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Hematological Diseases Related To Oral Cavity – A Review

¹MADHUMITHA.V, ²DR.JAYA KARTHIK.S.S, ³DR.MATHUMALA SUBRAMANIAN,
⁴DR.KARTHIGA.P, ⁵DR.SATHISH KUMAR.M

¹Under graduate, Department of oral pathology ,Karpaga Vinayaga Institute of Dental sciences,Chengalpattu.

²Post graduate, Department of oral pathology ,Karpaga Vinayaga Institute of Dental sciences,Chengalpattu.

³Post graduate, Department of oral pathology ,Karpaga Vinayaga Institute of Dental sciences,Chengalpattu.

⁴Professor, Department of oral pathology ,Karpaga Vinayaga Institute of Dental sciences,Chengalpattu.

⁵Head of the Department, Department of oral pathology ,Karpaga Vinayaga Institute of Dental sciences,Chengalpattu.

Abstract

Periodontitis, a widespread oral condition, can have far-reaching effects on overall bodily health. Research has increasingly explored the potential links between periodontitis and various blood disorders. This study reviews existing literature on the connection between periodontitis and certain blood conditions, including red blood cell disorders like aplastic anemia and sickle cell anemia, as well as white blood cell disorders such as cyclic neutropenia, leukemia, and multiple myeloma. By examining these relationships, healthcare professionals, including physicians and dentists, can improve diagnosis, monitoring, and treatment of patients with both oral and blood disorders, emphasizing the importance of collaborative care for those affected by these interconnected conditions.

KEYWORDS: Aplastic Anemia (AA), Multiple Myeloma (MM), Cyclic Neutropenia (CyN), Sickle Cell Disease (SCD), Non-Hodgkin lymphoma (NHL), Anemia of Chronic Disease (ACD), Acute Lymphoblastic Leukemia (ALL), Langerhans Cell Histiocytosis (LCH).

Introduction

Periodontitis is a chronic inflammatory condition that affects the periodontium, leading to the deterioration of periodontal ligaments and alveolar bone, and potentially resulting in tooth loss^{[1][2]}. The oral cavity is home to a diverse range of microorganisms, with approximately 700 species of bacteria present. The oral microbiota plays a significant role in the development of periodontitis, with certain bacterial pathogens triggering an inflammatory response that damages connective tissue.

Gram-negative bacteria, such as *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Prevotella intermedia*, and *Tannerella forsythia*, are commonly associated with periodontitis, with *Porphyromonas gingivalis* being a primary pathogen found in subgingival plaques^{[3][4]}. Additionally, there is evidence of a connection between certain periodontal diseases and blood diseases, such as anemia, leukemia, and multiple myeloma^{[5][6][7]}.

The connection between periodontal disease and hematologic diseases is significant, and it's essential for physicians and dentists to consider this relationship when diagnosing and treating patients^[8]. These findings underscore the importance of ongoing management of periodontitis to maintain not only oral health but also systemic health. By controlling periodontal disease, healthcare providers can potentially reduce the risk of developing or exacerbating hematologic diseases, and vice versa^[9].

Relationship between Hematological disorders and Periodontitis

Hematological disorders refer to a range of conditions that impact the hematopoietic system, which is responsible for the production and function of blood cells. Blood disorders can impact different parts of the blood, such as red blood cells, white blood cells, platelets, and plasma, leading to a range of health problems. Some of the most prevalent hematological disorders include anemia, a condition characterized by a lack of healthy red blood cells, as well as leukemia and lymphoma, which are types of blood cancers.

These changes are thought to reflect the body's inflammatory response to periodontal infection, which triggers a systemic inflammatory reaction. The presence of an inflammatory infiltrate rich in leukocytes can enter the systemic circulation, stimulating the bone marrow to produce more cells that participate in the inflammatory response. Furthermore, bacteria in the periodontium can penetrate the damaged epithelium and cause a systemic inflammatory reaction^[5].

Moreover, the immunomodulatory effects of periodontitis on hematopoietic stem cells suggest that periodontal pathogens and the inflammatory environment they induce may significantly influence the differentiation and function of these cells. Studies have revealed significant demographic and hematological differences between groups, indicating that stages of periodontitis are related to changes in hematological parameters. This comprehensive data set provides valuable information for both clinical practice and further research on periodontal disease, highlighting the importance of considering the impact of periodontitis on overall health^[10].

