Sickle Cell Crisis in the Hospital Setting

Definition and Epidemiology

Sickle cell crisis refers to acute complications of sickle cell disease (SCD), a genetic hemoglobinopathy caused by a point mutation in the β-globin gene (HBB), leading to hemoglobin S (HbS). Crises include vaso-occlusive, hemolytic, aplastic, and sequestration events, requiring urgent hospital management.

Prevalence SCD affects ~100,000 people in the U.S., primarily African Americans (1 in 365 births). Vaso-occlusive crises are the most common, with 50-60% of patients experiencing ≥1 crisis annually.

Risk Factors Dehydration, infection, hypoxia, cold exposure, stress, pregnancy.

Rare Demographics SCD variants (HbSC, HbS/β-thalassemia), fetal hemoglobin (HbF) persistence, neonatal crises.

Pathophysiology

Mechanisms HbS polymerizes under deoxygenation, acidosis, or dehydration, causing RBCs to sickle, become rigid, and occlude microvasculature. This leads to ischemia, inflammation, and pain. Hemolysis causes anemia and endothelial dysfunction.

Effects Vaso-occlusion results in tissue hypoxia (e.g., bone, spleen), while hemolysis releases free hemoglobin, scavenging nitric oxide (NO), promoting vasoconstriction and organ damage. Aplastic crises halt erythropoiesis; sequestration traps RBCs in spleen/liver.

Molecular Pathways HbS polymerization activates NLRP3 inflammasome, releasing IL-1β and IL-6. Free heme induces oxidative stress via Fenton reactions. P-selectin and VCAM-1 mediate RBC-endothelial adhesion.

Key Pathway HbS polymerization → Sickle RBCs → Vaso-occlusion and hemolysis → Ischemia, inflammation, and organ damage.

Causes

Category	Common Triggers	Rare Triggers	Notes
Vaso-Occlusive	Dehydration, infection, hypoxia	High-altitude, cocaine	Bone pain most common; 90% of crises
Hemolytic	Infection, oxidative stress	G6PD deficiency, drugs (e.g., sulfonamides)	Acute anemia, jaundice
Aplastic	Parvovirus B19	EBV, CMV	Sudden drop in Hgb, low reticulocytes
Sequestration	Infection, fever	Pregnancy, hypersplenism	Splenic/liver pooling, hypovolemia
Infectious	Pneumococcus, Salmonella	Haemophilus, Babesia	Encapsulated organisms due to asplenia
Systemic	Pregnancy, surgery	Hyperviscosity (high HbF)	Pregnancy increases crisis risk by 20%

Clinical Presentation

- Symptoms
  - Severe pain (bones, joints, abdomen; vaso-occlusive)
  - Fever, fatigue (infection, hemolytic)
  - Dyspnea, chest pain (acute chest syndrome)
  - Rare Jaundice (hemolytic), pallor (aplastic), shock (sequestration)
- Exam
  - Tachycardia, pallor, scleral icterus
  - Bone tenderness, joint swelling
  - Splenomegaly (sequestration, early SCD)
  - Rare Hypovolemia (sequestration), respiratory distress (acute chest)
- Red Flags SpO2 <92%, Hgb drop >2 g/dL, altered mental status, priapism

Labs and Studies

- Labs
  - CBC Hgb 6-8 g/dL (baseline), reticulocytes >3% (hemolytic), <1% (aplastic)
  - LDH, Haptoglobin Elevated LDH, low haptoglobin (hemolysis)
  - Bilirubin Total >2 mg/dL (hemolytic crisis)
  - Advanced Free hemoglobin, hepcidin (research), HbF levels
- Imaging
  - CXR Acute chest syndrome (infiltrates, 10-20% of crises)
  - Ultrasound Splenomegaly, hepatomegaly (sequestration)

    - MRI Bone marrow necrosis, avascular necrosis (chronic)
    - Advanced CT chest (PE, acute chest), PET-CT (osteomyelitis)
- Other
    - Blood Cultures Rule out sepsis (fever, leukocytosis)
    - Peripheral Smear Sickle cells, Howell-Jolly bodies (asplenia)
    - Advanced Parvovirus B19 PCR (aplastic), ADAMTS13 (TTP mimic)
    - Urinalysis Hemoglobinuria (hemolysis), proteinuria (SCD nephropathy)

Diagnosis

- Criteria Acute pain, fever, or organ dysfunction in known SCD + lab/imaging evidence (e.g., Hgb drop, CXR infiltrates) consistent with crisis type.
- Differential Osteomyelitis, septic arthritis, MI, PE, TTP, acute abdomen.
- Flowsheet
    - Step 1 History/Exam Pain location, fever, hypoxia; assess for infection, sequestration
    - Step 2 Labs CBC, reticulocytes, LDH, bilirubin; blood cultures if febrile
    - Step 3 Imaging CXR (acute chest), ultrasound (sequestration), MRI (bone)
    - Step 4 Classify Crisis Vaso-occlusive (pain), hemolytic (Hgb drop), aplastic (low retic), sequestration (splenomegaly)
    - Step 5 Differential Rule out osteomyelitis (MRI), sepsis (cultures), PE (CTA)

