White Blood Cells Disorders

(Part 2)

Lecture: 4 **Dr. Saif Saadedeen**

Leukemic patients whose disease has not been diagnosed may experience serious **bleeding** problems after any surgical procedure, may have problems with the **healing** of surgical wounds, and are prone to postsurgical **infection**. Thus, it is important for the dentist to attempt to identify these patients through history and clinical examination before starting any treatment.

Questions regarding blood disorders and cancer in family members, weight loss, fever, enlarged lymph nodes, and bleeding tendencies should be asked. After the history is complete, clinical examination is mandatory. Examination of the head, neck, and mouth should include a thorough inspection of the oropharynx, head, and cervical and supraclavicular lymph nodes. The dentist should be aware that an enlarged supraclavicular node is highly suggestive of malignancy. Cranial nerve examination is important for identifying abnormalities suggestive of invasive neoplasms. Panoramic films also will provide insight into potential osteolytic lesions associated with WBC disorders.

A patient who displays the classic signs or symptoms of leukemia or lymphoma should be referred directly to a physician. Screening tests should include total and differential WBC counts, hemoglobin and platelet count.

Treatment Planning Modifications

Dental management of patients in whom a WBC disorder is diagnosed requires consideration of the three phases of medical therapy. Planning involves:

(1) Pre-treatment assessment and preparation of the patient.
(2) Oral health care during medical therapy.
(3) Post-treatment management.

Pre-treatment Assessment and Preparation of The Patient

The dentist must be aware of the specific diagnosis and the severity of the disorder, the type of medical treatment. For example, a patient who is receiving only palliative treatment is not a good candidate for extensive restorative or prosthodontic procedures that require months for completion.

For the patient in whom leukemia or lymphoma has been recently diagnosed, the dentist should become involved early during the treatment planning stages of cancer therapy. Guidance regarding the health of the oral cavity and jaws can help prevent severe oral infections (the goal is to minimize or eliminate oral diseases before the start of chemotherapy). Inspection of radiographs for undiagnosed disease, retained root tips, impacted teeth is important for clearing the oral cavity.

Pretreatment care should include oral hygiene instructions that emphasize the importance of meticulous plaque removal. Caries should be eliminated, if possible before chemotherapy is begun. If pulpal disease is present, the dentist may recommend root canal therapy or extraction of teeth before chemotherapy. Dental attention is given to oral hygiene procedures, including using fluoride gels, encouraging a non-cariogenic diet, eliminating mucosal and periodontal disease and eliminating any source of mucosal injury.

Extraction should be considered if periodontal pocket depths are greater than 5 mm, periapical inflammation is present, the tooth is nonfunctional or partially erupted (as with third molars), or the patient is noncompliant with oral hygiene measures and routine dental care. Guidelines for extraction in patients before chemotherapy include scheduling a minimum of 3 weeks between the time of extraction and initiation of chemotherapy or radiotherapy, attaining primary closure, and avoiding invasive procedures if the platelet count is less than 50,000/μL.

It is important to note that chemotherapy is initiated in many cases of acute leukemia within a few days of diagnosis, so dental treatment may have to be provided promptly before the patient becomes neutropenic as a result of chemotherapy. Patients who are neutropenic should not undergo invasive dental procedures without special preparation and precautions. The patient's physician may select to use recombinant human granulocyte colony stimulating factor to promote growth and differentiation of neutrophils before surgical procedures.

After necessary treatment is cleared with the patient's physician, the use of prophylactic antibiotics is dictated by WBC and neutrophil counts. **Prophylactic antibiotics** often are recommended if the WBC count is less than 2000.

Oral Complications During Medical Therapy

Patients who are undergoing chemotherapy or radiotherapy are susceptible to many oral complications, including the following:

Mucositis:

Chemotherapy affects epithelial cells that have high replication rates (mucosa of the mouth). Thus, younger persons have a greater prevalence of mucositis. These patients often develop mucositis, which usually begins 7 to 10 days after initiation of chemotherapy and resolves after cessation of chemotherapy. Affected mucosa becomes red, raw, and tender. Breakdown of the epithelial barrier produces oral ulcerations that may become secondarily infected and can serve as a source of systemic infection.

Oral hygiene should be maintained to minimize infection complications. A bland mouth rinse (causing no irritation) can be used to clean the surface of the ulcer (commercial mouth rinses are not recommended because they contain alcohol and tend to irritate ulcerated tissues). After the bland mouth rinse, use of a topical anesthetic and systemic analgesics makes the mouth more comfortable.

A thin layer of Orabase is useful in protecting ulcers from surface irritation. This protocol can be repeated four to six times a day. In addition, removal of sharp edges of teeth and restorations is palliative. Antiseptic and antimicrobial rinses (e.g., chlorhexidine) are recommended to promote healing of oral ulcerations and to prevent oral infection.

Neutropenia and Infection:

Patients who have neutropenia are unable to provide a protective response against oral microbes. Accordingly, these patients develop acute gingival inflammation and mucosal ulcerations. Chronic neutropenia contributes to severe destruction of the periodontium with loss of attachment when oral hygiene is less than optimal. Periodontal therapy that includes instruction on oral hygiene, frequent scaling, and antimicrobial therapy can reduce the adverse effects associated with this disorder.

