

SICKLE CELL ANEMIA

- disease is a hemoglobinopathy that includes (SS) & sickle cell trait (AS).
- homozygous state in which both the β globin chains.

FEATURES:

- caused by mutation in β globin that produce sickle hemoglobin (HbS)
- HbS is more in than RBC than HbA.
- It is produced against falciparum malaria.
- Autosomal Recessive disorder

Genetic mutation

PATHOMECHANISMS

Substitution of glutamic acid by

valine in the 6th position of the β globin

Production of Abnormal sickle (HbS)

Sickling during low O_2 tension

Reversible sickling

Recurrent attack of sickling

Formation of Irreversible sickle cell

Microvascular occlusion
by Irreversible sickle cells

Extravascular hemolysis of
Irreversible sickle cells

ischemia pain
crisis

Moderate to severe
hemolytic anemia

MOLECULAR BASIS:

- During low O_2 tension $\rightarrow$ HbS molecules undergo aggregation & polymerization

These aggregated Hb molecules form long needle-like fibres.
(pseudocrystalline structures called fibrils) within RBC.

↓
These fibrils grow in length beyond the centre of RBC & distort RBC shape.

↓
RBC become elongated, assumes a shape of sickle (holly leaf).

Reversal of sickling → Sickling is reversible when O₂ returns to normal.

↓
Sickling returns to normal.

↓
RBC membrane gets destroyed during each episode of sickling → causes membrane skeleton.

Irreversibly sickled cells & hemolysis → with recurrent sickling causes cumulative membrane damage → RBC become more rigid & non-deformable.

↓
susceptible to hemolysis.

Factors favouring

slowing of blood stream

↑ HbC

↓ pH

Temp Above 37°C

PATHOLOGIC CONSEQUENCE OF SICKLING:

These rigid sickle cells are destroyed in spleen.

↓ lead to
hemolytic Anemia.

Life span of RBC is reduced to 20 days.

↑ unconjugated bilirubin & pigmented gallstones.

Vascular obstructions:

These cells are rigid & form Aggregates.
Block small B.V. → produce ischemic tissue damage & pain crisis.

- Vascular congestion, thrombosis & infarction mainly affect spleen, Bone Marrow → A.S.B.F is slow.
- sickle cell express higher level of Adhesion molecule & thus become Abnormally sticky to the endothelium.

Pain crisis:

Types:
 - vaso occlusive → sequestration crisis
 - hemolytic
 - Aplastic

Vasocclusive → most common type produce → hypoxic, infarction.

Hemolytic crisis → ↑ in hemolysis

Aplastic → ↓ Red cell production. Accompanied by Retiulo cytopenic.

Sequestration crisis → sudden trapping of blood in the spleen or liver cause Rapid enlargement of these organs.

Clinical features:

Symptoms appear after 6 months of Age

→ cause Hb F is in the 1st 6 months of life & has a protective Role

- severe infection.
- Acute chest syndrome.
- splenic sequestration, stroke.
- impairment of growth in children.
- chronic organ damage.

Lab Findings:

$\downarrow$ Hb, $\downarrow$ PCV, $\downarrow$ ESR $\rightarrow$ due to sickle cell anemia cannot form rouleaux

$\uparrow$ Reticulocyte count

MCV $\downarrow$ RDW $\uparrow$

Peripheral smear:

- $\rightarrow$ normocytic normochromic
- $\rightarrow$ Anisopoikilocytosis - size & shape
- $\rightarrow$ long elongated biconcave cells

Target cells

$\rightarrow$ $\uparrow$ Reticulocytes

nodular polychromatic cell

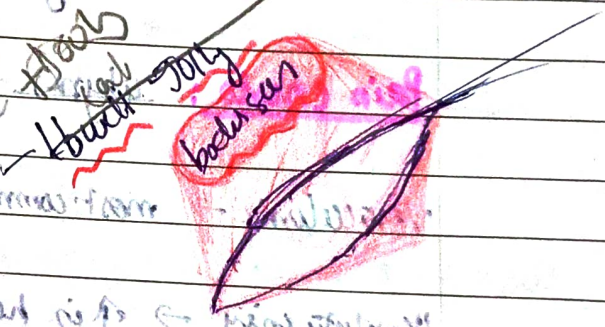
spec. blue, bluish gray or purplish

$\rightarrow$ WBC $\uparrow$

$\rightarrow$ Platelet $\uparrow$

BM

- $\rightarrow$ Hypercellular
- $\rightarrow$ nodular erythroid hyperplasia
- $\rightarrow$ Poor staining



Crescent appearance in Radiograph

$\rightarrow$ due to formation of newborn

Tests

- $\rightarrow$ sickle test $\rightarrow$
- $\rightarrow$ Hb electrophoresis
- $\rightarrow$ estimation of HbF
- $\rightarrow$ High performance liquid chromatography

Clinical features: