Available online at http://www.journalcra.com

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

International Journal of Current Research
Vol. 13, Issue, 03, pp.16654-16657, March, 2021

ISSN: 0975-833X

DOI: https://doi.org/10.24941/ijcr.41038.03.2021

REVIEW ARTICLE **OPEN ACCESS**

ORAL MANIFESTATIONS OF LEUKEMIA AND ITS DENTAL MANAGEMENT

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ARTICLE INFO

Article History:
Received 15th December, 2020
Received in revised form
12th January, 2021
Accepted 15th February, 2021
Published online 26th March, 2021

Key Words:
Leukemia; Oral Manifestations;
Dental management.

ABSTRACT

Leukemias are considered to be potentially lethal diseases in which there is neoplastic proliferation of bone marrow white blood cells. It presents varied clinical and oral manifestations. Thus the present review was aimed to describe the oral manifestations of leukemia and their dental management. This might be useful in early diagnosis of condition and improving patient outcomes.

Citation: Kratika Mohan, Shashwat Saxena and Jyoti Bisht. "Oral manifestations of leukemia and its dental management*", 2021. International Journal of Current Research, 13, (03), 16654-16657.*

INTRODUCTION

Leukemia is defined as a heterogeneous group of different hematological disorders that arise from hematopoietic stem cells due to uncontrolled proliferation of neoplastic cells.[1-2] The condition is characterized by impaired differentiation and programmed cell death[2]. Leukemia is the most common pediatric neoplastic disease of the white blood cells.The phenomenon behind the occurrence of leukemia is failure of precursor cells maturation leading to accumulation of blasts in the bone marrow.[3] This causessubsequentinhibition of normal hematopoiesis, resulting in deficiency of erythrocytes, mature leukocytes, and platelets.[4-5] The leukemias have been classified based on clinical-behavioural and histopathological criteria. They have been classified as lymphoid or myeloid lineage (according to the type of progenitor cell involved) and as acute or chronic leukemia (based on course of disease).[6-7]

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The incidence was observed to be 9 cases per 100,000 people, making it the most common neoplastic disease of the white blood cells.[7]Although the exact etiology of leukemia is still not known but it has been advocated by various researchers that several risk factorslikechemotherapy, ionizing radiation exposure, genetic disorders, viral infections, radiation exposure, smoking, chemical compounds, chromosomal abnormalities (Down syndrome), families with leukemic history/ members, and physical and chemical exposures can cause leukemia.[8-9] Various life-threatening complications are reported like recurrent infections, and severe bleeding episodes.[5] Leukemic cells can attackdifferent organs of our body likebone, spleen, liver, central nervous system (CNS), and oral tissues like gingiva.[3]The production of leukemic cells is detrimental to normal hematopoietic cells lines and various symptoms arise due to lack of normal blood cells. This causes marrow deficiency, decreased blood cell count and subsequently complications such infection, internal or external bleeding and finally leading to death. All these symptoms arise due to lack of normal blood cells.[8] It has been observed that oral manifestations are frequently seen in leukemic patients and may occur as an initial evidence of the disease or when disease relapses. Various symptoms are observed likeinfections, oral ulceration, petechia, mucosal pallor,

gingival enlargement and bleeding, noma, and trismus. Oral manifestations might result either from direct infiltration of leukemic cells (primary) or might be secondary to underlying conditions likeneutropenia, thrombocytopenia, or impaired granulocyte function.[9] Although various case reports and studies are available related to leukemia and its oral manifestations, but still the available literature lack the summarised details on oral changes of leukemia.[7-10]Thus the present review was aimed to describe the oral manifestations of leukemia and their dental management. This might be useful in early diagnosis of condition and improving patient outcomes.

