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A Leukemic Patient in a Dental Clinic

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Abstract: *Leukemia is common malignancy of white cell lineage of hematopoietic system.It affects individuals of any age group. Leukemia is also manifested in oral cavity. Apart from primary oral manifestations due to leukemia in oral cavity, there are numerous adverse effects of anti neoplastic therapy and stem cell transplantation, in these patients. Oral complications can compromise the protocols of chemotherapy, possibly making it necessary to decrease the administered dose, to change the treatment protocol, or even discontinuation of antineoplastic therapy, directly affecting patient survival.In this regard, the insertion of dentistry in the multidisciplinary speciality of hemato-oncology is an important part of the success of cancer treatment. Dentists in general and oral medicine specialists in particular, should have thorough and updated knowledge about the oral complications and their management considerations in such patients at different stages of disease and therapy. This paper is a brief review focusing at the oral manifestations and their management considerations which might serve as basic guide for dental clinician.*

Key Words: *Leukemia, Oral Manifestations, Dental considerations*

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I. Introduction

Hematopoietic system of human body,is a complex, highly organised system. It is comprised of blood and blood forming units, the bone marrow & reticuloendothelial system. Accordingly,the hematopoitic system has blood & blood cells as two main units.The pecularity of this system lies in fluid nature of blood which actually belongs to connective tissue category.[1]The components of the hematopoietic system have been traditionally divided into the myeloid tissues, which include the bone marrow and the cells derived from it (e.g., red cells, platelets, granulocytes, and monocytes), and the lymphoid tissues, consisting of the thymus, lymph nodes, and spleen.Hematopoietic Stem Cells(HSCs) have two essential properties that are required for the maintenance of hematopoiesis: pluripotency and the capacity for self-renewal. Pluripotency refers to the ability of a single HSC to generate all mature hematopoietic cells.[2]The disturbed hematopoietic system, secondary to various intrinsic & extrinsic factors of host, results in hematological malignancies like Leukemias. According to NCI dictionary of cancer terms,leukemia is " a rapidly progressing cancer that starts in blood-forming tissue such as the bone marrow, and causes large numbers of white blood cells to be produced and enter the blood stream." In simple terms, leukemia is an acute or chronic disease in humans and other warm-blooded animals characterized by an abnormal increase in the number of white blood cells in the tissues and often in the bloodstream.According to latest updated classification of Hematological malignancies(2016), leukemia has more than 20 subtypes.[3]

II. Discussion

2.1 *Leukemia manifested in oral cavity*

As it is truly said, "oral cavity is a mirror of systemic health", leukemia,being a systemic condition is also manifested in oral cavity. Apart from the primary effects of leukemia in oral cavity,it is also secondarily effected by therapy given for treatment of leukemia. As an oral health expert,dentist is an important & integral member of leukemia health care multidisciplinary team.[4] Leukemia being a disorder affecting common masses, such patients are frequently encountered with different oral manifestations by practising dentists. It is important for a dentist to be well aware of features of leukemia manifested in oral

cavity,the oral complications related to therapy and their management. Moreover, the fitness of a leukemic patient to undergo dental treatments should also be assessed prior to initiating any therapy.

2.2 Oral manifestations of leukemia secondary to disease

Different clinical manifestations falling under this category include the following.

2.2.1.Oral manifestations secondary to Anemia: The mucosa of oral cavity appears pale and bloodless instead of normal pinkish or reddish appearance. Anemia in leukemic patients results from infiltration of bone marrow by leukemic cells and hence resulting in reduction of red blood cells. Anemia is also a secondary contributor to poor wound healing in oral cavity due to reduced oxygenation to cells.[5]

2.2.2 Oral manifestations secondary to Thrombocytopenia: Infiltration of bone marrow by abnormal white blood cells(leukemic cells) results in impairment in production of platelets. The platelet counts in such patients may reduce severly resulting in bleeding episodes. Thrombocytopenia manifests in oral cavity as petechiae, ecchymoses, easy bruisibility, gingival bleeding and prolonged post op bleeding. These problems are encountered when platelet count drops below 20,000/cu.mm.[6]

