Review Article

Significance of Orofacial Manifestations Associated with Anemia: A Review

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ABSTRACT:

When there is decrease in total erythrocyte count and oxygen carrying tendency of blood, it results in anemia. The common clinical features include fatigue, weakness and pallor. The oral cavity is affected by this disease and the common sites are labial mucosa, gingiva, tongue, periodontium and dentition. Oral findings include changes in the oral mucosa, periodontal inflammation, angular cheilitis, glossitis, mucosal ulceration and dental anomalies. According to World Health Organization (WHO),one third of the world population suffers from anemia because of improper food consumption and improper nutrition. Careful assessment should be done to recognize the oral manifestations of this disease, so that correct diagnosis can be done.

KEY WORDS: anemia, hemoglobin, iron, deficiency, blood

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INTRODUCTION:

Anemia is a disease in which there is decrease in the total hemoglobin level. In this disease, the number of red blood cells are decreased.[1] The decrease in the total erythrocyte count causes reduction in the oxygen carrying tendency of blood and it results in hypoxia of the body tissues. According to World Health Organization (WHO), almost one third of the world population suffers from anemia because of improper nutrition. In India, about 80% of maternal deaths occur due to this disease.[2] When the hemoglobin level is less than 13 gm/dl (grams per deciliter) in males and less than 12 gm/dl in females, it results in anemia. According to an estimation done by WHO, 293 million children globally are suffering from this disorder and almost half of them are because of deficiency of iron. The clinical features include fatigue, pallor and dyspnea.[3] Blood loss due to trauma or internal bleeding, diseases such as malaria and autoimmune diseases can cause anemia.[4]

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OROFACIAL MANIFESTATIONS ASSOCIATED WITH ANEMIA:

Sickle Cell Anemia-

Sickle cell anemia is a chronic, hemolytic blood disorder. In this autosomal recessive disorder, there is sick ling of red blood cells due to presence of deoxygenated hemoglobin under decreased oxygen tension.[5] There is homozygous state of abnormal hemoglobin S which causes change in the DNA(deoxyribonucleic acid) molecule. There is replacement of the amino acid valine for glutamic acid.[6] There is polymerization of abnormal hemoglobin which leads to the production of tactoids, which are fluid polymers. The red blood cells attain sickle shape. There is ischemic tissue injury due to chronic hemolytic anemia and vasoocclusion.[7[The membrane lipids of the blood cells are destroyed which leads to decrease in

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the supply of oxygen to the tissues and obstruction of capillaries as these damaged cells attach to vascular endothelium. The destruction of these cells by the spleen takes place.[5] The clinical features are observed between 6 months and 3 years of age. The sickle shaped cells are C shaped, rigid and sticky and cause the formation of clumps. But the initiation of features is delayed because of the protection provided by fetal hemoglobin.[6] Hyperbilirubinemia can take place. Clinical features include fatigue, irritation, tachycardia, shortness of breath and dizziness.[8] Fever, joint pain, muscle pain and weakness can occur. Hyperplasia of bone marrow and thinning of cancelloustrabeculae is common in such cases.[5] There can be increased thickening of the skull due to widening of the diploicspace, mandibular infarction, osteomyelitis of the mandible, bonesclerosis, paresthesia of the mental nerve, necrosis of pulp, pain in the orofacialregion, diastema and hypomineralization of the enamel can be observed in such patients. Radiographic features include step ladder shape of the alveolar bone and osteoporosis, due to reduction in the volume of trabecular bone. There is pain in the mandible, neuropathy involving inferior alveolar nerve and paresthesia of lower lip in such patients.[7] Mucosal pallor and jaundice is common. Thinning of cortical plate and diminished trabeculation can be seen radiographically. The inferior border of mandible loses its normal shape. There can be presence of denticle like calcified bodies in dentinal tubules and pulp chambers. Delayed eruption of teeth, enamel hypoplasia and dentin hypoplasia can occur, which can further lead to development of dental caries in such patients.[8]

