A Case of Hemoglobinopathy-Thalassemia Syndrome

Michele C. Khurana, B.S. and Gene Gulati, Ph.D.

Department of Pathology, Anatomy and Cell Pathology, Jefferson Medical College of Thomas Jefferson University, Philadelphia, PA

Patient Presentation

- 43 year-old **African American** female presents with **left lower extremity pain**
- **Physical exam**: unremarkable
- **Past medical history**:
  - Anemic since childhood
  - Avascular necrosis of left hip
  - DVT
  - Chronic illnesses: asthma, depression
  - Surgical history: appendectomy, tubal ligation, splenectomy, cholecystectomy, L hip replacement
- **Family history**: mother has lupus

Initial workup

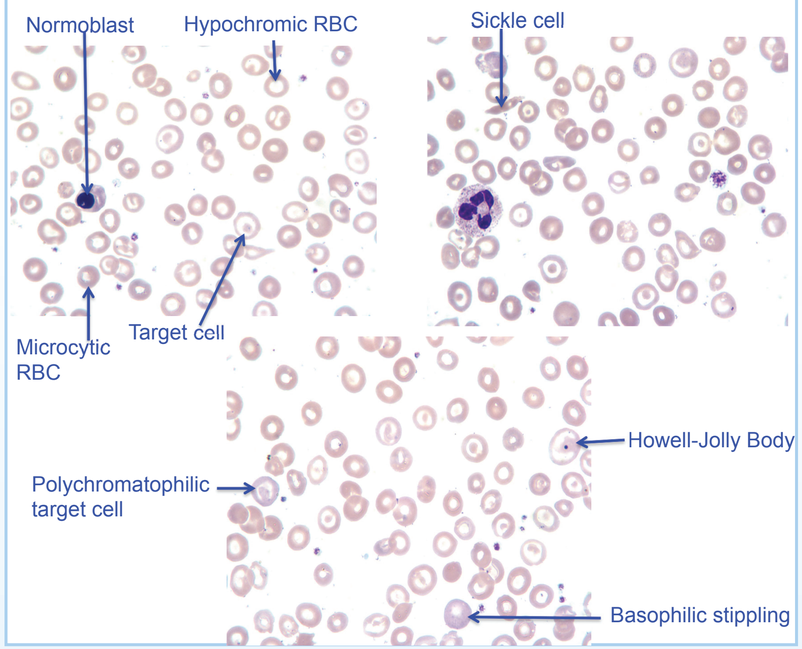
CBC	Value	Normal
WBC count (x10^3/uL)	9.0	3.5-11
RBC count (x10^6/uL)	3.46	3.7-5.2
Hemoglobin (g/dL)	6.8	12.5-15
Hematocrit (%)	22.5	36-46
MCV (fL)	65	80-99
MCH (pg)	19.7	26-34
MCHC (g/dL)	30.2	32.0-37.5
RDW (%)	20.5	11.0-15.8
Platelets (x10^3/uL)	403	140-400
Nucleated RBCs (per 100 WBCs)	6.3	0.0

Differential	Relative (%)	Normal	Absolute (x10^3/uL)	Normal (x10^3/uL)
Neutrophils	85	40-73	7.7	1.6 – 8.0
Lymphocytes	10	20-44	0.9	0.8 – 4.8
Monocytes	4	3-13	0.4	0.1 – 1.4

Reticulocyte Results	%	Normal	Absolute (x10^3/uL)	Normal (x10^3/uL)
Reticulocytes	5	0.5-1.5	173	25 – 75
IRF	45.6	0.0-12.5		

- **Bilateral lower extremity Doppler ultrasound**: negative
- **Hip, femur, knee X-rays**: negative

Peripheral Blood Smear



Differential Diagnosis

- Iron deficiency anemia
- Thalassemia
- Anemia of chronic disease
- Hemoglobinopathy
  - Sickle cell anemia
  - Hemoglobin SC disease
- Hemoglobinopathy/thalassemia syndrome
  - Sickle-α thalassemia
  - Sickle-β$^+$ thalassemia
  - Sickle-β^0 thalassemia

Additional workup

- **LDH:** 249 IU/L
- **Haptoglobin**: 140 mg/dL
- **Bilirubin** (mg/dL): total: 0.4 direct: 0.2

Iron Studies	Value	Normal
Iron (mcg/dL)	36	40-155
TIBC (mcg/dL)	377	250-400
Iron saturation (%)	10	20-55
Ferritin (ng/mL)	77	13-150

- **High performance liquid chromatography (HPLC)**
  - HbA= 16%
  - HbA2= 5.7%
  - HbF= 1.3%
  - HbS= 77%
- **DNA analysis:** mutation in exon II of β globin chain

Final Diagnosis

- Sickle-β$^+$ thalassemia with or without iron deficiency

Treatment

- Chronic pain:
  - IV saline
  - Opioid analgesic

Summary of sickle-β$^+$ thalassemia syndrome

- A form of sickle cell disease
- Pathogenesis and pathophysiology:
  - Compound heterozygous condition—mutation in both β-globulin genes:
    - 1 point mutation causing formation of abnormal sickle hemoglobin (HbS)
    - 1 point mutation causing decreased production of normal β-globin chains
  - Abnormal hemoglobin polymerizes when deoxygenated, forming rigid sickled RBCs:
    - Obstruct microcirculation and result in ischemic injury to organs
    - Undergo extravascular hemolysis
- Clinical presentation:
  - Presents initially in childhood and seen throughout adulthood
  - May develop acute painful episode, stroke, acute chest syndrome, infection, osteonecrosis of hip and shoulder joints, gallstones, pulmonary hypertension
- Diagnosis:
  - CBC + differential and peripheral blood smear: microcytic, hypochromic anemia with reticulocytosis, target cells, and sickle cells
  - HPLC: HbS + elevated HbA2 + HbA
  - DNA analysis and/or family studies often necessary for definitive diagnosis
- Management: supportive and symptomatic
  - General: IV saline, opioid analgesic, transfusion (whole or RBC), iron chelation
  - Other: folic acid, hydroxyurea as needed

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