Thalassaemia

By
Dr. Najaf Masood
Definition

- Group of hereditary disorders characterized by a genetic deficiency in the synthesis of alpha or beta-globin chains
Historical background
Beta thalassemia

- First described by Cooley and Lee in 1925.
- Mediterranean ancestry.
  - Cooley's Anemia
  - Mediterranean Anemia
Review of hemoglobin structure

- In the adult ......three hemoglobin types
  - Hgb A.... 2 alpha & 2 beta chains - 95% of total
  - Hgb A2... 2 alpha & 2 delta chains - 3% of total
  - Hgb F... 2 alpha & 2 gamma chains - 2% of total
Geografical Distribution

- Mediterranean Italians
- Greeks,
- Arabian Peninsula, Iran, Africa, Southeast Asia, southern China.
Indian/Pakistani origin

- **b-thalassemia trait**
  - 1-15%

- **α-thalassemia**
  - 5–10%

- **Hemoglobin D trait**
  - 1-3%
Genetics

- Autosomal Recessive
Pathophysiology:

- Imbalance between the normal rate of alpha-chain production and the impaired rate of beta-chain production.
- Beta+ thalassemia
  - Decreased beta-chain production
- Beta -0 thalassemia
  - Absent beta-chain production.
- less hemoglobin deposited in each RBC.... hypochromasia.
- The Hb deficiency ....... microcytosis.
- In Silent carrier state both Hb level and RBC indices remain normal.
Elevated A2 Hb

- delta chains that, by pairing with the alpha chains, produce Hb A2 (about 2.5-3% of the total Hb).
- due to the increased utilization of delta chains by the excessive free alpha chains
- The delta gene has physiological limitation in its ability to produce adequate delta chains
Hemolysis in thalassemia

- The remaining alpha chains precipitate in the cells → reacting with cell membranes → intervening with normal cell division acting as foreign bodies → destruction of RBCs.
- Ineffective erythropoiesis
- Erythroid hyperplasia and extramedullary hematopoiesis.
TYPES OF BETA THALASSEMIA

1- Heterozygous States
   Thalassemia Minor

2- Homozygous States
   Thalassemia Intermedia
   Thalassemia Major
Clinical feature
Thalassemia Major

- Age of presentation
  - 6-12 months of life
- Fatigue, poor appetite, and lethargy
- Abdominal distention
- Failure to gain weight
- History of consanguinity
- Similar history in family
Systemic review

- Polyuria & polydipsia
- Jaundice
- Constipation, lethargy
- Breathlessness on exertion, edema
- Tetany, fits
Examination

- Pallor
- Jaundice
- Height & weight
- Greenish yellow hue pigmentaion
- Typical facies (maxillary hyperplasia, flat nasal bridge, frontal bossing)
- Hepatosplenomegaly
Thalassemia Minor

- asymptomatic mild microcytic anemia
- Detected through routine blood tests
Investigations

- Blood count, ESR, RBC morphology & Retic Count
- Hb Electrophoresis
- Serum Ferritin
- Chest X-Rays
Hemoglobin Electrophoresis

- **Thalassemia Minor**
  - Decreased HbA1
  - Elevated HbA2 up to 10% (normal 2.5%)
  - Elevated HbF up to 7% (normal <2.0%)

- **Thalassemia Intermedia**
  - Decreased HbA1 (20-40%)
  - HbA2 always elevated
  - HbF is 60-80% of total hemoglobin

- **Thalassemia Major**
  - Absent HbA1
  - Elevated HbA2 (>3%)
  - HbF (>90% HbF may be 100% at birth)
Skull X-Rays
Bone Marrow Aspiration
Management

- General
  - Counselling of parents
  - Diet
  - Tab folic acid
  - Vitamin C
- Vaccination
  - Hepatitis B
Specific

- Regular blood transfusion
  - Keep Hb upto 10 gm%

- Super blood transfusion
  - Keep Hb upto 12 gm%

- Packed cells transfusion
  - Three or four weekly
    - 15 to 20 ml/kg
Chelation Therapy

- **Desferoxamine**
  - 20-60 mg/kg Subcutaneously over 8-12 hrs
  - 5-6 night /week

- **Defriperone**
  - Oral chelator
  - Alone has poor response and severe side effects

- **Asunra**
  - Expensive with good response
Other modalities

- Splenectomy
  - Hypersplenism
  - Increased blood transfusion requirement
  - Large Spleen

- Bone Marrow Transplantation
  - Definitive
Complications

- Congestive heart failure
  - Severe anemia
  - Cardiomyopathy
- Transfusion reactions
  - Acute
  - Late
- Blood borne infections
- Hemosidrosis
  - Endocrinopathy
    - Diabetes mellitus
    - Hypoparathyroidism
    - Hypothyroidism
    - Hypogonadism

- Chronic liver disease
Side effect of chelation therapy

- Retinopathy
- Deafness
- Metabolic bone disease
- Agranulocytosis
PROGNOSIS

- Increase quality of life with proper management
- Death due to congestive heart failure is common
- Bone marrow transplantation is curative