On analyzing orofacial manifestations of sickle cell disease, it was found that mucosal pallor and jaundice is common in such patients due to early breakdown of red blood cells in the spleen. The decreased number of red blood cells can cause hemolytic anemia and hyperbilirubinemia. Gingiva,buccal mucosa and labial mucosa undergo discoloration in such patients. A microradiography study of dental tissues was conducted in such patients and it was observed that there were hypomineralized and diffused areas present in the tooth enamel. The presence of calcified structures in pulp chambers was also observed in the study.[8] The portion of enamel, which had undergone hypocalcification, would allow the development of cariogenic bacteria as these bacteria are connected to the base of the defects and are close to exposed dentin, thus leading to the development of dental caries in such patients. Fakuda et al conducted a study and observed that if patients, suffering from sickle cell disease, are given penicillin prophylaxis for a long time, it delays the acquisition of *Streptococcus Mutans*, thus, decreasing the risk of development of dental caries in such patients. Vaso-occlusive crisis can occur in such patients, due to disturbance of microcirculation in the pulp causing pulp necrosis. Blood thrombosis can cause calcified pulp stones in the pulp chamber.[8] There can be presence of radiopaque areas caused by repairs to bone infarction. Coarse trabecular pattern of staircase shape can be observed in the interproximal bone. Radiolucency can be observed due to decreased trabeculae and increased medullary spaces secondary to compensatory hyperplasia.[6]

In cases of mildly anxious patients, the treatment includes pain management anxiolytics and sedatives. Nitrous oxide gas also helps in reducing anxiety in patients undergoing dental treatment but in cases of severe anxiety, general anesthesia should be given. If such patients are suffering from infections then antibiotic therapy should be given. Acetaminophen is advised for pain relief in such patients as salicylates can cause acidosis.[8] In 1980, Konotey-Ahulu observed a disorder, known as mental nerve neuropathy, in such patients. In this disorder, vasculo-occlusion can occur in the maxillofacial region and can cause infarction of the blood supply to the nerves, which are mental nerve and inferior alveolar nerve. This can lead to loss of sensation, persistent anesthesia and neuropathy in lower lip and chin and this condition can continue upto 24 months. During sickle cell crisis, it was found that 4% of the patients complained of pain in mandible which varied in severity from moderate to severe. The development of burning sensation and numbness of lower lip occurred in such patients and the condition continued for months. The signs and symptoms developed along the path of mental nerve in such patients. In another case, a 40 year old male patient complained that his right mandibular first premolar, canine and incisors felt like wooden blocks.

After conducting a needle prick test, it was observed that profound anesthesia had developed in areas supplied by mental nerve. On radiographic analysis of right mental nerve, it was found that an ovoid radiolucency was present as a result of decreased trabeculation. It could also be due to sickle cell crisis causing production of acute bony infarct of the mandible. A follow up for 12 months was conducted, during which the pain disappeared but loss of sensation in the lower lip was present. No changes in the radiographic findings was observed.[8]

Iron deficiency anemia:

Iron deficiency anemia results from insufficient

iron in the normal red blood cells. Hepcidin is a hormone that is generated in the liver and it stops absorption of iron from intestine.[9] Iron is an important constituent of hemoglobin protein, helps in the movement of electrons within the cell, and helps in oxygen enzyme reactions.[10] In this disorder, the iron supply to the bone marrow is decreased and erythropoiesis is disturbed. Low plasma ferrit in and reduction in plasma iron transferrin saturation occurs with decreased hemoglobin.[9] The major causes include less consumption of iron, internal bleeding, blood loss because of menstruation and obstruction in the absorption of iron. Infants, children suffering from malnutrition, females of child bearing age, individuals who consume less iron in diet and people who donate blood multiple times are susceptible to this disorder.[10] The predominant reason of microcytic hypochromic anemia is iron deficiency anemia and mostly infants and children suffer from this disorder. The clinical features include headache, weakness, fatigue and nails of such patients attain spoon shape, which is called koilonychia.[11] Lethargy, tiredness, palpitations and breathlessness can occur.[12] Oral manifestations include glossitis, oral candidiasis, angularcheilitis, recurrent oral ulcers and erythematous mucositis.[3] There can be oral mucosal atrophy, which is generalized, in such patients. There can be angular stomatitis and cheilosis in such patients. Destruction of filiform and fungiform papillae causes atrophic tongue. Burning sensation and glossodyniacan occur in the oral cavity.[7] Iron deficiency anemia is related to Plummer Vinson syndrome and the features include iron deficiency anemia, dysphagia, atrophicglossitis, angularcheilitis, esophageal webs and presence of ulcers in the pharyngoesophageal region.[3] The treatment includes oral and parenteral iron preparations such as ferrous fumarate, ferroussulphate and ferrous gluconate.[13] In cases of fissured tongue, there are several fissures and grooves over the dorsum of the tongue. Many studies have been conducted which showed hereditary association in the etiology of the development of fissured tongue. It can be associated with various syndromes and conditions like Melkersson-Rosenthal syndrome, Acromegaly, Downsyndrome, Sjogren'ssyndrome, Geographictongue, orofacial granulomatosis and psoriasis. Alsheik E et al conducted a study and observed that 24.4% of the Egyptian patients suffering from iron deficiency anemiahave fissured tongue. Mostly such cases are asymptomatic but burning sensation can occur in patients suffering from iron deficiency anemia due to thinning of epithelium of the tongue. Per Lin et al observed that diffusion of spicy salivary elements through the epithelium of tongue, which has undergone atrophy, and their entry into the subepithelial connective tissue causes irritation of free sensory nerve endings. This leads to burning sensation, pain and numbness in the tongue. The presence of glossitis in patients suffering from iron deficiency anemia is indicated as a patchy or diffuse papillae atrophy affecting the dorsum of the tongue. Onhistopathological analysis, hypochromic microcytic cells in a peripheral blood smear can be observed. Such patients have decreased serum ferritin levels and increased Red Cell Distribution Width in the body.[14]

