

Orofacial Manifestations associated with Anemia

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ABSTRACT

Oral cavity is the window to the body and is often the area where systemic disease first presents itself. The various tissues including lips, tongue, gingiva, mucosal surfaces, dentition, and bone are involved in the presentation of disease state. The most frequently affected is the periodontium, followed by the oral mucous membrane and the periapical inflammations. The review is not all inclusive; however, it does address some of the most common, as well as a few of the more rare anemia-associated disease states observed in both adults and children.

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INTRODUCTION

Examination of the oral cavity can reveal signs and symptoms of immunologic diseases, endocrinopathies, hematologic conditions, systemic infections, and nutritional disorders. Careful examination should include the assessment of mucosal changes, periodontal inflammation and bleeding, and general condition of the teeth. Identifying these oral findings may enable early diagnosis and treatment.¹

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In India, anemia is a common and serious health disorder. It is not a disease, but rather the expression of an underlying disorder or disease. Anemia is said to be present when the hemoglobin (a protein in red blood cells that carries oxygen to the muscles, brain, and other organs) level in the blood is below the lower extreme of the normal range for the age and sex of the individual. It is a functional inability of the blood to supply the tissue with adequate oxygen for proper metabolic function.²

ORAL LESIONS ASSOCIATED WITH ANEMIA

Fanconi Anemia

Fanconi anemia (FA) is an autosomal recessive disorder characterized by physical abnormalities, bone marrow failure, and predisposition to hematologic and solid malignancies. Oral findings associated with FA include lesions of oral mucosa like generalized erythroleukoplakia with focal ulcerations, diseases of periodontium, and dental anomalies. Fanconi anemia patients are at high risk for oral squamous cell carcinoma.³ Clinical findings in FA are *café au lait* spots, short stature, hand abnormality, micrognathia, developmental delay, hyperpigmentation of the neck, cardiac malformation, and many others. Fanconi anemia requires a multidisciplinary follow-up so that appropriate clinical management of patients and their families is achieved.⁴

Iron Deficiency Anemia

Nutritional iron deficiency is the most common cause of anemia throughout the world. Iron deficiency occurs on a sequential basis in three stages of progression. The first one is a negative oral balance, in which the demands for iron (or iron losses) exceed the body's ability to absorb iron from the diet. As long as iron stores are present, and can be mobilized, red cell morphology and indices are normal in this phase. The next stages are the iron-deficient erythropoiesis, characterized by the first appearance of microcytic cells on peripheral blood smear, and the iron deficiency anemia (IDA) itself, presenting as low levels of hemoglobin and hematocrit.⁵ Oral manifestations include angular cheilitis and atrophic glossitis or generalized oral mucosal atrophy.⁶ Painful fissures at the corners of the mouth (angular stomatitis) and dry scaling of the lips and corners of the mouth (cheilosis) are also common findings related to IDA (Fig. 1).⁷ The atrophic tongue is a



Fig. 1: Angular cheilitis



Fig. 2: Depapillation of tongue

result of depapillation and loss of filiform and fungiform papillae (Fig. 2). Moreover, glossodynia is a common complaint.⁵ Glossitis is significantly more common in those individuals who are deficient in vitamin B12 and folate. So, glossitis remains a valuable sign of vitamin B12 and folate deficiency. Iron deficiency glossitis has been described as a diffuse or patchy atrophy of the dorsal tongue papillae, often accompanied by tenderness or a burning sensation. Such findings are also evident in oral candidiasis. Some investigators have suggested that iron deficiency predisposes the patient to candidal infection, which results in the changes seen at the corners of the mouth and on the tongue.⁶

Clinical manifestations of vitamin B12 deficiency are paresthesia, peripheral neuropathy, combined systems disease (demyelination of dorsal columns and corticospinal tract), psychiatric irritability, personality change, mild memory impairment, dementia, depression, psychosis, possible increased risk of myocardial infarction, and stroke.⁸