2.2.3 Oral manifestations secondary to leukemic cell infiltration: Gingival hyperplasia secondary to infiltration of the gingival tissue with leukemia cells is characterized by progressive enlargement of the interdental papillae as well as the marginal and attached gingival. In the condition's most pronounced form, the crowns of the teeth may be covered. Gingiva appear swollen, devoid of stippling and pale red to deep purple in colour. Gingival infiltration by leukemic cells will also predispose the patient with leukemia to bleeding.[7]According to Sinrod et al[8] & Boggs et al. [9]Indicated that gingival enlargement in such cases is due to leukemic infiltration of gingiva while as the local irritants act as co factors. Because, even in patients having meticulous oral hygiene maintenance, gingival enlargement was noted. Clinically, gingiva appears as swollen, glazed, shiny, reddish or bluish red, non stippled, soft, edematous and tender on palpation. Initially, interdental papilla is involved which gradually extends to involve marginal gingiva too. In oral cavity, gingival tissues remain selective to be infiltrated by leukemic cells. According to Barrett,[10] the selective infiltration of gingival tissues is partially due to the inherent extravascular infiltrative properties of the leukemic cell, and partially due to the unique gingival microanatomy. Some reserchers[11]concluded thatapparent acceleration in the mitotic rate and the absolute number of leukemic cells are key factors in initiating gingival infiltration.These two concepts have partly explained the selective infiltration of gingiva, although the actual mechanism remains obscure and more research is needed in this regard.

2.2.4 Oral manifestations secondary to Neutropenia/Leukopenia:Although leukemia is condition of increase in white blood cells, but the cells are functionally & structurally impaired and are unable to fight infections in body. Apart from this functional impairment, the excess number results in reduction in number of functional WBCs, RBCs & platelets. The functional leukopenia finally results in variety of complications like oral ulcers which includes Chronic recuurent ulcers, Recurrent aphthous stomatitis, Deep gangrenous ulcers, Acute Necrotizing Ulcerative Gingivitis(ANUG).Oral mucosal ulcers are common findings in leukemic patients receiving chemotherapy and are frequently caused by the direct effect of chemotherapeutic agents on the oral mucosal cells. Bacterial invasion following a severe neutropenia also plays a role in the development of oral ulcers, that could be an early sign of disease. The ulcers are characteristically large, irregular, foul smelling, and surrounded by pale mucosa caused by anemia and a lack of nonnal inflammatory response.

2.2.5 Oral features secondary to lymphadenomegalia: Dysphagia, Odynophagia.

2.2.6 Oral features secondary to nervous system involvement: Paresthesia of lower lip, tenderness on mental foramen, Bell,s palsy, Hypoglossal nerve paralysis, Herpes zoster, Hunt zoster

2.2.7 Swelling of salivary glands:It occurs secondary to infilitration of glands by leukemic cells.

2.2.8 Periodontitis: Manifested as periodontal attachment loss, tooth mobilty & loss of teeth & periodontal Pain.

2.3 R*adiographic features of leukemia in jaws & teeth[12]*

2.3.1 Jaws:

Marrow replacement by proliferating cells results in generalized rarefactions of bone. Effects on jaws are more pronounced if patient is young & disease is more severe. Multiple radiolucent lesions to solitary moderately defined osteolytic lesions, generalized rarefaction, moth eaten appearance, occasionally osteosclerosis, thinning of jaw cortices, destruction of marrow spaces,unilateral or bilateral involvement of jaws are found to be common manifestations in jaws..

2.3.2 Teeth:[13]

The features include;Incomplete/ delayed formation of tooth crowns,Cortices of tooth crypts are partially or completely destroyed,Enlargement of crypt with failure of bone formation around it, Asymmetric position of tooth in crypt due to destruction, Crowns situated above crest being completely elevated from the bone,Partially formed teeth show rapid eruption.Lamina dura may be missing.

2.4 O*ral complications secondary to therapy*

Patients with leukemia are recieving various cytostatic treatments. There are various side effects noted in oral & maxillofacial regions secondary to chemotherapy or stem cell transplants. Most common are described as follows:

2.4.1 xerostomia: is primarily a complication related much more to radiotherapy than chemotherapy, but several times children undergoing chemotherapy may experience temporary changes and decrease in saliva amount. In leukemic patients,radiotherapy is not part of main treatment but is used when brain, spinal cord or testes are involved. In such patients the radiation induced injury to salivary glands followed by replacement of glandular tissue by fibrous tissue results in reduction in salivary flow. Apart from this, in leukemia salivary gland function is reduced due to infiltration of leukemic cells into salivary glands.The oral changes often encountered in these patients are: dry mouth (the mucous membranes appear atrophic and hyperemic with fissured tongue and dry lips), difficulty in eating and talking, burning sensation, changes in taste perception. In xerostomia, following periodontal inflammation there is reduction of vascularization and the less cellular conditions take to few alterations at Sharpey's fibers and periodontal sulcular depth. Cemental dysfunction, with a drastic decrease in its regenerative capacity is also noted. Reduced salivationalso promotes the accumulation of plaque, stimulating indirectly the onset of periodontal disease. Moreover nocturnal disorders (polydypsia due to xerostomia followed by polyurea) and increased tooth sensitivity has also been reported.[14]

2.4.2.oral mucositis: It is common complication, and contributes to the severity of the disease. The mechanism of its development is not yet fully known, but, since it is a syndrome of multifactorial etiopathogenesis, its prevention and treatment are also multifactorial. The most common reasons for mucositis, according to different researchers are graft-versus host disease(GVHD) secondary to allogenic transplant which may also have numerous other oral manifestations (such as lichenoid mucositis, xerostomia, erythema, mucosal atrophy, scleroderma, and pyogenic granuloma). The development of these manifestations indicate poor prognosis and their timely detection is of paramount importance. Mucositis is most common oral manifestation and found to be in 20 to 40% o f patients under antileukemic treatment. For most of the researchers the most common cause for mucositis is chemotherapy which leads to destruction of basal cells. Another proposed mechanism is by direct effect of antineoplastic agents on oral mucosa resulting in tissue damage.

2.4.3.**oral ulcers**:The most common cause of oral ulcers in leukemic patients receiving chemotherapy is recurrent HSV infections which involve the intraoral mucosa and the lips. The lesions frequently begin with the classic cluster ofvesicles typical of recurrent HSV, and quickly spread out causing large ulcers that often have a raised white border. In all patients receiving chemotherapy, HSV should be ruled out as a cause of oral ulcers with a cytology smear stained with fluorescence for HSV antibody and a viral culture.Viral infections especially the reactivation of herpes simplex virus type I (HSV- I) is serious because they can cause pain and problems with hydration and nutrition. HSV I is the virus most frequently associated with the onset of infections during the chemotherapy. The lesions may occur in the nose, the lips, eye lids and different areas of skin as well.Herpes zoster occurs with a higher frequency in immunosuppressed patients or during chemotherapy treatment. Oral lesions rarely include intact vesicle. In rare casesorofacial tissue necrosis has also been observed. In children undergoing chemotherapy, oral lesions of chickenpox appear to be more pronounced, accompanied by pain anddifficulties in alimentation. Apart from ulcers of viral origin, these patients may also encounter chronic non healing ulcers secondary to low number of neutrophils and change in quantity and quality of saliva.

2.4.4.poor wound healing: In patients who are on chemotherapy or who have received chemotherapy in recent past, alveolar osteitis is noted followed by extraction. Soft tissue wound healing is also effected. It occurs due to collagen derangement secondary to toxic effect of antineoplstic therapy.

2.4.5.chemotherapy induced odontalgia: Toothaches noted in patients on chemotherapy do not respond to even narcotic analgesics and are very difficult to manage.Several anti cancer medications result in peripheral neurotoxicity & neuropathic pain. This is the cause for vague pain in orofacial region, numbness & dental pain in patients on chemotherapy.[15]

2.4.6.bleeding tendency: Increased bleeding tendency in buccal mucosa, gingiva etc is also a common finding.. Purpura of hard palate, tongue and spontaneous bleeding is also noted. The reason for increased bleeding tendency being thrombocytopenia and anemia.

2.4.7 gingivitis: The chemotherapy phase also showed an association with the onset of gingivitis. Research supports that the severity of gingivitis in such patients is directly related to the oral hygiene of the patient. The poorer the oral hygiene,the severe the gingivitis.

2.4.8 dental caries:Higher incidence of caries in such patients results from change in flora, change in quality & quantity of saliva, due to expression of cytotoxic drugs into saliva and exposure of root surface secondary to periodontal compromise.