Megaloblastic Anemia-

Vitamin B12 deficiency associated with pernicious anemia, small intestinal diverticula, folic acid deficiency because of malnutrition, or surgical procedure involving ileum, can result in megaloblastic anemia.[7] There are characteristic morphological changes in the precursors of red blood cells.[15] Morphological changes can occur in bone marrow and gastrointestinal tract. Oral manifestations include magenta colouredtongue, recurrentaphthousulcers, glossitis and stomatitis.[7]

In megaloblasticanemia, there is obstruction in DNA formation and obstruction in the progression of the cell cycle. The cells develop abnormally without dividing, which results in megacytosis. Major causes are vitamin B12 deficiency or folic acid deficiency. There is presence of various immature, large and poorly functioning red blood cells, which are known as megaloblasts, in the bone marrow. Vitamin B12 deficiency is characterized by decreased vitamin B12 in blood and it is also called cobalamindeficiency. Common features include initiation of neurological problems, cardiacdisorders, poorreflex, poor muscle function, glossitis and altered taste sensation. Improper gastric or intestinal absorption is one of the major causes. This decreased absorption occurs due to pernicious anemia, which is a type of vitamin B12 deficiency anemia. Loss of intrinsic factors results in disturbed absorption of vitamin B12 as there is damage to gastric parietal cellsin chronic atrophic gastritis and this kind of megaloblastic anemia is called pernicious anemia. The treatment of megaloblastic anemia includes administration of vitamin B12 orally or with the help of injection. In pregnant women, vitamin supplements are advised.[16]

Pernicious Anemia-

Pernicious anemia occurs due to malabsorption of vitamin B12 causing its deficiency. This occurs due to insufficient intrinsic factor, which is important for

normal absorption of vitamin B12, as it leads to production of red blood cells. Therefore, the deficiency causes autoimmune atrophic gastritis.[1] It is an autoimmune disorder in which gradual atrophy of gastric mucosa is observed, which leads to reduction in the number of parietal cells, which is important for absorption of cobalamin, called vitamin B12.[17] The clinical features include breathlessness, fatigue, pain in chest, loss of normal colour of skin, difficulty in coordination and balancing of body, poor reflexes and depression.[4] Oral manifestations include burning sensation in the oral cavity, atrophy of tongue, disturbance in taste sensation, dysphagia and aphthous like ulcerations.[1] Females of more than 50 years of age are mostly affected.[12]

Oral manifestations include Hunter glossitis in which a shiny, erythematous tongue is observed in such patients. The management involves intramuscular injections of cyanocobalamin, hydroxocobalamin or methyl cobalamin. There should be regular evaluation of vitamin B12 levels and iron deficiency in the body. Sometimes administration of intramuscular injection is difficult in elderly patients suffering from sarcopenia and coagulopathy, so oral supplementation is preferred in such cases. In patients suffering from immune driven inflammatory mucosal lesions, the use of topical corticosteroids and low level laser therapy is preferred. In cases such as oral lichen planus, oralmucositis and neuropathic orofacialpain, low level laser therapy, with optical spectral range between 600 and 1100 nm (nanometer) is important for nerve inhibition and pain relief.[17]