Megaloblastic Anemia

Megaloblastic anemia 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). Deficiency of vitamin B12 manifests in the oral cavity as part of megaloblastic changes in gastrointestinal tract, and these changes are well demonstrated morphologically in the bone marrow. The oral manifestations of 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 have long been recognized. These oral changes may ensue in the absenteeism of symptomatic anemia or of macrocytosis. "Magenta tongue," which is said to be rather characteristic, may herald a B12 deficiency.⁹

Congenital Hypoplastic Anemia (Diamond-Blackfan Anemia)

Congenital hypoplastic anemia is a rare disease developing in early childhood. This disease is characterized by a normochromic, normocytic anemia, and a deficiency of erythroblasts in the bone marrow, and normal or near-normal leukocyte and platelet counts. Diamond and Blackfan (1938) were the first physicians to describe congenital hypoplastic anemia as a separate entity. The oral findings reported were severe gingivitis, multiple carious lesions, and poor healing of recent extraction sites.¹⁰

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- β thalassemia, and sickle cell HbC disease. Sickle cell anemia (HbSS) is the utmost common type and characterizes the homozygous form where the individuals inherit a double dose of abnormal gene which 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. With decreased oxygen tension, the abnormal hemoglobin polymerizes, forming fluid polymers (tactoids) that cause the red cells to deform into a characteristic sickle shape that may plug different areas of the microcirculation or large vessels. The trademark features of sickle cell disease are chronic hemolytic anemia and vaso-occlusion causing ischemic tissue injury. While a wide spectrum of complications result from these, the major manifestation of concern is "sickle crisis" of aplastic, hemolytic, or painful (vaso-occlusive) types, leading to devastating multisystem complications, including stroke, pulmonary disease, delayed growth, osteomyelitis, organ damage, and psychosocial dysfunction. Entire tissues and organs of the body are at jeopardy of injury due to sickling. Comparatively infrequent number of orofacial changes has also been observed in sickle cell disease. The basic pathogenicity is analogous to that in other organs. These orofacial changes in HbSS as reported in the literature include midfacial overgrowth attributable to marrow hyperplasia, other skull and jaw changes, such as increased thickening of the skull and osteoporotic changes, mandibular infarction that may be followed by

osteosclerosis, osteomyelitis of the mandible, anesthesia or paresthesia of the mental nerve, asymptomatic pulpal necrosis, orofacial pain, enamel hypomineralization, and diastema. The step-ladder appearance of the alveolar bone and areas of decreased densities along with coarse trabecular pattern is very easily seen between the root apices of the teeth and the inferior border of the mandible, which is a characteristic radiographic feature of dentofacial deformities. Mandibular osteomyelitis is commonly observed, which is rarely manifested with other complications, making its diagnosis and treatment easy. The mandible is the most affected part of the face when compared with the maxilla because the blood supply is relatively insufficient. Mandibular ache is preceded by extensive tender crises and is escorted by neuropathy which involves the inferior alveolar nerve and paresthesia of lower lip. Intravascular impairment can result in ischemic infarct and osteonecrosis and this allows proliferation of bacteria (*Streptococcus* or *Salmonella*). The likelihood of blood extravasations and hematoma secondary to sickle cell anemia-induced hemorrhage must be considered as a working diagnosis of a facial swelling in sickle cell disease. The higher number of malocclusions is associated with muscular imbalance, absence of labial sealing, or fluctuations in the osseous base, thus leading to augmented orthodontic intervention.⁸

