Influence Of Hematological Disorders On The Periodontium

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Blood cells play essential role in maintenance of healthy Periodontium

WBC

- Inflammatory reactions
- Cellular defense,
- Proinflammatory cytokine release

RBC

- Gas Exchange
- Nutrient Supply

Platelets

- Normal Hemostasis
- Recruitment of cells during inflammation and wound healing

- Abnormal gingival bleeding or from other areas of oral mucosa that is difficult to control may suggest some underlying hematological disease.
- Hemorrhagic tendencies occur when normal hemostatic mechanisms are disturbed
- Petechiae and ecchymosis of soft palate may suggest underlying bleeding disorder

- It is essential to diagnose the specific etiology in order to address any bleeding or immunologic disorder appropriately.

Leukemia

- Malignant neoplasm of WBC precursors

Characterized by:

1. Replacement of bone marrow with proliferating leukemic cells
2. Abnormal number and form of immature WBCs in circulating blood
3. Infiltration in liver, spleen, lymph node and other body sites.

Classification

- According to lineage of WBC, Leukemia are classified as:

1. Lymphocytic
2. Myelocytic
    1. Monocytic

- According to evolution Leukemia can be:

1. Acute
2. Subacute
3. Chronic

- **Acute Leukemia** the **primitive blast cells** are released in peripheral circulation.

- **Chronic Leukemia** the **abnormal cells are more mature** with normal morphologic characteristics and function when released into circulation.

- All leukemic cells tend to displace normal component of bone marrow elements with resulting in decreased production of

- RBC → Anemia
- WBC → Leukopenia
- Platelets → Thrombocytopenia

Anemia

- **Poor Tissue Oxygenation**
- Tissue become more friable
- Susceptible to breakdown

Leukopenia

- Reduction in Normal WBCs
- Susceptibilty to infection increases

Thrombocytopenia

- Bleeding tendency
- Particularly effects oral cavity especially gingiva

Aleukemic leukemia:

- Patients have normal blood counts while leukemic cells primarily reside in bone marrow.
- The peripheral blood does not consists any leukemic or malignant cell.

Periodontium in leukemia

- Oral and periodontal manifestation of leukemia consist of
  - ✓ Leukemic infiltration
  - ✓ Bleeding or hemorrhage
  - ✓ Oral ulcerations
  - ✓ Infections
- The expression of above signs are more common in acute and subacute form of leukemia than chronic.

Leukemic infiltration

- Leukemic cells **infiltrate gingiva** and less frequently alveolar bone
- Gingival infiltration results in leukemic **gingival enlargement.**

- **Highest incidence of leukemic gingival enlargement** is found in patients with

  -Acute monocytic leukemia (66.7%)

  -Acute myelocytic-monocytic leukemia(18.7%)

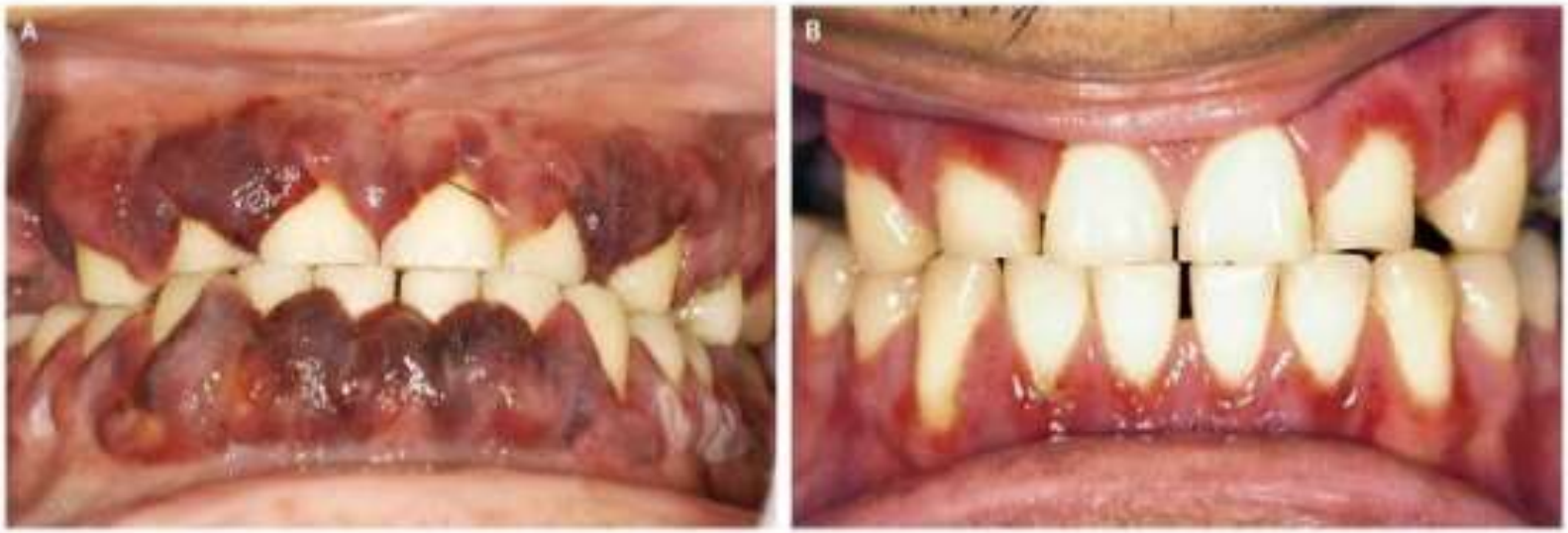
  -Acute myelocytic leukemia (3.7%)

- Leukemic gingival enlargement is not found in edentulous patients or in patients with chronic leukemia

- Leukemic gingival enlargement consists of
  - Infiltration of **gingival corium** by leukemic cells
  - Increased gingival thickness, periodontal pocket formation, bacterial plaque accumulation and secondary inflammation
  - Increase in gingival size at interdental papilla covering the crown of teeth.

Leukemic Gingival Enlargement

Leukemic Gingival Enlargements



Clinical Features

- Gingiva appears bluish-red and cyanotic.
- Rounding and tenseness at gingival margin

Figure 17-7 Petechiae evident on the soft palate of patient with underlying bleeding disorder.

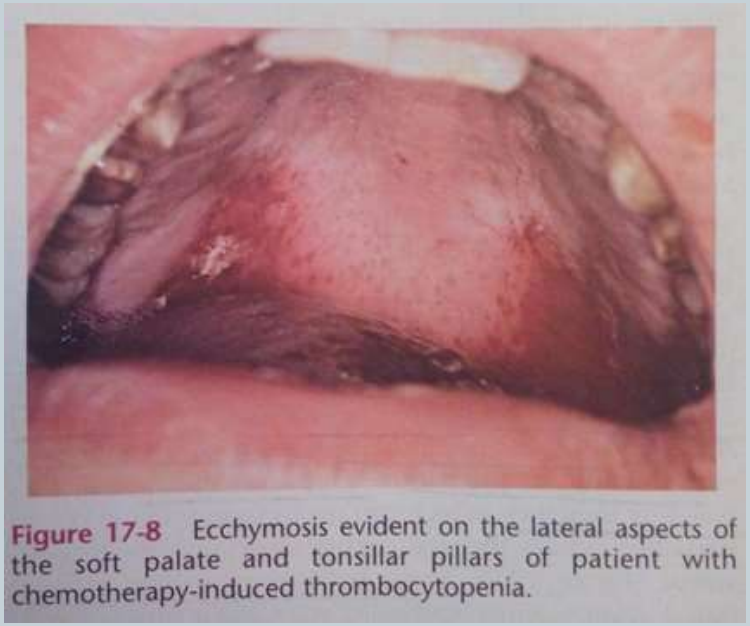
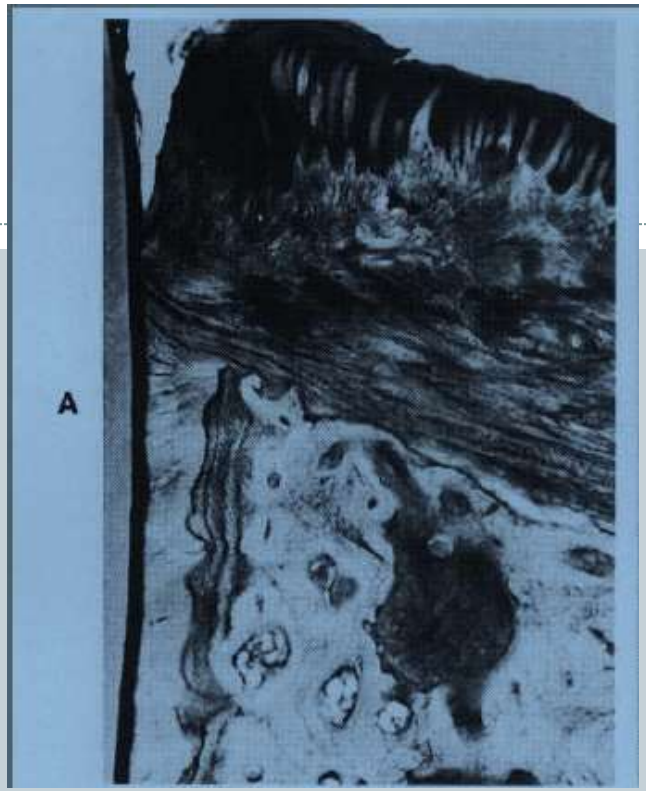