Oral manifestations: According to the oral signs and symptoms and their response to dental treatment, the dentist should get the specific additional tests done concerned with the disease, so that the final diagnosis of associated systemic disease can be made possible. General manifestations of leukemia include anemia, fever, recurrent infection, bleeding, fatigue, lymphadenopathy, bone and abdominalpain, and purpura.[6] Oral lesions can arise in both acute and chronic forms of all types of leukemia.[8]The most common oral manifestations encountered with leukemia are pale oral mucosa, abnormal gum colour, ecchymosis, gingival petechiae, painless gingival hyperplasia, hemorrhages, gingival bleeding, buccal infections, and ulcerative necrotic lesions. Blood clotting and petechiae is observed due to decrease in platelet count. The decrease in white blood cells makes patient prone to frequent infections, such as oral sores, pneumonia, etc.The deficiency of red blood cells leads to anaemia, dyspnea and pallor, causing headaches, seizures, and migraine.[8]

Acute myeloid leukemia (AML) is an aggressive unusual disease that mainly occurs in elderly people accounting for approximately 25% of all types of leukemia, with a median age of over 65 years at diagnosis and with a slight male predominance.[10-12]The incidence of acute leukemia is less than 3% of all malignancies, but still it is the leading cause of death in childhood.[13] Acute promyelocytic leukemia is a subtype of acute myeloid leukemia with specific clinical and molecular features accounting for 5-8% of all cases of AML.[12] Theother is hypogranular variant that accounts for approximately 10-25% of adult APL cases. It has unique biological characteristics such as a higher white blood cell count at presentation.[13]

Oral Manifestations of AML: The common oral symptoms are easy fatigue, weakness, infections of variable severity, hemorrhagic findings likeecchymoses, gingival bleeding, epistaxis or menorrhagia. All these symptoms are related to complications of pancytopenia.[14] As compared to other types of leukemia, oral manifestations are commonlyencountered in AML. Signs and symptoms are 1) mucosal pallor because of anemia;2) spontaneous bleeding and petechial hemorrhages of palate, tongue, gingivae, or lips arising from thrombocytopenia; 3) gingival hyperplasia due to leukemic infiltration. Oral ulcerations are quite common and might occur due to neutropenia or direct infiltration by leukemic cells.[14] Patients may also exhibit infections like herpes and candidiasis because of immunosuppression.[15] The manifestations like gingival bleeding, oral ulceration and gingival hyperplasia are the early signs of AML[16]Rare clinicalfindings have also been observed in some cases likecracked lips, paresthesia of chin, tooth pain and mobility, and hemorrhagic bullae on labial, buccal mucosa and anterior dorsum of tongue, noma-like lesion.[15] Oral manifestations of pancytopenia due to leukemia are noticable from other causes of pancytopenia, like immune conditions, adverse drug reactions, and viral infections.[17] Rarely unusual maxillary mixed osteoblastic and osteolytic lesions have also been observed as an initial manifestation of AML.[18] As in AML the platelet counts decrease from 25 000 mm^{-3} to 60 000 mm^{-3} resulting in spontaneous bleeding. It has been observed that the prevalence of thrombocytopenia was more in patients with acute leukemia than those with chronic leukemia.[19] The oral manifestations manifest earlier in AML than in other types of Leukemia. The prognosis of the patients is variable, and is dependent on age, performance status, poor risk cytogenetics.[20] For survival, an effective early diagnosis is required. Thus dentists play a significant role for early detection of leukemia and referring the patient to a hematologist. For final diagnosis, a complete hemogram is required, with a bone marrow biopsy and immunophenotyping of peripheral blood film.[20] Early diagnosis and effective management are very important to minimize the complications and increase survival rate.

Chronic Myeloid Leukemiaisfeatured by the presence of large number of well-differentiated cells present in the peripheral blood film, bone marrow, and tissues. Disease has a prolonged clinical course. Chronic myeloid leukemia (CML) is one of the myeloproliferative disorders, accounting for 20% of all leukemia cases, predominantly seen in adults aged 30 to 50 years.[21] Signs and symptoms include hepatosplenomegaly due to infiltration by leukemic cells. The peripheral blood film shows leukocytosis with excess of myelocytes, neutrophils, and metamyeolocytes. Oral manifestations involve gingival and mucosal tissue enlargements due to direct leukemic cell infiltration.[22]Few rare oral manifestations are granulocytic sarcoma of the jaws is that represents a localized deposit of myeloid cells.