Thalassemia-

Thalassemia is also called Cooley's anemia or Mediterranean anemia. It is a hereditary disease and there is improper formation of hemoglobin. There is decrease in hemoglobin and deformed red blood cells with decreased life span.[5] There is fault in the generation of alpha or beta polypeptide chains of hemoglobin. The various forms include homozygous, heterozygous or compound heterozygous.[7] Thalassemia minor is heterozygous type and is mild whereas thalassemia major is homozygous type and is severe, affecting mostly infants. Oraofacial manifestations include abnormally extending premaxilla and bulging cheekbones causing rodent like facial appearance in such patients. There is hyperplasia of the affected bone marrow and expanding of the frontal region of the skull with granular radiographic presentation.[5] Malocclusion,enlargement of maxilla and decrease in cortical dimensions can occur.[7] Large and coarse trabeculae, diminished lamina dura and decreased length of roots can be observed radiographically. There is radiolucency with thickened diploic space.[5] The treatment includes latest medical advances in transfusion, bone marrow transplantation and use of drugs aimed to remove excess iron, known as iron chelators.[18]

In a study involving 54 children and adolescents suffering from Thalassemia Major (which included 31 males, 23 females and thalassemia free controls),it was found that dental caries can occur in such patients, along with poor oral hygiene and gingivitis. The average DMFT value(decayed, missing, filled tooth) was found to be 6.26 for15 year old patients compared with 4.84 in the control group. Poor oral hygiene was present in 61.1% and gingivitis was present in 92.2% of the patients. Orofacial manifestations included chipmunk like face, frontalbossing, saddlenose, discoloration of the dentition, deterioration of labial mucosa, abnormal protrusion of maxilla and discoloration of oral mucosa. Radiographic features included hypoplasia of maxillary sinus, Class II malocclusion, diminished mandibular cortex, thickenedfrontal bone, obstruction in development of teeth and decrease in normal size of teeth. In 75.9% of patients, growth retardation was observed.[18]

Aplastic anemia-

Aplastic anemia is a blood disorder, which is fatal. There is damage to pluripotent stem cells in the bone marrow which leads to peripheral pancytopenia and hypoplastic bone marrow.[2] Clinical features include breathlessness, fatigue, dizziness, headache, pain in chest, abnormal sensation in limbs, paleskin, gingiva and nail beds.[12] Other features associated with neutropenia and thrombocytopenia can be observed in such patients.[2] Oral manifestations include multiple hemorrhages, candidiasis and oral ulceration.[7] Platelet deficiency may cause gingival bleeding, petechialpurpuric spots and mucosal hematomas in the oral cavity. The immunity of the patient is affected which can lead to the development of ulcers in the oral cavity.[2] Treatment for aplastic anemia comprises of blood and marrow stem cell transplants, blood transfusion and medication.[12]

Fanconi Anemia-

Fanconi anemia is an autosomal recessive disorder. The clinical features include bone marrow failure, physical discomfort and susceptibility to malignancy. The presence of café au lait spots, retarded growth, micrognathia, disturbance in functioning of limbs, obstruction in normal physical development of

the body, hyperpigmentation of neck and cardiovascular disorders can be observed in such patients. Oral manifestations include generalizederythroleukoplakia, periodontal problems, dental anomalies and focal ulceration in the oral cavity. The proneness of such patients to oral squamous cell carcinoma is common.[7]

CONCLUSION:

Anemia is a public health problem that results in damaged mental and psychomotor activity, obstruction in normal physical development of children, high rate of child and maternal mortality and high risk of parasitic infections. Nutritional deficiency such as iron deficiency, vitamindeficiency, foliatedeficiency, loss of blood due to hookworm infection, malaria, helminthic infections and low socioeconomic status are some of the causes of anemia. Patient should understand the severity of blood disorders and nutritional deficiencies. The patient should be aware of early signs and symptoms of such diseases. On the basis of various clinical features such as pallor, nailchanges, pedaledema, epithelial changes and diagnostic procedures such as routine blood investigations, bone marrow analysis and peripheral smear examination, an assessment about the diagnosis should be done. There should be proper understanding about the pattern of anemia whether it is acute or its initiation is insidious. Preventive dental therapy should be advised to the patients. Some patients visit dental clinics for emergency treatment rather than preventive care. The dental treatment should never be started during crisis unless it is unavoidable as in emergency cases. Periodic oral health examination every 6 months should be advised to such patients so that comprehensive care can be done.

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Conflicts of Interest

There are no conflicts of interest.

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