Among the drugs most often associated with oral manifestations, teniposide, paclitaxel, methotrexate, idarubicin, epirubicin, doxorubicin, cisplatin, and cytarabine are associated with mucositis, xerostomia, gingival bleeding, and other diseases of the oral cavity.[125] Methotrexate, bleomycin, doxorubicin, cisplatin, vinblastine and

vincristine are drugs that produce direct toxicity by some of their antimetabolites and other synthetic agents, such as hydroxyurea and procarbazine hydrochloride, which lead to glandular degeneration, changes in collagen, and epithelial dysplasia. Drug combinations used during chemotherapy have shown to cause more severe oral adverse effects.

2.5 ***Oral manifestations related to human stem cell transplant (HSCT):***

Theoral manifestations have found to be slightly variable in differnt phases, that is, pre-, immediate post-, and late post-HSCT phases.[16]

(1) **Preconditioning phase:** oral infections, ulceration, bleeding, and temporomandibular joint dysfunction;

(2) **Neutropenic phase conditioning**: mucositis, dysgeusia, xerostomia, bleeding, oral pain, opportunistic infections, neurotoxicity, and temporomandibular dysfunction, usually manifesting with high prevalence and severe forms. At this stage, the patient may develop hyperacute Graft Versus Host Disease(GVHD) with further severe oral complications.

(3) **Engraftment to hematopoietic recovery**: Opportunistic infections are common and acute GVHD becomes a concern; bleeding may be present, xerostomia, neurotoxicity, granulomas/papillomas, and temporomandibular dysfunction is also noted.

(4) **Immune reconstitution/recovery from systemic toxicity**: salivary dysfunction, late viral infections,craniofacial growth abnormalities,cGVHD, and squamous cell carcinomas.

(5) T**he long-term survival**: in pediatric patients, particularly children under 6 years, one can observe complications in the development of bones and teeth; at this stage, recurrence and malignant neoplasms can be observed.

GVHD, mainly manifests in oral cavity as mucositis, gingivitis, erythema,pain,lichen-type features,hyperkeratoticplaques, mucocele, atrophic mucosa, ulceration, fibrosis with limited mouth opening, hyposalivation, and xerostomia. In addition, secondary to cGVHD, the patients have a greater tendency to develop malignancies.The gingival status and tooth mobility have a potential risk factor for complications, especially periodontal pockets greater than 6 mm. Gingival pockets of this size favor greater accumulation of bacteria and necrotic tissue, and increase the risks for dentaland oral disease. Another common observation, in approximately 80% of the patients, is gingival hyperemia, probably due to toxic reactions to drugs used during conditioning. Another likely cause is oral mucosa sensitization due to antiseptic mouthwash (chlorhexidine) used for oral hygiene. Patients do not brush their teeth for fear that trauma caused by the brush can cause bleeding, due to thrombocytopenia. The lack of brushing can result in an increase in bacterial plaque, causing gingivitis. Researchers have reported that orthodontic devices and dentures are also risk factors for stomatitis.[17]

2.6 ***Dental treatment considerations in leukemia patients***

2.6.1 General considerations: For the oral complications manifested in leukemic patients due to leukemia/treatment, the dental treatment should be planned on the basis of antineoplastic therapy which can be chemotherapy with or without radiotherapy and bone marrow transplantation. In addition, performing dental procedures at different stages of treatment (before, during, or after) certain protocols need to be followed in relation to the haematological indices of patient. The main aim of dental treatment is to maintain health as well as to contribute to the effectiveness of the results of antineoplastic therapy. If dental treatment is not carried out appropriately, it not only makes patient's life difficult but also interferes with delivery of effective antineoplastic therapy and hence reduces the survival. For the US National Cancer Institute[18]the multidisciplinary team should have oncologists, nurses, dentists (general and stomatological practitioners), social workers, nutritionists, and other health professionals, which may contribute to the prevention and treatment of oral complications in these patients.

2.6.2 Patient categories:The feasibility to perform dental procedures in leukemia patients depends on the overall state of health of the patient, as well as the stage of the disease and/or antineoplastic therapy or hematopoietic stem cell transplantation. A simplified guide has been developed for guidance of residents in dentistry for the dental care of oncohematological patients at University Hospital, Federal University of Santa Catarina.They have adapted the classification proposed by Sonis et al.[19] Sonis et al. proposed the classification of patients into categories of high, moderate, and low risk for dental treatment, based on the type of leukemia (acute or chronic) and chemotherapy.

High-risk patients are those with active leukemia, which have a high number of neoplastic cells in the bone marrow and peripheral blood; because of this, they are thrombocytopenic and neutropenic. This risk group also includes antileukemic patients under treatment, and as a result of therapy, present bone marrow suppression.

Moderate risk patients are those who successfully completed the first phase of treatment (induction) and are undergoing the maintenance phase, thus not showing signs of malignancy in the bone marrow or peripheral blood; however, they present myelosuppression due to chemotherapy.

Low-risk category are patients who successfully completed treatment and present no evidence of malignancy or myelosuppression.

2.6.3 Objectives of oral care:

- Prevention of infection
- Pain control
- Maintenance of oral functions, and
- Management of complications of antineoplastic therapy, aimed at improving the quality of life of patients .

2.*7 Role of dentist at three different levels**:[21-22]***

(1) Pre-antineoplastic Phase
(2) Antineoplastic phase
(3) Posttreatment Phase.

2.7.1.Pre-Antineoplastic Treatment Assessment and Patient Preparation

Dental treatment at this stage is based on priorities and should be directed to the acute needs; elective treatment can be postponed to a time when the patient is appropriate for clinical and laboratory conditions.

(1) Identify and eliminate sources of existing or potential infection, without, however, promoting complications or delaying cancer therapy.

(2) Educate the patient (or their relatives) about the importance of maintaining oral health in reducing problems and oral discomfort before, during, and after cancer treatment.

(3) Warn about the possible effects of antineoplastic therapy in the oral cavity, such as mucositis.

(4) Identify specific issues of the diagnosis of leukemia, such as leukemic infiltrates in oral tissues.

The hematological values that should be considered before performing dental procedures vary according to different authors. The one most commonly followed is presented below.

PLATELET COUNT	NEUTROPHIL COUNT
● >60,000 Cells/mm^3- without additional support. ● 30,000-60,000cells/mm^3-optional transfusion for non invasive procedures. ● <30,000 cells/mm^3 -transfusion 1 hour before procedure,obtain immediate post transfusion count. Transfuse regularly to maintain platelet count >30,000 till healing.	● > 2000 cells/mm^3 - without antibiotic prophylaxis. ● 1000-2000 cells/mm^3 -antibiotic prophylaxis(low risk). ● <1000 cells/mm^3 -antibiotic prophylaxis with Amikacin 150mg/m^2 1 hr before surgery & Ticarcillin 75 mg/Kg IV 1hr before surgery. Repeat both 6 h postoperative.

Table1. Minimum hematological values required in prechemotherapy phase(US National cancer institute 2011)[18]

Dental treatments in prechemotherapy phase

The American Academy of Dentistry[22] guidelines:

- If all dental needs cannot be addressed before the start of cancer therapy, priority should be eliminating sources of infection and trauma, extractions and periodontal care.
- Extractions should be made, preferably three weeks prior to chemotherapy or radiotherapy and at least 10 to 14 days earlier.
- Endodontic treatment of symptomatic nonvital teeth should be done at least a week before the start of chemotherapy in order to have sufficient time to evaluate the success of treatment; if this is not possible, extraction is indicated.
- Teeth that cannot receive endodontic treatment in one session also have extraction as a treatment of choice, with antibiotic prophylaxis (penicillin or clindamycin) for about a week.
- In asymptomatic teeth, endodontic treatment should be delayed until the haematological indices of the patient stabilize (this includes endodontically treated teeth with periapical lesions, without signs and symptoms of infection).
- Teeth unable to be restored, with periodontal pockets greater than 6 mm, with acute symptomatic infection, significant bone loss, furcation exposure, mobility, and impacted and residual roots should be removed. Ideally, extraction should occur two weeks before the start of the antineoplastic treatment or at least 7 to 10 days before.
- Surgical procedures should be as atraumatic as possible, without leaving remnant bone edges and with satisfactory suture of the wound. If there is infection associated with the tooth, antibiotic prophylaxis should be done for a week and by the drug ideally chosen by antibiogram.
- Partially erupted molars can be a source of infection due to pericoronitis. If the gingival tissue which partially covers the tooth is a potential factor for infection, the tissue should be excised, if the hematological levels permit.

- The American Academy of Pediatric Dentistry[22] argues that orthodontic appliances should be removed if the patient has deficient oral hygiene and/or in cases where the protocol of antineoplastic treatment confers risk for developing moderate or severe oral mucositis. It is important that the dentist is aware of the signs and symptoms of periodontal disease, since these can be subtle when the patient is immunosuppressed.
- After treatment of acute needs, other procedures such as smoothing of rough restorations, rounding, or restoration of tooth fractures may be performed, in addition to the assessment of dentures.
- Scaling procedures and root planning should be performed to prevent periodontal infections, as well as enhancing oral hygiene instructions and the use of mouthwash with fluoride in preventing dental caries.

2.7.2.Oral Health Care during Antineoplastic Treatment

Patients undergoing chemotherapybecome immunosuppressed and therefore,are susceptible to systemic infections. They are classified as high-risk patients, not only by the possibility of developing infection, but the extent and severity of this potential, which can have quick course and be potentially fatal.[23]

OBJECTIVES OF CARE:

(1) Maintain optimal oral health

(2) Treat side effects of anti-neoplastic therapy

(3) Reinforce to the patient the importance of oral health in reducing problems/discomforts arising from chemotherapy.

It is important to realize that infections in the oral cavity can progress to systemic infections, worsening the health status of the patient.[23]

PLATELET COUNT	NEUTROPHIL COUNT
<50,000 Cells/mm^3- Invasive procedures contraindicated.	<1000 cells/mm^3 - invasive procedures contraindicated.

Table2.minimum hematological values required in chemotherapy phase. (Brennan et al 2008)[24]

Dental treatment in transchemotherapy phase

In high-risk patients (active or under leukemia bone marrow suppression) dental intervention is limited to emergency care.

- Oral hygiene must be maintained by the use of mouthwashes and mild antimicrobial and antiseptic solutions, in order to promote ulcer healing and minimize complications from infection. 0.12%, solution-based nonalcoholic chlorhexidine gluconate should be used in the form of daily mouthwash or applied with gauze or swab.
- When there is evidence of oral infection, high-risk patients should receive broad-spectrum antibiotics intravenously.

In patients at moderate risk (maintenance phase), the myelosuppression peak is most evident, usually after 14 days of drug administration, and at this time, dental treatment should be avoided.

- Before or 21 days after the start of chemotherapy the treatment can be performed; however, the oncologist should be consulted prior.
- Type I procedures can be performed according to standard protocols, &in types II, III, and IV procedures, antimicrobial prophylaxis is recommended.
- In oral surgical procedures during chemotherapy, the benefit/risk to the patient must be considered, as well as the consequences of chemotherapy cycles; these procedures should therefore be planned and agreed on an interdisciplinary level.[23]
- It is claimed, in addition, that an absolute neutrophil count greater than 1000 cells/mm^3 and platelet count of at least 60,000 cells/mm^3 are acceptable rates for oral surgeries.
- When there is spontaneous bleeding resulting from minor trauma, the dentist should strive to improve the oral hygiene of the patient and use local measures to control the bleeding. If these measures are not sufficient, platelet transfusion may be required.The management for control of oral bleeding includes the use of vasoconstrictor agents, clots, and tissue guards. To reduce the flow of blood from bleeding vessels, one can use epinephrine; to organize and stabilize blood clots, topical thrombin and/or collagen hemostatic agents can be used; and to stanch the bleeding sites and protect organized clots, the application of the mucosa adhesive products, such as those based on cyanoacrylate, may be performed. The topical aminocaproic acid can be useful in patients with friable clots and intravenous administration may be considered, in some cases, to improve coagulation and the formation of stable clots,topical use of tranexamic acid is also cited as an effective hemostatic in reducing the incidence of postoperative bleeding in patients with continuous use of oral anticoagulants. 500 mg crushed tablets of tranexamic acid ground in

moist cotton at the site of the surgical wound after tooth extraction, or diluted in water for mouthwash, can also be used.

2.7.3 Post-Antineoplastic Treatment Oral Health Care

In the post-antineoplastic treatment phase, patients are considered cured of leukemia and not having oral manifestations due to illness or chemotherapy, with the exception of those with sequelae of radiotherapy or children who received chemotherapy in the stage of tooth formation, which may present hypoplastic areas on tooth enamel (mineralization disorder) and changes in the development of dental roots (which are presented short and V-shaped).

Dental treatment after chemotherapy

- Patients who were cured of leukemia are considered to be of low risk and can be met with normal dental treatment regimens. After completion of cancer therapy and only after two years free of disease, the orthodontic treatment that was interrupted can be restarted.
- Antibiotic prophylaxis during oral and maxillofacial surgical procedures should be performed for at least six months after the completion of chemotherapy.[25]

2.8 Special considerations in patients on HSCT

According to American Academy of Pediatric Dentistry[22]dental treatment is dependent on each phase of HSCT.

