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Periodontal Manifestations of Hematological Diseases- A Review

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Abstract:- Numerous literature assessments have shown that periodontitis, despite inducing local inflammation, can also cause diverse systemic effects, similarly presence of any systemic conditions such as diabetes mellitus, hypertension, hematological diseases, cardiovascular disease, respiratory disorders, endocrine disorders, etc. can individually or collectively attribute to local inflammatory reaction resulting in complete loss of teeth and its associated structures. Among these systemic factors hematological disorders are uncommon and rare disorders that demonstrate non-specific oral and periodontal manifestations. The present review was undertaken to discuss briefly on the impact and role of various hematological disorders manifesting with substantial periodontal disease.

Keywords:- *Anemia, Cellular infiltration, Inflammation, Leukemia, Polymorphonuclear leukocytes, Tooth loss.*

I. INTRODUCTION

Dental plaque and calculus along with bacterial colonization are considered as the major etiological factors in the prevalence of gingivitis progressing to periodontitis if untreated. Periodontitis, a frequent multifactorial infection of the tooth-bearing supportive tissues that manifests as local inflammation influenced by wide-ranging determinants and contributing factors such as individual features, environmental factors, social and behavioral factors, genetic influences, systemic diseases, anatomical factors of teeth, dental plaque, calculus, microbial compositions and other emerging factors [1,2].Over the years, numerous studies have revealed that periodontal inflammation besides triggering a local inflammatory reaction, can also reveals extensive systemic effects, similarly presence of any systemic conditions such as diabetes mellitus, hypertension, hematological diseases, cardiovascular disease, respiratory disorders, endocrine disorders, etc. can individually or collectively attribute to local inflammatory reaction resulting in complete loss of teeth and its associated structures [3].

Among these systemic factors hematological disorders are uncommon and rare disorders that reveal non-specific as well as characteristic oral and periodontal clinical manifestations. Hematological disorders can be largely categorized into red blood cell (RBC) disorders that include anemia, sickle cell disease (SCD), hemochromatosis and inherited erythropoietic porphyria; white blood cell disorders including cyclic neutropenia, leukemia, lymphomas; and platelet cell disorders such as thrombocytopenia and plasma cell dyscrasias [4]. The white blood cell disorders remains as the notable hematological diseases of oral mucous membranes, teeth, periodontal tissues and Para-oral structures characterized by direct infiltration of atypical leucocytic cells, deposition of uncharacteristic proteins, and anomalous formation of blood components [5]. It has also been postulated that white blood cells and thrombocytes may be more reactive to periodontal pathogens and the subsequent activation might contribute to elevated athero-thrombotic changes in coronary artery diseases [6]. Investigations have similarly shown that patients with periodontitis have higher levels of WBCs, C-reactive protein, plasma fibrinogen and increased platelet activation in cardiovascular disease patients [7]. However the exact mechanism of these changes resulting in local inflammatory reaction with complete loss of teeth and its associated structures is still unknown. The present review was undertaken to discuss briefly on the impact and role of various hematological disorders manifesting with substantial periodontal disease.

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II. RED BLOOD CELL DISORDERS

Red blood cell or disorders of erythrocytes does not severely harm the periodontal tissue. However, certain diseases such as aplastic anemia, sickle cell anemia and acatalasia have been related with aggressive periodontal destruction and marked gingival inflammation.

❖ *APLASTIC ANEMIA (AA) :*

Aplastic anemia is an uncommon complex disease of hematological origin illustrated by decreased cellularity of the bone marrow resulting in production of insufficient hematopoietic stem cells leading to deficient production of leucocytes, erythrocytes and thrombocytes. The etiology is unknown; nonetheless studies have shown certain medications, exposure to benzene compounds, insecticides and viruses are frequently associated with the diseased state. Reduced neutrophil counts (<500/µL), reduced platelet counts (<20,000/µL) along with symptoms like fatigue, bleeding from nose, bruising and gingival hemorrhage are seen in severe disease [8, 9]. Several quantitative and qualitative defects of neutrophil, including neutropenia (cyclic), increased/decreased agranulocytes, and leukocyte adhesion disorders are characterized by severe or rapidly progressing aggressive periodontitis. Brennan et al in his study suggested that individuals with Aplastic Anemia rarely presents with an increased risk of alveolar bone loss. However minimal bone loss of about 10% was significantly noted. Apart from periodontal diseases oral manifestations such as sub-mucosal bleeding, spontaneous gingival bleeding, hemorrhage, swelling and herpetic lesions have also been reported [10].