Oral infection is less of a problem in patients with chronic leukemia than in those with acute leukemia because the cells are more mature and functional in chronic leukemia. However, in the later stages of both CML and CLL, an infection can become a serious complication. Splenectomy due to massive splenomegaly may also increase the risk of infection.

Because of neutropenia, signs of infection are often masked in patients with leukemia; the swelling and erythema usually associated with oral infection are often less marked. In these patients, severe infection can occur with minimal clinical signs, which can make clinical diagnosis more difficult. When an oral infection develops in such patients, a specimen of exudate should be sent for culture and antibiotic sensitivity testing.

Opportunistic infections (bacterial, fungal, and viral) are common in leukemic patients because:

(1) Malignant leukocytes are immature
(2) Chemotherapy induces an immunocompromised state
(3) Use of broad-spectrum antibiotics

A common opportunistic infection is acute pseudomembranous candidiasis; should be treated with one of the antifungal medications. Infrequently, unusual oral fungal infections (mucormycosis) occur, or fungal septicemia may originate from the oral cavity. These patients require potent systemic antifungal agents such as fluconazole or amphotericin B.

Another common infection in patients receiving chemotherapy is recurrent HSV (Herpes Simplex Virus) infection. Herpetic lesions tend to be larger and take longer to heal than herpetic lesions found in non-leukemic patients. Generally, to prevent a recurrence, antiviral agents (such as acyclovir) are prescribed to HSV antibody-positive patients who are undergoing chemotherapy. In patients in whom HSV infection develops, diagnosis can be made rapidly using an enzyme-linked immunoassay.

Bleeding:

Small or large areas of submucosal hemorrhage may be found in the leukemic patient. These lesions result from minor trauma (e.g., tongue biting) and are related to thrombocytopenia. Leukemic patients also may report spontaneous and severe gingival bleeding that is aggravated by poor oral hygiene. The dentist should make efforts to improve oral hygiene and should use local measures to control bleeding. A gelatin sponge with thrombin or microfibrillar collagen can be placed over the area, or an oral antifibrinolytic rinse may be used. If local measures fail, medical help will be needed and may involve platelet transfusion. Platelet counts should be at least 50,000/μL before performance of invasive dental procedures.

Graft-versus-Host Disease (GVHD):

GVHD is a common sequela of patients who undergo bone marrow or stem cell transplantation. It occurs when immunologically active donor T cells react against antigens of the host. It produces features that mimic Sjögren syndrome, including thickening and lichenoid changes of the skin and mucosa, arthritis, xerostomia, xerophthalmia, mucositis, and dysphagia.

To prevent this complication, patients who are preparing for transplantation typically undergo T cell depletion of the graft and prophylactic treatment with immunosuppressive agents, such as corticosteroids, cyclosporine, methotrexate, or tacrolimus.

Adverse Drug Effects:

A small number of leukemic patients describe paresthesia that results from leukemic infiltration of the peripheral nerves or as adverse effects of chemotherapy (vincristine). An adverse effect of cyclosporine use in bone marrow transplant patients is gingival overgrowth.

Growth and Development:

Chemotherapy during childhood can affect the growth and development of the teeth and facial bones. This effect is not observed in adults. Restricted growth of the jaws leads to micrognathia, retrognathia, or malocclusion. Damage to the teeth that occurs at the time of chemotherapy can manifest as shortened or blunted roots, dilacerations, calcification abnormalities, pulp enlargement, microdontia, and hypodontia.

Post-treatment Management

Patients who have WBC disorders and are in a state of remission can receive most indicated dental treatment. Patients who have advanced disease and a limited prognosis, as occurs in many cases of leukemia, should receive emergency care only. In Hodgkin lymphoma, the spleen may be involved and surgically removed. Subsequently, the patient is at risk for bacterial infection. The risk for such infection is greatest during the first 6 months after splenectomy. Antibiotic prophylaxis should be provided for invasive procedures during the first 6 months after splenectomy.

Up to 80% of patients with Multiple Myeloma (malignant neoplasm of plasma cells) are presented with osteopenia, osteolysis, and pathologic fractures. Patients often are treated with **bisphosphonates**; drugs that inhibit osteoclast activity. An infrequent adverse effect of bisphosphonates is osteonecrosis of the jaws.

The greatest risk for this complication is associated with the use of intravenous bisphosphonates for at least 1 year. The condition often is triggered by the extraction of a painful tooth or teeth, most commonly a mandibular posterior tooth. The typical presenting lesion is a severely painful and unexpected non-healing extraction socket or exposed area of bone. However, the necrotic bone may be asymptomatic for weeks and may be noticed only on routine examination. Treatment is directed toward controlling and limiting progression by means of local debridement (bone and wound irrigation with antiseptics), together with suitable antibiotics.

To minimize the likelihood that osteonecrosis will develop in these patients, the following recommendations should be followed:

(1) Treat infections early.
(2) Nonsurgical approaches are preferredable to surgical approaches.
(3) Limit the extraction to as few teeth as possible and to one quadrant.
(4) Wait two months before performing surgery in a different quadrant.
(5) Provide antibiotic coverage during the extraction and healing period and consider alveolectomy.

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- E. Donnall Thomas (1920 – 2012) was an American physician who developed (with other partners) bone marrow transplantation as a treatment for leukemia. In 1990 he gets the Nobel Prize in Physiology or Medicine.