Diseases related to Red blood cell disorders and Periodontitis

Aplastic anemia(AA)

Aplastic anemia is a rare and complex disease characterized by a significant reduction in the production of blood cells, resulting in pancytopenia, a condition characterized by a reduction in the count of red blood cells, white blood cells, and platelets in the peripheral blood, resulting in a decrease in the overall blood cell count. This condition is often caused by an immunological response, where the immune system attacks the bone marrow, leading to a decrease in the production of blood cells. While some cases of aplastic anemia are inherited, most cases are acquired and can be triggered by various factors, including exposure to certain drugs, viruses, toxins, and genetic mutations. In some cases, the exact cause of the disease remains unknown^[11].

Thrombocytopenia

Thrombocytopenia, a common feature of AA, can lead to coagulation disorders, manifesting as bleeding gingiva and hemorrhagic ecchymoses^[12].

Sickle Cell Disease (SCD)

Sickle cell anemia is the most common form of hemoglobinopathy, a group of inherited blood disorders^[13]. Due to their compromised immune system, patients with sickle cell disease are more susceptible to infections, including periodontal disease, which is characterized by systemic inflammation^[14]. These patients have a higher incidence of periodontal inflammatory disease, which is associated with elevated levels of acute phase biomarkers, compared to healthy individuals^[15].

Anemia of Chronic Disease (ACD)

Anemia of chronic disease is a type of anemia that occurs in individuals with chronic infections, chronic immune system activation, or malignant tumors^[16]. Chronic periodontitis is a chronic inflammatory disease marked by persistent inflammation^[17]. It is hypothesized that the low-grade systemic inflammation associated with periodontal disease may disrupt erythropoiesis, leading to a decrease in red blood cell count and

hemoglobin concentration^{[18][19]}. However, the relationship between periodontal disease and anemia is not fully understood, and conflicting results have been reported in the literature^{[19][20]}

Diseases Related to White Blood Cell Disorders and Periodontitis

Cyclic Neutropenia (CyN)

Cyclic neutropenia (CyN) is a rare hematological disorder that is a form of congenital neutropenia. It is characterized by a periodic decrease in the absolute number of neutrophils in the blood, which occurs approximately every three weeks and lasts for a few days^[16]. Oral symptoms of CyN include oral ulcers, angular cheilitis, periodontitis, and premature tooth loss. These symptoms can be severe and resemble those of recurrent aphthous stomatitis and aggressive periodontitis, making differential diagnosis challenging. Further hematological tests are necessary to confirm the diagnosis of CyN and distinguish it from other conditions. The oral symptoms of CyN highlight the importance of interdisciplinary collaboration between hematologists and dentists in the diagnosis and management of this condition^[21]

Multiple Myeloma (MM)

Multiple myeloma (MM) is a type of cancer characterized by the uncontrolled growth of plasma cells in the bone marrow, leading to the production of abnormal immunoglobulins. This condition can cause significant skeletal destruction, including osteolytic lesions, osteopenia, and pathological fractures^[22]. Treatment can also lead to dental complications, such as increased caries and periodontal disease, and bisphosphonate therapy can cause osteonecrosis of the jaw^[23]

Acute Lymphoblastic Leukemia/Lymphoma (ALL/LBL)

Acute Lymphoblastic Leukemia/Lymphoblastic Lymphoma (ALL/LBL) is a type of cancer that affects the lymphatic system and can occur in both children and adults. It is characterized by the abnormal proliferation of lymphocytes, which can lead to a range of symptoms, including anemia, neutropenia, and thrombocytopenia^[16]. Oral manifestations of ALL are well-documented in the literature, and a systematic review of studies shows that oral symptoms in patients with ALL are quite common. The most common oral lesions found in children with ALL undergoing chemotherapy are mucositis, candidiasis, periodontitis, and gingivitis, and the most commonly affected sites are the oral and labial mucosa^{[24][25]}

Others

Non-Hodgkin lymphoma (NHL)

Periodontal disease has been identified as a potential risk factor for Non-Hodgkin Lymphoma, but the exact relationship between these two conditions is still not well understood. It is possible that periodontal disease may contribute to the development of NHL through direct or indirect mechanisms, or that it may be a marker of underlying systemic inflammation or immune system dysfunction. Further investigation is needed to determine the nature of this relationship and to explore the potential implications for the prevention and treatment of NHL.^[25]