❖ *SICKLE CELL ANEMIA:*

Sickle cell disease (SCD) is an autosomal recessive hereditary disorder resulting from abnormal formation of hemoglobin (HbS) in red blood cells (RBCs) during polymerization under hypoxia. The common oral manifestations are unilateral fractures of the mandible, pulpal necrosis, osteonecrosis, facial swelling, diastema, and gingival enlargement, mandibular osteomyelitis, and Oro-facial pain. Numerous studies have shown that increased adherence of neutrophil cells to the endothelium in the microcirculation is seen in SCD. Neutrophil and eosinophil derived mediators contribute to the inflammatory response in localized aggressive periodontitis and increased superoxide levels. As a result, severe periodontal damage that cannot be described by microbial invasion is significantly seen leading to loss of teeth and alveolar bone [11].

III. WHITE BLOOD CELL DISORDERS

An intense leukocyte infiltration is one of the most appreciable histo-pathological features of gingival inflammation and aggressive periodontal disease. These leukocytes play a crucial role in tissues reactions to the noxious and antigenic stimulants from the sub-gingival plaque microbes. The immune and inflammatory components are critical, complexly associated systems that dependent on each other for survival of the healthy tissues. Reserve systems are often existing which represent several functional deficiencies that are not lethal but do cause susceptibility to non-specific diseases such as chronic periodontitis. In general, quantitative Polymorphonuclear leukocytes (PMN's) deficiencies like neutropenia and leukemia are frequently accompanied by generalized aggressive periodontal destruction. Functional deficiencies as seen in multiple myeloma, Leukocyte adhesion deficiencies, Chediak-Higashi syndrome and Histiocytosis X (LCH) are often presented with localized periodontal destruction affecting only specific teeth [4, 5].

❖ *CYCLIC HEMATOPOIESIS:*

Cyclic hematopoiesis also known as cyclic neutropenia is an unusual condition illustrated by episodic hematopoietic breakdown of progenitor cells resulting in intense alternations in agranulocytes, granulocytes, thrombocytes and immature red blood cell counts with systemic manifestations like fever, lymphadenopathy, respiratory and dermal infections. The oral manifestations include Recurrent Aphthous ulcers, (RAS), persistent gingivitis, hemorrhage or necrotic gingiva, hyper-salivation and fetid odor [12]. The periodontal manifestations include fiery red, hyperplastic, edematous gingivitis accompanied by severe or aggressive periodontal tissue or alveolar bone loss. In the severe disease form marginal gingival ulcers, necrosis is seen associated with soft tissue bleeding and infrequent attached gingival tissue involvement. Histo-pathologically, the ulcerated areas demonstrate minimal or absence of neutrophil infiltration. The gingiva is often edematous, hyperemic and hyperplastic with areas of incomplete or loss of squamous cell layer. These features are often illustrated by deep periodontal pockets and severe aggressive alveolar bone loss [13].

❖ *LEUKEMIA:*

Leukemias are the most common malignancies of hematopoietic origin characterized by the abnormal, uncontrolled, increased production of leukocytes (WBC's) associated with destruction and complete replacement of the bone marrow with immature white blood cells. Loss of normal leukocyte function, destruction of hematopoietic cell lines, suppression or direct infiltration of leukemic cells into tissues produce diverse clinical manifestations such as anemia, tiredness or fatigue, lymphadenopathy, frequent infection, bone and gastro-intestinal pain, bleeding, and rash of purple spots (Purpura). Gingival hyperplasia or enlargement of the gingival tissue is the most common oral and periodontal manifestation seen in acute promyelocytic or monocytic leukemia resulting from leukemic infiltration [14]. Barrett proposed a grouping system for the gingival lesions based on etiological factors in leukemic patients [15]. It consists of four categories as follows:

- **Category 1:-** typical lesions caused by direct leukemic infiltration associated with clinical gingival overgrowth with or without bleeding.
- **Category 2:** direct drug toxicity caused by chemotherapeutic drugs with diverse gingival changes such as hyperplasia along with mucosal erosion and ulceration.