Figure 17-8 Ecchymosis evident on the lateral aspects of the soft palate and tonsillar pillars of patient with chemotherapy-induced thrombocytopenia.

Microscopically

- **Dense, diffuse infiltration** of predominantly **immature leukocytes** in attached and marginal gingiva
- Normal connective tissue component of gingiva is **replaced** by **leukemic cells**
- **Mitotic figures** indicative of **ectopic hematopoiesis** may be seen
- **Nature of cell infiltrate depends on type of leukemia**



- Cellular accumulation is **denser** in entire **reticular** connective tissue layer
- **Papillary layer** contains comparatively **few leukocytes**
- **Blood vessels** are **distended** and contain predominantly **leukemic cells**

- Epithelium presents with variety of changes and may be **thinned** or **hyperplastic**

- **Degeneration** associated with i**ntercellular and intracellular edema** and leukocyte infiltration with diminished surface keratinization

- **Microscopic picture of marginal gingiva** shows **notable inflammatory component** in addition to leukemic cells

- Scattered **foci of plasma cells** and **lymphocytes** with edema and degeneration are common findings

- **Inner aspect of marginal gingiva** is usually **ulcerated** with **marginal necrosis** and **pseudomembrane formation.**

- Periodontal ligament and alveolar bone may also be involved in acute and subacute leukemia
- Periodontal ligament may be infiltrated with mature and immature leukocytes
- Marrow of alveolar bone exhibits localized area of necrosis, thrombosis of blood vessels, infiltration with mature and immature leukocytes
- Replacement of fatty marrow with fibrous tissue.

Bleeding

- Gingival hemorrhage is common in leukemic patients
- Bleeding gingiva can be early sign of leukemia.
- Oral bleeding has been seen in **17.7% patients with acute leukemia** and **4.4% in patients with chronic leukemia**

- Caused by **thrombocytopenia** by replacement of bone marrow cells by leukemic cells
- Also **by inhibition of normal stem cells function** by leukemic cells or their products
- Bleeding may be **side effect** of **chemotherapeutic agents** used to treat leukemia

Oral ulceration and infection

- **Granulocytopenia (diminished WBC count)** results from the displacement of normal bone marrow cells by leukemic cells
- **Discrete, punched-out ulcers penetrating deeply into submucosa and covered by a firmly attached white slough**
- **Recurrent herpetic oral ulcers**
- **Atypical oral ulcer**

- Gingiva is peculiar bluish red, is sponge like and friable, and bleeds persistently on slightest provocation or even spontaneously in leukemia patients
- Acute gingival necrosis
- Pseudo membrane formation

- Loss of appetite, nausea, blood loss from persistent gingival bleeding and constant gnawing pain

- Eliminating or reducing local factors (dental plaque)

- In chronic leukemia clinical oral changes suggesting hematologic disturbances are rare

- Gingival biopsy in patient with chronic leukemia may reveal typical gingival inflammation without any suggestion of a hematologic disturbance

Anemia

- Deficiency in the quantity or quality of the blood
- Manifested by reduction in the number of erythrocyte and the amount of hemoglobin
- Anemia results from
  - Blood loss
  - Defective blood formation
  - Increased RBC destruction

Anemias are classified according to cellular morphology and hemoglobin content

1. Macrocytic Hyperchromic anemia (Pernicious anemia)
2. Microcytic Hypochromic anemia (iron deficiency anemia)
3. Sickle cell anemia
4. Normocytic Normochromic anemia (Hemolytic and Aplastic anemia)

Pernicious anemia

- vitamin B12, folic acid, and intrinsic factor from the stomach mucosa required for the reproduction of erythroblasts in the bone marrow

- **Tongue**: red – **smooth and shiny** – due to **loss/atrophy of papillae**
- Pallor of the gingiva

Iron deficiency anemia

- Tongue: red – smooth & shiny – due to loss/atrophy of papillae
- Pallor of the gingiva
- **Plummer-Vinson syndrome**: Iron deficiency anemia - glossitis – ulceration of the oral mucosa and oropharynx

Sickle cell anemia

- Hereditary
- Chronic hemolytic anemia
- Exclusively in black
- Presents with
  - Pallor
  - Jaundice
  - Weakness
  - Rheumatic manifestation
  - Leg ulcers

Oral changes:

- Generalized osteoporosis of jaw
  - Stepladder arrangement of trabeculae of interdental septa
- Pallor/yellowish discoloration
- Periodontal infection may precipitate sickle cell crisis

Thromocytopenia

- Reduced platelet count either due to
  - Lack of platelet production or
  - Increased platelet destruction
  - Increased loss
- Purpura is
  - Purplish appearance of skin or mucous membrane that occurs as a result of decreased platelets
- Thrombocytopenic purpura may be
  - Idiopathic (Werlhof's disease) or
  - Secondary to some known etiologic factor

Etiology of thrombocytopenia

- Aplasia of bone marrow
- Displacement of megakaryocyte in marrow as with Leukemia
- Replacement of marrow by tumor
- Destruction of marrow by irradiation, radium or drugs - Benzene, Aminopyrine, Arsenical agents

- **Thrombocytopenia is characterized by**

- **Low platelet count**
- **Prolonged clot retraction and bleeding time**
- **Normal or slightly prolonged clotting time**
- **Petechiae and hemorrhagic vesicle** occur in the palate, tonsillar pillar and buccal mucosa
- **Spontaneous bleeding in gingiva**

Neutropenia

- Low levels of circulating neutrophils absolute neutrophil count (ANC) less than 1500cells/µl is considered neutropenia
- Neutropenia
  - Genetic
  - Drug induced
  - Viral infection

- Neutropenia is serious , can leads to life threatening infection which are difficult to control
- It may be
  - Chronic or cyclic
  - Severe or benign

Agranulocytosis

- It is more severe neutropenia that involves not only neutrophils but also basophils and eosinophils.
- It is defined as an ANC of less than 100 cells/µl.
- Severe ulcerative infections if oral mucosa, skin, GIT and genitourinary tracts
- Drug Idiosyncrasy main cause of agranulocytosis
  - Aminopyrene, barbiturates and their derivatives, benzene ring derivatives, sulfonamides, gold salts and arsenical agents

- Agranulocytosis
- Generally occurs as acute disease
- Chronic / periodic with recurrent neutropenic cycles (cyclic neutropenia)
- Disease onset with fever, malaise, general weakness and sore throat

- Ulceration in oral cavity , oropharynx and throat is characteristics
- Mucosa exhibits isolated necrotic patches
- Black and grey in color demarcated from adjacent uninvolved areas
- Absence of inflammatory reaction caused by lack of granulocytes is striking feature

- Gingival hemorrhage , necrosis, increased salivation and fetid odor
- Cyclic neutropenia gingival changes recur with recurrent exacerbation of disease
- Aggressive periodontitis has been seen in cyclic neutropenia
- D/D- ANUG, Diphtheria, NOMA, acute necrotizing infection of tonsil

Papillon-Lefevre Syndrome

- ***Papillon-Lefèvre syndrome***, first described by two French physicians ***Papillon*** and ***Lefèvere*** in 1924 - extremely rare genodermatosis - *autosomal recessive* trait - affecting children between the ages 1-4 years.
- Prevalence: 1- 4 cases per million
- Males and females are equally affected - no racial predominance
- The disorder is characterized by diffuse *palmoplantar keratoderma* and *premature loss of both deciduous and permanent teeth*

- The sharply demarcated *erythematous keratotic plaques* may occur focally, but usually involve the entire surface of the *palms and soles,* sometimes extending onto the *dorsal surfaces of the hands and feet.*
- Often, there is associated *hyperhydrosis* of the palms and soles resulting in a foul-smelling odor.
- Well-demarcated *psoriasiform plaques* occur on the *elbows and knees*.
- The findings may worsen in winter and be associated with painful fissures.

Hyperkeratotic scaly lesions

- The second major feature of PLS - *severe periodontitis* - starts at age 3 or 4 years. The development and eruption of the deciduous teeth proceed normally - eruption is associated with gingival inflammation and subsequent *rapid destruction of the periodontium*.
- The resulting periodontitis - *unresponsive to traditional periodontal treatment* modalities and the primary dentition is usually exfoliated prematurely by age 4 years.
- After exfoliation, the inflammation subsides and the gingiva appears healthy.

- However, with the eruption of the permanent dentition the process of gingivitis and periodontitis is usually repeated and there is subsequent premature exfoliation of the permanent teeth, although the third molars are sometimes spared.
- The degree of dermatologic involvement may not be related to the level of periodontal infection.
- *By age of 15 years, patients are usually edentulous* except for the third molars. These also may get lost a few years after they erupt.

- *Tooth extraction sites heal uneventfully.* Microscopically, *marked chronic inflammation* of the lateral wall of the pocket - predominantly plasma cell infiltrate - *considerable osteoclastic activity* - *apparent lack of osteoblastic activity* - an extremely thin cementum.
- *Bacterial flora similar to bacterial flora in chronic periodontitis*
- No significant alterations have been found in peripheral blood lymphocytes and PMNs.
- intracranial calcification of dura mater (***Gorlin et al***)

Chediak-Higashi syndrome

- *Rare disease* that *affects the production of organelles found in almost every cell*.
- It *affects mostly the melanocytes, platelets, and phagocytes*.
- It causes *partial albinism, mild bleeding disorders, and recurrent bacterial infections*.
- Neutrophils contain abnormal, *giant lysosomes* that can fuse with the phagosome, but their ability to release their contents impaired. As a result, *killing of ingested microorganisms is delayed.*

Oral Manifestations

- Ulcerations of the oral mucosa, severe gingivitis, and glossitis
- Periodontal breakdown, probably related to defective leukocyte function
- *Aggressive periodontitis*

Lazy Leukocyte Syndrome

- *Defective chemotactic response* by neutrophils,
- Susceptibility to *severe microbial infections, neutropenia,*
- Abnormal inflammatory response.
- Aggressive periodontitis with ***destruction of bone*** and ***early tooth loss***.

Leukocyte Adhesion Deficiency Disorder

- Leukocyte adhesion deficiency (LAD) - rare disease with fewer than 200 patients reported in the literature.
- *Autosomal recessive*
- Localized bacterial infections - difficult to detect until progressed to an extensive life-threatening level
- The infections act similarly to those observed in neutropenic patients because *phagocytes are unable to adhere to the endothelium (lack of CD18)and transmigrate into tissues*.

Down Syndrome *(Trisomy 21 Syndrome; Mongolism)*

- Congenital disease cause by chromosomal abnormality
- Trisomy 21
- Mental deficiency and growth retardation

- *Abnormalities in host response*
- Decreased number of mature T lymphocytes and functional defects in polymorphonuclear leukocytes, resulting in *reduced chemotaxis*, as well as *impaired phagocytosis*.
- These alterations in immune response may contribute to the *development of periodontal disease*

- Patients with Down syndrome are characterized by a flat face, a large anterior fontanel, open sutures, small slanting eyes with epicanthal folds, open mouth, frequent prognathism, sexual underdevelopment, cardiac abnormalities and hypermobility of the joints

- *The prevalence of periodontal disease in Down syndrome is high* (occurring in almost 100% of patients younger than 30 years).
- Although plaque, calculus, and local irritants (e.g., diastema, crowding of teeth, high frenum attachments, malocclusion) are present and oral hygiene is poor, *the severity of periodontal destruction exceeds that explainable by local factors alone*.
- More severe in the lower anterior region.
- Marked recession is also sometimes seen.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THANK YOU