Lec 9: Aplastic anemia

Aplastic anemia is a rare and serious condition where the bone marrow fails to produce enough blood cells. This results in a deficiency of red blood cells, white blood cells, and platelets, which can lead to fatigue, infections, and bleeding issues.

Causes of Aplastic anemia

1. Idiopathic (unknown cause) - Most cases have no identifiable cause.
2. Autoimmune conditions - The immune system attacks bone marrow stem cells.
3. Exposure to toxins - Benzene, pesticides, or certain chemicals.
4. Medications - Such as chemotherapy, antibiotics (e.g., chloramphenicol), or anti-inflammatory drugs.
5. Infections - Hepatitis, Epstein-Barr virus, HIV, or parvovirus.
6. Inherited disorders - Such as Fanconi anemia or dyskeratosis congenita.
7. Radiation - High levels of radiation exposure.

The pathogenesis of aplastic anemia

involves damage to the hematopoietic stem cells in the bone marrow, leading to failure in the production of red blood cells, white blood cells, and platelets.

The underlying mechanisms can be grouped into several major pathways:

1. **Immune-mediated destruction**
2. **Direct injury to hematopoietic stem cells**
3. **Genetic and telomere dysfunction**
4. **Viral infections**
5. **Defective microenvironment**
6. **Secondary causes**

1. Immune-mediated destruction

This is the most common mechanism, particularly in idiopathic aplastic anemia.

A. Autoimmune attack: T-cells become abnormally activated and target hematopoietic stem cells, likely triggered by:
B. Viral infections (e.g., hepatitis, EBV).
C. Aberrant immune signals.
D. Cytokine involvement: Pro-inflammatory cytokines like interferon-gamma (IFN-γ) and tumor necrosis factor-alpha (TNF-α) suppress bone marrow function by:
E. Inducing apoptosis in hematopoietic stem cells.
F. Blocking stem cell proliferation.

2. Direct injury to hematopoietic stem cells

A. Toxins and radiation: Substances like benzene or radiation can directly damage DNA in stem cells.
B. Drugs and chemicals: Certain medications (e.g., chemotherapy, chloramphenicol) impair DNA replication or damage stem cells directly.

3. Genetic and telomere dysfunction

A• Inherited bone marrow failure syndromes:

• Fanconi anemia: DNA repair defects lead to chromosomal instability and marrow failure.

• Dyskeratosis congenita: Defects in telomerase result in shortened telomeres, causing stem cell exhaustion.

B• Acquired genetic changes: Mutations in stem cell survival or repair genes may lead to marrow failure.

4. Viral infections

• Certain viruses, such as parvovirus B19, hepatitis viruses, and HIV, can:

• Infect and directly destroy progenitor cells.

• Trigger immune responses that harm stem cells.

5. Defective microenvironment

The bone marrow microenvironment provides support and signals to maintain stem cell survival and proliferation. Disruption of this environment (e.g., due to fibrosis or inflammation) can impair hematopoiesis.

6. Secondary causes

Secondary aplastic anemia occurs when external factors like medications, autoimmune diseases, or infections initiate one of the mechanisms described above.

Key Pathological Features

1. Bone marrow hypoplasia or aplasia: Replacement of cellular marrow with fatty tissue
2. Peripheral blood pancytopenia:Reduction in all three blood cell lines (red cells, white cells, and platelets).
3. Normal or slightly elevated erythropoietin levels: Reflects compensation for anemia.

In summary, the pathogenesis of aplastic anemia involves a complex interplay of immune-mediated destruction, environmental insults, and genetic predispositions leading to stem cell failure. This results in reduced production of blood cells and the associated clinical manifestations.

Symptoms

1. Fatigue and weakness (due to anemia).
2. Frequent infections (due to low white blood cells.
3. Easy bruising or bleeding (due to low platelets.
4. Paleness.
5. Shortness of breath.
6. Dizziness or headaches.

Diagnosis

1. Blood tests - Complete blood count (CBC) shows low counts of all blood cell types (pancytopenia)
2. Bone marrow biopsy - Shows a reduction in marrow cellularity.
3. Other tests - To rule out other causes like vitamin deficiencies or leukemia.

Treatment

1. Immunosuppressive therapy:

Drugs like antithymocyte globulin (ATG) and cyclosporine to suppress the immune system.

2. Bone marrow (stem cell) transplant:

Especially for younger patients or those with severe cases.

3. Blood transfusions:

To manage symptoms by increasing blood cell counts temporarily.

4. Medications:

Eltrombopag (stimulates bone marrow to produce more blood cells.(

Antibiotics and antivirals to prevent or treat infections.

5. Lifestyle adjustments:

Avoid exposure to infections, toxic chemicals, and unneeded medications.

Prognosis

With advancements in treatments like bone marrow transplants and immunosuppressive therapies, the prognosis has improved significantly. Early diagnosis and tailored treatment are critical.