Treatment

- General Principles Relieve pain, correct hypoxia, prevent organ damage, and treat underlying triggers.
- Supportive Care
    - Hydration NS 1.5-2x maintenance IV (e.g., 100-150 mL/h), avoid overhydration
    - Oxygen 2-6 L/min NC for SpO2 <92%; BiPAP for acute chest
    - Folate 1 mg PO daily (chronic hemolysis)
- Specific Therapies
    - Pain Management Morphine 0.1 mg/kg IV q15-30min (PCA preferred), ketorolac 30 mg IV q6h (short-term)
    - Antibiotics Ceftriaxone 2 g IV q24h (fever, sepsis), azithromycin 500 mg IV (acute chest)
    - Hydroxyurea 15-35 mg/kg/day PO (escalate post-crisis, ↑HbF)
    - Transfusion PRBCs for Hgb <5 g/dL or symptomatic anemia; exchange for acute chest, stroke

    - Advanced Voxelotor 1500 mg PO daily (↑Hgb affinity), crizanlizumab 5 mg/kg IV q4w (anti-P-selectin)
    - Rare Triggers Parvovirus (IVIG 1 g/kg), hypersplenism (splenectomy)
- Monitoring
    - Pain scores q2h, SpO2, urine output
    - Daily CBC, LDH, bilirubin; CXR q24h (acute chest)
    - Blood cultures until afebrile, monitor for alloimmunization

Complications

- Acute
    - Acute Chest Syndrome Pneumonia-like, 10-20% mortality without treatment
    - Stroke 5-10% of crises, MCA occlusion
    - Priapism 5% of males, risks impotence
- Long-Term
    - Avascular Necrosis Hip/shoulder, 20-30% by age 30
    - SCD Nephropathy Proteinuria, CKD in 20%
    - Rare Osteomyelitis (Salmonella), pulmonary hypertension, retinal detachment

Clinical Scenarios

Case 1 Vaso-Occlusive Crisis

Presentation 25 y/o M with SCD (HbSS) presents with severe leg pain, fever. Vitals BP 120/80, HR 100, SpO2 95%, RR 18. Exam Bone tenderness, no swelling.

Labs/Studies Hgb 7 g/dL, reticulocytes 5%, LDH 600 U/L, blood cultures negative.

Interpretation Vaso-occlusive crisis, likely dehydration-triggered.

Management Morphine PCA (0.1 mg/kg/h), NS 150 mL/h, ceftriaxone 2 g IV q24h. Hydroxyurea escalated to 20 mg/kg. Pain resolves by day 4, discharge with pain clinic follow-up.

Case 2 Acute Chest Syndrome

Presentation 30 y/o F with SCD presents with chest pain, dyspnea, fever. Vitals BP 110/70, HR 110, SpO2 90%, RR 24. Exam Crackles, scleral icterus.

Labs/Studies Hgb 6 g/dL, reticulocytes 4%, CXR RLL infiltrates. Bilirubin 3 mg/dL.

Interpretation Acute chest syndrome, vaso-occlusive.

Management O2 4 L/min, exchange transfusion (HgbS <30%), morphine 0.1 mg/kg IV q20min, azithromycin 500 mg IV. ICU monitoring. CXR clears by day 5.

Case 3 Aplastic Crisis (Rare)

Presentation 10 y/o M with SCD presents with pallor, fatigue, no pain. Vitals BP 100/60, HR 120, SpO2 96%, RR 16. Exam Pallor, no splenomegaly.

Labs/Studies Hgb 4 g/dL, reticulocytes 0.5%, parvovirus B19 PCR positive.

Interpretation Aplastic crisis, parvovirus-induced.

Management PRBC transfusion (Hgb to 8 g/dL), IVIG 1 g/kg, folate 1 mg PO daily. Isolation (droplet). Hgb stabilizes by day 3, discharge with hematology follow-up.

Expert Tips

- Use PCA for pain; avoid under-dosing due to opioid stigma (monitor respiratory status)
- Check for acute chest syndrome in all febrile crises; CXR even if SpO2 >92%
- Suspect parvovirus in aplastic crisis; low reticulocytes and rash are clues
- Monitor for alloimmunization post-transfusion; use phenotype-matched blood
- Consider voxelotor or crizanlizumab in recurrent crises; genetic counseling for HbF variants
- Pitfall Missing osteomyelitis; MRI if pain persists >7 days or ESR >100 mm/h
- Advanced Anti-NLRP3 therapies (research), hepcidin modulators for iron overload

Key Pearls

- Vaso-occlusive crisis is most common; pain and fever require rapid management
- Acute chest syndrome needs exchange transfusion, antibiotics, and O2
- Hgb <5 g/dL or severe symptoms warrants transfusion; avoid over-transfusion
- Hydroxyurea reduces crisis frequency; escalate post-recovery
- Rare aplastic crises (parvovirus) require IVIG and isolation

References

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