Mycosis fungoides

Mycosis fungoides is a type of cutaneous T-cell lymphoma that can progress to affect areas beyond the skin, including the oral mucosa, in its advanced stages. While gingival involvement is uncommon, it is essential for periodontists to be familiar with the oral manifestations of this disease. This is because patients with mycosis fungoides may not always present with visible skin lesions, especially if they are seeking treatment on an outpatient basis, making it crucial for dental professionals to recognize the potential oral signs of this condition.^[26]

Thalassemia

Thalassemia patients were found to have significantly higher gingival inflammation, emphasizing the need for targeted preventive strategies to reduce the risk of periodontal diseases. By implementing evidence-based guidelines, healthcare providers can help prevent periodontal diseases and minimize the complexity of oral health care for individuals with Thalassemia, improving their overall quality of life and health outcomes.^[27]

Langerhans Cell Histiocytosis(LCH)

Langerhans cell histiocytosis (LCH) is a rare and poorly understood inflammatory disorder that affects both children and adults, characterized by the uncontrolled growth of Langerhans cells.

This condition can affect any part of the body and may present with a range of symptoms.

Notably, oral manifestations of LCH can be the initial sign of the disease, and when it affects the periodontal tissues, it can be easily misdiagnosed as more common conditions such as chronic periodontitis, aggressive periodontitis, or necrotizing ulcerative periodontitis. Therefore, it is essential for dental professionals to be aware of the oral signs of LCH to ensure timely and accurate diagnosis.^[28]

Molecular Mechanisms Linking periodontists and Hematologic Diseases

Recent studies have shed light on the molecular mechanisms that connect periodontitis to hematologic diseases. A study published in the Journal of Proteome Research highlights the significance of proteomic changes in patients with periodontal disease and their systemic effects^[29]. The research emphasizes that proteins involved in inflammation, immune response, and tissue regeneration are differentially expressed in periodontal disease, potentially impacting hematologic health. Interdisciplinary care for patients with Hematologic diseases and periodontitis.

The management of patients with hematologic diseases who also suffer from periodontitis requires a coordinated interdisciplinary approach to ensure comprehensive care. Hematologic diseases, such as anemia, leukemia, and neutropenia, can significantly impact periodontal health, and conversely, severe periodontitis can exacerbate systemic conditions and complicate the management of hematologic diseases. Effective collaboration between dentists and hematologists is essential to address the complex needs of these patients.

Experimental studies have provided insights into the disease mechanisms of periodontitis, and these findings could pave the way for new therapeutic approaches in periodontal disease management^[30]. Subgingival instrumentation has been shown to have a positive impact on reducing systemic inflammation and serum bone resorption markers in premenopausal women with periodontitis.^[31]

The use of antibiotics as an adjuvant to subgingival instrumentation can significantly reduce systemic inflammation in periodontitis patients. Advanced regenerative procedures, such as the use of biomaterials like platelet-rich fibrin (PRF) and hyperacute serum (HAS), can offer promising alternatives to traditional methods, particularly for patients with systemic conditions like diabetes^[32].

Conclusions and Clinical and future perspective

The conclusions of this synthesis highlight the interconnected nature of systemic disease and oral health, emphasizing the critical role of oral health in the management of hematologic malignancies. The key findings include:

1. Oral manifestations, such as periodontal disease and gingivitis, serve as important indicators of underlying hematologic conditions and treatment side effects.
2. The compromised immune status of patients with hematologic malignancies increases the risk of oral infections, making vigilant oral hygiene and preventive care essential.
3. Interdisciplinary collaboration among healthcare providers is crucial for early recognition and treatment of oral health problems, improving overall patient outcomes.
4. As part of their comprehensive care, patients with blood cancers should receive regular dental care to prevent and alleviate oral health issues that can be exacerbated by their condition, ensuring optimal overall health and well-being.
5. Additional studies are necessary to create effective, personalized approaches to address oral health issues in patients with blood cancers, highlighting the crucial role of oral hygiene in the overall treatment and management of these conditions.

The association between periodontitis and hematologic cancer has been demonstrated in a cohort study in Taiwan, suggesting that periodontal health may play a crucial role in cancer prevention strategies.^[33]

Emerging evidence suggests a connection between periodontal disease and a higher risk of developing specific types of cancer, including hematological malignancies. This association highlights the critical role of oral health in preventing and managing systemic diseases, particularly those affecting the hematopoietic system. As a result, dentists must be proactive in managing periodontal health in patients with hematologic disorders, promoting a comprehensive approach to care that addresses both oral and systemic health challenges.

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