifestations of hematological diseases, with emphasis on anemia. Mesh phrases used in the search were: oral diseases AND anaemia; orofacial diseases AND anaemia; orofacial lesions AND anaemia; orofacial diseases AND anaemic disorders. The Boolean operator "AND" was used to combine and narrow the searches. The full texts of these articles were thoroughly examined. References in these articles were also manually searched for non-Medline articles. Only relevant articles were selected for the review.

DISCUSSION

IRON DEFICIENCY ANEMIA

In India, anemia is a common nutritional deficiency and a serious health disorder with women being more frequently affected than men and its prevalence is higher in the developing countries. It's not a disease, but rather an expression of the underlying disorder or disease.(2) In India, the prevalence of anemia is high because of low dietary intake, which is less than 20 mg /day, poor bio-availability of iron in Indian diet. Anaemia is defined as a haemoglobin concentration in blood below the lower limit of the normal range for the age and sex of the individual. The development of iron deficiency depends upon one or more of the factors - increased blood loss, increased requirements, inadequate dietary intake, decreased intestinal absorption.(3)

ORAL MANIFESTATIONS:

Mucosal pallor, recurrent oral ulcers, atrophic mucosa, loss of normal keratinization, angular chelitis, glossitis(diffuse or patchy atrophy of dorsal tongue papillae, giving a smooth, glazed appearance of the tongue. This is often accompanied by tenderness or a burning sensation, migratory glossitis, cheilosis, glossodynia which is burning sensation of mouth, candida infection (changes seen at the corners of the mouth and on tongue), dehydration and ulceration due to atrophy of mucosa. Dysphagia can be seen in chronic or long standing cases which are due to development of oesophageal strictures or webs. These are the main oral manifestations of iron deficiency anemia.

Lactoferrin is a protein contained in body fluids such as saliva, tears, and vaginal secretions. It provides a defense function because it binds with iron and withholds the iron from pathogens such as Candida. When lactoferrin levels are low, Candida can proliferate on the free iron. This is one of the reasons for the soreness of the tongue.(4)

Plummer-vinson syndrome: -

It is also called Paterson-Brown-Kelly syndrome and sideropenic Dysphagia. Main features include Dysphagia, iron deficiency anemia, dystrophy of nails (koilonychias). Oral manifestations include atropic glossitis, angular cheilitis, hyperkeratotic lesion, Dysphagia (due to esophageal webs), pharyngoesophageal ulcerations.(5)

TREATMENT

Dental patients presenting with symptoms of anemia or oral signs suggestive of this condition should have a complete blood count, including differential blood count. If significantly lowered hemoglobin values are obtained, the patient should be referred to his or her physician for a more thorough medical history, laboratory diagnosis, and treatment.(6)

Precautions to be taken: Elective oral surgical or periodontal procedures should not be performed on patients with marked anemia because of the potential for increased bleeding and impaired wound healing. When hemoglobin levels fall below 10 g/dL, the low oxygen tension affects the rheologic interactions between the cellular components of blood, mainly platelets and endothelium, decreasing their ability to clot effectively.'(6) General anesthesia should not be administered unless the hemoglobin is at least 10 g/dL. The patient should never be treated with iron until the cause of the microcytic hypochromic anemia is found.

When angular cheilitis is due to opportunistic infections brought on by decreased resistance secondary to nutrient deficiencies, treatment should focus on antifungal therapy, correction of the nutrient deficiency and diet modification to make eating a more comfortable experience.(1)(7)

MEGALOBLASTIC ANEMIA

This may be caused by a vitamin B12 deficiency (commonly from pernicious anemia, surgical resection of the ileum or small intestinal diverticula) or by a folic acid deficiency (most commonly from malnutrition). Vitamin B12 deficiency manifests in the oral cavity as part of megaloblastic changes in the entire gastrointestinal tract, which are so well demonstrated morphologically in the bone marrow.(3)

ORAL MANIFESTATIONS:

The oral manifestations are painful atrophy of the entire oral mucous membranes and tongue (glossitis). Stomatitis as well as mucosal ulceration (recurrent aphthous ulcers) in vitamin B12 and folate deficiency has long been recognized. These oral changes may occur in the absence of symptomatic anemia or of macrocytosis. "Magenta tongue," which is said to be rather characteristic, may be proclaimer of B12 deficiency. The tongue usually presents a fiery-red appearance, principally at the tip and lateral margins. Atrophy of the filiform papillae occurs and progresses unless vitamin B12 is given. Other mucosal surfaces may appear atrophic, and erosions are not uncommon.(1)(8)