Thalassemia

These are a group of inherited hemolytic anemia involving defects in the synthesis of either the α - or the β -polypeptide chains of hemoglobin (α -thalassemia, β -thalassemia). Depending on genetic and clinical entities, thalassemia is classified as homozygous, heterozygous, or compound heterozygous. The heterozygous form of the disease (thalassemia minor) is mild and usually asymptomatic, the only manifestation being hypochromic microcytic anemia. Homozygous β -thalassemia, also known as Cooley's anemia or Mediterranean anemia, is chiefly seen in Mediterranean populations with prevalence as high as 15 to 20% in Greece, Turkey, Cyprus, and southern Italy. 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: Bossing of the skull, enlargement of the maxilla, and prominent molar eminences. Overdevelopment of the maxilla frequently results in an increased over jet and spacing of maxillary teeth and other degrees of malocclusion.⁸

Aplastic Anemia

Aplastic anemia commonly presents with oral manifestation and can be the first clinical manifestation of the

disease. The most common orofacial manifestation of the disease is multiple hemorrhages, which most often develop in patients with platelet counts $<25 \times 10^9/L$. The other common manifestations are oral ulceration, candidiasis, and viral infection.⁸

Minkowski–Chauffard Hemolytic Anemia

Hemolytic anemias occur as a result of the excessive destruction of the erythrocytes, as a result of some intracorporeal effects of theirs (frequently of hereditary origin) or by the existence of some extracorporeal factors. Some oral and dental signs and symptoms are common to all hemolytic anemias. The pallidness of the oral mucous membrane is especially obvious at the level of the soft palate, tongue, and sublingual tissue, being more and more visible as anemia advances. Unlike the anemias produced through bleeding or deficiency of factors, the hemolytic anemias cause yellowing, as a result of the hyperbilirubinemia which accompanies the destruction of erythrocytes.¹¹

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 orofacial manifestations are nonspecific, but ought to alert the hematologist and the dentist to the potentials of a concurrent disease of hemopoiesis or hemostasis or a dormant one that may consequently manifest itself. These manifestations must be accurately recognized and patient must receive proper diagnosis and referral for treatment.

REFERENCES

1. Bolat M, Chiriac MI, Trandafir L, Ciubara A, Diaconescu S. Oral manifestations of nutritional diseases in children. Romanian J Oral Rehabil 2016 Apr-Jun;8(2):56-60.
2. Limaje JS, Choudhary NG. Oral complications associated with different types of anaemia: a mini review. IJRMF 2016 Oct;2(10):134-139.
3. Stoopler ET, Homeida L, Sollecito TP. Oral lesions associated with Fanconi anemia. Rev Bras Hematol Hemoter 2017 Apr-Jun;39(2):175-176.
4. Zen PR, de Moraes FN, Rosa RF, Graziadio C, Paskulin GA. Clinical characteristics of patients with Fanconi anemia. Rev Paul Pediatr 2011 Sep;29(3):392-399.
5. Braunwald, E.; Fauci, AS.; Kasper, DL. et al. Harrison's principles of internal medicine. New York: McGraw-Hill, Medical Publishing division; 2001.
6. Neville, BW.; Damm, DD, Allen.; CM., et al. Oral & maxillofacial pathology. Philadelphia: W.B. Saunders Company; 1995.
7. Pierro VS, Maia LC, Primo LG, Soares FD. Case report: the importance of oral manifestations in diagnosing iron deficiency in childhood. Eur J Paediatr Dent 2004 Jun;5(2): 115-118.

8. Oh R, Brown DL. Vitamin B12 deficiency. *Am Fam Physician* 2003 Mar;67(5):979-986.
9. Adeyemo TA, Adeyemo WL, Adediran A, Akinbami AJ, Akanmu AS. Orofacial manifestations of hematological disorders: anemia and hemostatic disorders. *Indian J Dent Res* 2011 May-Jun;22(3):454-461.
10. Willis TB, Seale NS. Oral manifestations in congenital hypoplastic anemia (Diamond-Blackfan anemia): clinical report. *Pediatr Dent* 1984 Sep;6(3):162-163.
11. Botez C, Cristina BI, Murariu VR. Study of the oral lesions caused by the Minkowski-Chauffard hemolytic anemia. *Int J Med Dent* 2011 Apr-Jun;1(2):118-121.