Acute Lymphoblastic Leukemia: Is a malignancy that occurred due to uncontrolled clonal proliferation of a transformed lymphoblast characterised by overgrowth and displacement of normal bone marrow precursors.[23-24]. It accounts for 97% of all types of leukemia with male predilection, commonly seen in 2-5yrs and after 50yrs of age.[25] ALL represents 75% of childhood leukemia cases and 20% of adult leukemias.[25]

Oral manifestationsof ALL: Signs and symptoms includefever, mucosal pallor, fatigue, dyspnea, weight loss, gingival bleeding, or echymoses, bone pain, hepatosplenomegaly, and lymphadenopathy. Rare complications reported are pericoronitis, trismus that might be due to intensive infiltration of leukemic cells into the deeper portion of the muscles of mastication.[23] Various mucosal anomalies like fetor oris, shallow papillae, extensive ulcers, coated tongue, tender oral mucosa and oral mucosal infections like candidiasis, mucositis, herpes simplex, varicella/zoster and cytomegalovirus has been observed.[26]

Chronic Lymphocytic Leukemia: Accounts for 25% to 35% of all types of leukemia, most commonly seen in Western countries, in people aged 50-80yrs.[27]**Oral Manifestations of CLL**include predisposition to involve the tonsillar tissues, lymphoid-bearing soft tissues in the oral mucosa.[17] Oral manifestations accounts for 5% of all cases involving vestibule, gingival, palatal regions with rare involvement of

alveolus and buccal vestibule.[28]Recurrent oral bleeding, purpura, palatal enlargement and gingival bleeding are encountered due to thrombocytopenia.

Management of Leukemic Oral Manifestations: Oral health care professionals should have a thorough knowledge of oral manifestations of systemic diseases. They play a trivial role in early diagnosis of condition thus directing the patient for appropriate investigations and referring them to a specialized professional.[28-29] Sonis et al.[29]classified leukemic patients into three categories high, moderate, and low risk for dental treatment. This categorisation is based on the type of leukemia and chemotherapy given. They advocated that dental treatment should be done based on treatment needs. Elective treatments should be delayed till the patient get into good clinical and hematological conditions.Potential sources of trauma like dental calculus, orthodontic appliances, unsatisfactory restorations, ill-fitting dentures, and traumatized teeth should be eliminated. Nonrestorable teeth must be extracted. [29]

Before the start of cancer therapy, priority should be removing sources of trauma and infection and giving appropriate treatment like extractions and periodontal care. Endodontic treatment of symptomatic nonvital teeth should be done at least a week before the start of chemotherapy so as sufficient time is there to evaluate the success of treatment.[28] Extraction is the treatment of choice if endodontic treatment cannot be done. All treatments should be preceded by antibiotic prophylaxis (penicillin or clindamycin) for about a week.[28] In asymptomatic teeth, endodontic treatment can be delayed until the haematological indices get stabilized. Teeth with periodontal issues like periodontal pockets greater than 6 mm, furcation exposure, significant bone loss, acute symptomatic infection, mobility, impacted and residual roots should be removed with priority.[28]Extractions should be done about two weeks or at least 7 to 10 days before the start of antineoplastic treatment. All surgical procedures should be atraumatic, without leaving any remnant bone edges.

Depending on the state of health and phase of therapy patient is undergoing, dental procedures can cause risk to the patient. Thus, noninvasive procedures (type I and type II) can be performed at any stage of the disease or treatment. Type III procedures may require special care. Finally, invasive procedures (types IV, V, and VI) offer higher risk.[30] In emergency situations involving pain (acute cases), the patient should be assisted in a hospital setting, with the institution of measures to increase the hematological indices (transfusions) with antibiotic coverage.[30]

CONCLUSION

Based on the literature review we observed various dental manifestations in different types of leukemia. The dental treatment of leukemia patients should follow some judicious protocols, mainly related to neutrophil and platelet counts. The presence of the dentist is essential in a multidisciplinary team, as maintenance of oral health contributes significantly to the overall health and quality of life.

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