TREATMENT

Most cases of megaloblastic anaemia need therapy with appropriate vitamin. This includes hydroxycobalamin and oral folic acid. Severely-anaemic patients in whom a definite deficiency of either vitamin cannot be established with certainty are treated with both vitamins concurrently. Blood transfusion should be avoided since it may cause circulatory overload. Packed cells may, however, be infused slowly. The marrow begins to revert back to normal morphology within a few hours of initiating treatment and becomes normoblastic within 48 hours of start of treatment.(3)

SICKLE CELL ANEMIA

Sickle cell disease is generically used to describe a group of disorders characterized by the production of abnormal hemoglobin S (HBS). The entities include sickle cell anemia (HbSS), sickle cell Hb C disease (HbSC) and sickle cell-β thalassemia.(9) Sickle cell anemia (HbSS) is the most common type and represents the homozygous form where the individuals inherit a double dose of the abnormal gene that codes for hemoglobin S. The sickle hemoglobin abnormality is caused by substitution of valine for glutamic acid in the sixth position from the NH2 terminal end of the β-globin chain.

In the homozygous form, the substitution results in polymerization of hemoglobin on deoxygenation, leading to deformed dense red blood cells in patients with SCD. The predominant pathophysiological feature of SCD is vaso-occlusion, which leads to acute and chronic complications such as: painful crises; increased risk of infection; acute chest syndrome; and stroke. It may also cause severe painful episodes with dramatic hemolysis that can progress to involve multiple organs; including teeth, bones, lungs, liver, kidneys central nervous system, and cardiovascular system.(10)

ORAL MANIFESTATIONS:

Oral manifestations are discussed as three major headings: dental, oral soft tissues, and maxillofacial complications.

Dental: Delayed eruption of teeth has been reported in SCD patients, where disturbances in growth and development of maxilla and mandible are seen. In a cross-sectional study done by Mendes, et al., SCD patients were found to have a 1.7 times greater chance of delayed eruption in comparison to healthy individuals.(11) Abnormal tooth formation has been documented in SCD. Enamel and dentin hypomineralization and hypomaturation have been reported in SCD patients.(12) Due to hypomineralization and hypomaturation of teeth in SCD patients, tooth structure is at higher risk of developing dental caries.(13) Interestingly, such abnormalities were observed in both heterozygous and homozygous states of sickle cell disorders. The maxillary and mandibular bone marrows attempt to compensate for the low numbers of red blood cells by becoming hyperplastic, and cause jaw expansion. Such compensatory hematopoietic expansion is believed to induce changes in dental tissues in general.(14) Hypercementosis also has been associated with SCD, where excessive deposition of non-neoplastic cementum is laid over the root's primary cementum.(15)SCD patients can present with tooth discoloration, where teeth appear abnormal in comparison to the normal range of variation in color and shade of the teeth. One explanation for SCD-related tooth discoloration is the release of hemoglobin and its by-products due to erythrocytosis into the peripheral circulation where they incorporate into the dentin and enamel and cause intrinsic discoloration.(16) Asymptomatic pulp necrosis was reported in higher frequency among SCD patients than healthy people. Such a phenomenon was attributed to abnormal blood flow to the dental pulp.'(17)

Oral soft tissues alterations: Depapillation of the tongue, atrophic glossitis, is observed in anemic patients, while the frequency of such features is undetermined among SCD patients. (18) Several studies have indicated that SCD patients tend to express high plaque scores and subsequently develop gingivitis. As opposed to adults, children with SCD are more prone to develop periodontitis. In general, SCD patients are more susceptible to infections and periodontal disease(18)(19) The oral mucosa in SCD patients presents with pallor to yellow discoloration, which is the result of deposition of blood pigments secondary to hyperbilirubinemia caused by erythrocytosis.(20) In addition, atrophy and recurrent aphthous ulcerations have been observed. Furthermore, erythematous macular lesions, bleeding, and hemorrhage can involve the buccal and labial mucosa.

Maxillofacial Alterations: Due to compensatory hematopoiesis, hemolysis, and vaso-occlusive events in the maxilla and mandible, radiographic bone changes are noticed in SCD patients. These changes include (a) increased radiolucency which leads to decreased trabeculae numbers, (b) increased medullary spaces, (c) thinning of the inferior mandibular border, (d) staircase pattern noticed mainly in the alveolar interproximal bone due to horizontal trabecular rows, (e) thickening of the lamina dura, (f) resorption in alveolar bone, and (g) radiopacities due to repaired mechanism of bony infarctions.(21) Pain in the jaws is common due to vaso-occlusion, which might lead to acute and chronic ischemia and infarction followed by osteonecrosis. Vaso-occlusion could also cause anesthesia or paresthesia of the mandibular nerve. Hypovascularity in the mandible can induce mandibular osteomyelitis and osteonecrosis in SCD patients. Disturbances of growth and development could occur among SCD patients, which lead to dentofacial deformities such as malocclusion.(22) In addition, craniofacial anomalies are associated with SCD and the most common bone abnormalities reported in the literature are maxillary protrusion and mandibular retrusion, which subsequently result in overjet, overbite, and spacing of both dental arches [36]. Malocclusion in its different classes can be observed in SCD patients due to bony changes. Class I malocclusion is the most prevalent form of malocclusions among SCD patients, even more prevalent than normal occlusion, and there is no clear consensus concerning its etiology.(23)

TREATMENT

SCD patients need to dodge sickle cell precipitating factors such as extreme hot and cold weather, low oxygen pressure atmosphere, severe muscular exercise to avoid vaso-occlusive crises. Antibiotics and painkillers must be taken during the sickle cell crises. Such patients necessitate regular dental visits to identify early dental abnormalities or maxillary osteonecrosis to be treated afore major dental complications develop. The treatment of choice consists of folic acid, hydroxocobalamin, mouth wash, rehydration, opioid analgesics and non-steroidal anti-inflammatory drugs to manage the severe pain and reduce inflammation, or even a blood transfusion to reduce the anemic crisis. Healthcare professionals should be aware that SCD may also provoke aseptic jaw arthritis.'(24)

THALASSEMIA

Thalassemia is a genetic disorder that involves abnormal haemoglobin formation. Defects in the synthesis of either α or the β polypeptide chains of hemoglobin (α-thalassaemia, β-thalassaemia) are seen. Based on genetic and clinical entities, thalassaemia are classified as homozygous, heterozygous or compound heterozygous. The heterozygous form of the disease (thalassaemia minor) is mild and usually asymptomatic, the only manifestation being hypochromic microcytic anemia. Homozygous β-thalassaemia, also known as Cooley's anemia or Mediterranean anemia, is chiefly seen in Mediterranean populations with prevalence as high as 15–20% in Greece, Turkey, Cyprus and southern Italy. The homozygous form of β-thalassaemia (thalassaemia major) exhibits the most severe clinical symptoms with marked orofacial deformities. The onset of symptoms occurs early in infancy and the patients are severely anemic and have a short life expectancy. Patients with the most severe form of the disease rarely survive into adulthood because of cardiac failure, chronic anemia and hypoxia. However, with modern management, the prognosis has greatly improved.(25)

ORAL MANIFESTATIONS:

The most common orofacial manifestations are due to intense compensatory hyperplasia of the marrow and expansion of the marrow cavity and a facial appearance known as "chipmunk" face: enlargement of the maxilla, saddle nose, frontal bossing of the skull and prominent malar eminences. Overdevelopment of the maxilla frequently results in an increased over jet and spacing of maxillary teeth and other degrees of malocclusion. Brodie syndrome (Mandibular arch is telescoped within the maxillary arch), malocclusion, high caries index, mucosal pallor, atrophic glossitis, severe gingivitis, inflammation of salivary glands, dark coloured gingiva, thin mandibular cortex, multiple diastemas roots- short and spike shaped, taurodontism. (26) Radiographic features include coarsening of trabecula and blurring resulting “salt and pepper effect”, thickening of diploe of skull. Inner and outer plates become elongated producing bristals like crew cut or hair on end appearance.(5)

TREATMENT

Treatment includes blood transfusion, chelating agent, bone marrow transplantation, splenectomy, folic acid supplementation. Any invasive procedure in thalassemia patients should be done under antibiotic cover and immediately after transfusion. Liver function and coagulation tests should be done before dental procedures are carried out. Orofacial defects and malocclusions in less severe types of thalassemia can be treated surgically followed by orthodontic treatment for alignment of teeth. Less severe malocclusions can be corrected by orthodontic treatment at an early age. Prescription of hepatotoxic drugs should be given cautiously. Tetracycline, metronidazole and erythromycin estolate should be avoided. Paracetamol is a safe alternative to NSAIDS and aspirin. Sedation or anaesthesia may be used during dental treatment of thalassemia patients for better control and cooperation. Caution should be exercised in thalassemia patients due to complications related to compromised immunity, liver function, splenectomy and cardiovascular issues. Multidisciplinary approach involving dental surgeon, haematologist and orthodontist should be practiced.(26)

CONCLUSION

A wide array of disorders of red cells and hemostasis encountered in internal medicine has manifestations in the oral cavity and the facial region. Most of these manifestations are non-specific, but should alert the hematologist and the dental surgeon to the possibilities of a concurrent disease of hemopoiesis or hemostasis or a latent one that may subsequently manifest itself. These manifestations must be properly recognized if the patient must receive appropriate diagnosis and referral for treatment. Proper diagnosis is essential to initiate the correct treatment.

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