2.8.1 Preconditioning Phase:

- All dental treatment should be completed before the patient becomes immunosuppressive.
- Elective treatment should be delayed until the reestablishment of immunity (at least 100 days after transplant, or more in the case of oral complications or other cGVHDs).

2.8.2 Neutropenic conditioning phase:

- The focus is the monitoring and management of oral complications, with reinforcement of maintenance guidelines of good oral hygiene.
- Dental procedures should not be performed at this stage; in the case of emergencies, dental approach should be developed with the participation of the medical staff.

2.8.3 Engraftment phase to hematopoietic recovery:

- A dental assessment should be performed, with special attention to xerostomia and GVHD.
- Invasive procedures should be made only with the approval of the medical staff.
- The patient should be encouraged to maintain good hygiene with a noncariogenic diet.

2.8.4 Immune reconstitution/recovery phase:

- A periodic evaluation with dental radiography can be performed.
- Invasive procedures should still be avoided.
- Clarifying the risks and benefits of the use of orthodontic appliances is recommended.

The US National Cancer Institute[18] points out that the time of reconstitution of the immune system in transplant patients can range from 6 to 12 months and that the dental care routine should not be done in this period, including scaling and periodontal planning. Procedures that produce aerosol, such as ultrasound equipment and high speed instruments, can also present a risk of aspiration of debris and bacteria and cause pneumonia in these patients. If emergency treatment is required, strategies for reducing aerosol aspiration and antibiotic prophylaxis should be used. Finally, it is recommended that the use of IgG, antibiotics, corticosteroids, and/or platelet transfusion should be considered before implementing invasive procedures.

2.8.5 Long-term survival phase:

Aroutine dental evaluation with interdisciplinary and multidisciplinary involvement is necessary.

III. Conclusion

From the literature, it is evident that leukemia and anti neoplastic therapy,both are associated with various oral manifestations. Often these oral manifestations are first signs of leukemia. These may present clinically as leukemic infiltration in oral tissues as well as simulating a periapical lesion. Other symptoms may occur such as pale mucosa, poor wound healing, bleeding (petechiae and ecchymoses), atypical or recurrent candidiasis, recurrent herpes infections, and ulcerations in the oral mucosa. During antineoplastic treatment (chemotherapy, mostly), the main complication is mucositis. Various other conditions include bleeding, increase the rate of caries, infection, gingival abscess, recurrent herpetic stomatitis, candidiasis, salivary gland

dysfunction, xerostomia, dysgeusia, and pain. In the posttherapy period, patients are considered cured and usually present no sequelae of treatment.Moreover, special features are observed in patients undergoing allogeneic HSCT, such ascGVHD, which typically manifests as lichen-type features, hyperkeratotic plaques, mucocele, and fibrosis with limited mouth opening, and are more likely to develop malignancies such as squamous cell carcinoma.In such patients, performing dental procedures can offer risk to the patient, depending on state of health and phase of therapy. Furthermore, different procedures carry different levels of risk. 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. Invasive procedures (types IV, V, and VI) offer higher risk. In emergency situations of risk considered, particularly those involving pain (acute cases), the patient should be assisted,in a hospital setting, with the institution of measures to increase the hematological indices (transfusions) and, if applicable, with antibiotic coverage.In assessing patients for dental procedures, two hematological indices are particularly important: neutrophil and platelet counts. Apart from basic knowledge of oral complications & their management, dentists should have thorough, updated knowledge about the potential complications & adverse effects of newer antineoplastic drugs that are being introduced from time to time. The presence of the dentist in a multidisciplinary team is essential, since maintaining oral health contributes significantly to the overall health and improved quality of life for patients through the use of dental approaches based on scientific evidence which are preventive, curative, and palliative in nature.