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- **Category 3:**encompasses the harmful effects caused as a result of graft-versus-host reactions.
- **Category 4**: haemorrhage, neutropenic ulceration and increased susceptibility to microbial infections caused by secondary effects of marrow/lymphoid tissue suppression.

Patients characteristically present with moderately edematous, bluish-red colored, fragile, erythematous gingiva that may impinge on the teeth with spontaneous bleeding due to thrombocyte deficit with compromised resistance to infection due to reduced immune and inflammatory cell infiltrates. In leukemic patients bleeding from gingiva is a common finding even in the absence of visible gingivitis. Also petechiae are frequently found with or without leukemic infiltrates and often diffuse submucosal bleeding appear as ecchymosis.

- *MULTIPLE MYELOMA (MM):*

Multiple myeloma is a rare malignant plasma cell disorder characterized by excessive production of immunoglobulin light chains clinically presenting with gingival tissue bleeding in the retromolar areas, severe bone pain caused by osteolytic lesions, pathologic fractures, alveolar bone destruction and expansion of the buccal cortical plates. Radiographically multiple "punched-out" bone lesions are pathognomonic. Approximately 30% of patients illustrate involvement of the mandible with associated swelling, pain, paresthesia, mobility and loss of tooth [16].

- *CHEDIAK-HIGASHI SYNDROME:*

Chediak-Higashi syndrome is an uncommon hereditary disease transmitted as an autosomal recessive inheritance caused by aberrations in the cytoplasmic granules resulting in compromised phagocytosis or lysis of bacterial microbes. The primary deficiency may be in the membrane activation regulation or decreased enzymatic potential, fusion of phagosome and lysosome. These affected cells are highly predisposed to bacterial infections due to the defective or reduced functional capacity of the Polymorphonuclear (PMN's) cells [17].

- *LANGERHANS CELL HISTIOCYTOSIS:*

Langerhans cell histiocytosis (LCH) is an unfamiliar disorder of indefinite etiology illustrated by destructive tissue infiltration by abnormal proliferation of histiocytes mixed with lymphocytes and eosinophils. LCH has a comprehensive spectrum of clinical manifestations. 10 to 20% of cases have shown localized osteolytic lesions radiographically termed as "floating tooth" with pathologic fractures of maxilla or mandible, resulting in edema and mucosa ulceration, gingival inflammation, necrosis, recession and increased tooth mobility with tooth loss prematurely [18,19].

IV. PLATELET DISORDER

- *THROMBOCYTOPENIA:-*

It is a term used to describe the disorder of decreased platelet count resulting from either lack of platelet assembly, platelet production or increased loss of platelets associated with prolonged clot retraction and bleeding time under normal or marginally elongated clotting time. Oral manifestations include petechiae and hemorrhagic vesicles occur in the soft palate, tonsillar pillars, oral mucous membrane and the buccal mucosa. Gingival changes signify an abnormal response caused by local irritation.

- *MANAGEMENT:-*

- *Thrombocytopenicpupura*

Periodontal therapy for these hematologically compromised patients should be directed towards reducing inflammation and its associated mediators by mechanical removal local irritants such as plaque and oral biofilm to avoid need for more aggressive therapy. Oral hygiene instructions, diet counseling and frequent self or professional prophylactic management are necessary in these patients to improve prognosis.

- *Leukemia:*

Improved or advanced periodontal treatment for patients with leukemia is based on increased susceptibility to infections, bleeding tendency and the effects of chemotherapy. A physician's close cooperation is required. In the acute phases, only emergency periodontal therapy should be given. Antibiotic therapy is a treatment of choice. For chronic remission patients scaling and root planing can be done without complications.

- *Agranulocytosis:*

During the period of disease remission conservative periodontal treatment can be done. Under antibiotic protection scaling and root planing should be performed carefully.

V. CONCLUSION

Several disorders of erythrocytes and leukocytes may affect the course of periodontal therapy. Alteration in wound healing, bleeding tissue appearance and susceptibility to infection may occur. One should be should be aware of the clinical signs and symptoms. Hemo-Diagnosis should be done prior to periodontal therapy. Clinicians should measure various clotting mechanism indicators like hemostasis, coagulation or lytic phase factors. Investigations such as bleeding and clotting time, total blood cell count, thrombin time, pro-thrombin time and partial thromboplastin time should be properly evaluated.

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