References

[1] Manisha pokharel, Leukemia: A Review Article:IJARPB, 2012; Vol.2 (3):397-407.
[2] Hematological malignancies, Basic pathology by Robinn's; p 1087.
[3] Daniel A. Arber et al; The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia; Blood 2016 127:2391-2405
[4] Caroline Zimmermann et al; Dental Treatment in Patients with Leukemia;Journal of Oncology:Volume 2015, Article ID 571739, 14 pages
[5] Franch AM et al; Oral manifestations and dental management of patient with leukocyte alterations. J Clin Exp Dent. 2011; 3(1):53-59.
[6] Demirer S et al;Gingival Hyperplasia as an Early Diagnostic Oral Manifestation in Acute Monocytic Leukemia: A Case Report. Eur J Dent. 2007 Apr; (2):111–114.
[7] Elitsa g. Deliverska1 et al; Oral signs of leukemia and dental management – literature data and case report;journal of imab - annual proceeding (scientific papers) 2013, vol. 19, issue 4.
[8] Sinrod H S;Leukemia as a dental problem.;J Am Dent Assoc. 1957 Dec; 55(6):809-18.
[9] Boggs DR et al;The acute leukemias. Analysis of 322 cases and review of the literature;Medicine (Baltimore). 1962 Sep; 41():163-225.
[10] Barrett AP;Oral changes as initial diagnostic indicators in acute leukemia;J Oral Med. 1986 Oct-Dec; 41(4):234-8.
[11] Dreizen S et al;Malignant gingival and skin "infiltrates" in adult leukemia;Oral Surg Oral Med Oral Pathol. 1983 Jun; 55(6):572-9.
[12] Radiographic manifestations of leukemia in jaws and teeth;malignant diseases;oral radiology principles & interpretation by white & pharoah; chapter 24;p 449.
[13] H.M Worth; Jaw changes due to abnormal conditions of the blood; Principles & practice of oral radiologic interpretation:chap 12: p370-371.
[14] Ed. Lauritano et al.Oral manifestations in children with acute lymphoblastic leukemia;European journal of inflammation vol. 10, no. 2 (s), 65-68 (2012).
[15] Cyehuda zadik et al; Cytotoxic chemotherapy-induced odontalgia:A differential diagnoss of dental pain;j of endodontics; vol 36,issue 9 p 1588-1592.
[16] OEverton Freitas de Morais et al. Oral manifestations resulting from chemotherapy in children with acute lymphoblastic leukemia;Braz. j. otorhinolaryngol. vol.80 no.1 São Paulo Jan./Feb. 2014
[17] Regina Haddad Barrach, Mair Pedro de Souza et al.Oral changes in individuals undergoing hematopoietic stem cell transplantation.Braz. j. otorhinolaryngol. vol.81 no.2 São Paulo Mar./Apr. 2015
[18] US National Cancer Institute, Oral Complications of Chemotherapy and Head/Neck Radiation, US National Cancer Institute, 2011,
[19] .S. T. Sonis, R. C. Fazio, and L. Fang, Principles and Practice of Oral Medicine, WB Saunders, 1995.l.
[20] J. W. Little, D. A. Falace, C. S. Miller, and N. L. Rhodus, "Disorders of white blood cells," in Dental Magenement of the Medically Compromised Patient, pp. 373–395, 2007.
[21] S. Elad, J. E. Raber-Durlacher, M. T. Brennan et al., "Basic oral care for hematology–oncology patients and hematopoietic stem cell transplantation recipients: a position paper from the joint task force of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) and the European Society for Blood and Marrow Transplantation (EBMT)," Supportive Care in Cancer, vol. 23, no. 1, pp. 223–236, 2015.
[22] American Academy of Pediatric Dentistry, "Guideline on dental management of pediatric patients receiving chemotherapy, hematopoietic cell transplantation, and/or radiation," Journal of Pediatric Dentistry, vol. 35, no. 5, pp. E185–E193, 2013.
[23] D. C. Tong and B. R. Rothwell, "Antibiotic prophylaxis in dentistry: a review and practice recommendations," Journal of the American Dental Association, vol. 131, no. 3, pp. 366–374, 2000.
[24] Michael T.Brennan, MHSa et al;Dental Treatment Planning and Management in the Patient Who Has Cancer;Dental Clinics of North America:Volume 52, Issue 1, January 2008, Pages 19-37.
[25] K. Yamagata, K. Onizawa, H. Yoshida et al., "Dental management of pediatric patients undergoing hematopoietic stem cell transplant," Pediatric Hematology and Oncology, vol. 23, no. 7, pp. 541–548, 2006.

Dr Nazia Qurashi. "A Leukemic Patient in a Dental Clinic". IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 18, no. 6, 2019, pp 55-62.