Sickle Cell Disease in Athletes

Objectives

- Be familiar with the classification, diagnosis, and complications of sickle cell disease/trait.
- Be equipped to guide the management of sickle cell disease/trait in athletes.

Case Study

- In January, a 22 y/o collegiate football athlete with known sickle cell disease competed in morning conditioning drills at 6 am.
- He developed left-sided arm and upper leg pain during breakfast and presented to Student Health.
Case Study

• EMS was contacted immediately and the athlete was transported by ambulance to the nearest Emergency Department due to concern for sickle cell crisis.

![EMS vehicle]

Case Study

• Intravenous fluid resuscitation was initiated in the ED and hydromorphone was given as needed for pain.
• Admitted to the hospital for further work-up and management.

![Emergency Department]

History

• Past Medical History
  — Sickle cell disease
  • Initial crisis at 5 years old; most recent crisis 1 year prior
• Surgical History
  — None
• Medications
  — Folic acid, Multivitamin
• Allergies
  — None
• Family History
  — Father and mother in good health
• Social History
  — Student athlete originally from Amsterdam, Netherlands
  — No smoking history or illicit drug use
Physical Examination

- VITALS: T 97.8, P 96, RR 20, BP 126/80, spO2 99%
- GENERAL: Well-developed. No acute distress.
- HEART: Regular rate and rhythm, no murmurs.
- LUNGS: Clear to auscultation bilaterally.
- ABDOMEN: Normal bowel sounds, non-tender.
- SHOULDERS: Tender to palpation over distal biceps and triceps, pain with resisted elbow flexion/extension. Otherwise, normal.
- HIPS: Tender to palpation over greater trochanter and lateral quadriceps. Otherwise, normal.

Differential Diagnosis

- Complication of sickle cell disease
  - Sickle cell pain crisis
  - Exertional rhabdomyolysis
  - Spleenic infarct
- Unrelated musculoskeletal issue
  - Muscle strain/contusion
- Medical issue
  - Referred pain (angina, pulmonary embolus)

Labs on admission

- WBC 11 (87% neutrophils)
- Platelets 182
- **Hemoglobin 11.6**
- **Hematocrit 34.2**
- **Reticulocyte count 4.1**
- CMP within normal limits
- Cardiac enzymes negative (CK 228) (normal <308)
- ABG within normal limits (lactate 0.33) (nl <1.25)
- Urinalysis and toxicology screen negative
Additional diagnostics

• Imaging
  – Chest x-ray (2 views): No acute process
  – CT Chest: Bibasilar atelectasis
  – Shoulder films (2 views): Unremarkable
  – Pelvis films (2 views): Unremarkable
  – Repeat CXR (1 view): Mild pulmonary edema
• Cardiac work-up
  – Electrocardiogram: Normal sinus rhythm
  – Transthoracic echocardiogram: Unremarkable

Additional labs

• Hemoglobin electrophoresis
  – Hemoglobin S: 49.8%
  – Hemoglobin C: 43.9%
  – Hemoglobin A2: 4.9%
  – Hemoglobin F: 1.4%
• Diagnosis: Hemoglobin SC disease

Management

• Sickle cell pain crisis
  – 5-day hospital stay for hydration and pain control
    • IV fluid resuscitation
    • Patient-controlled analgesia (hydromorphone)
  – Transitioned to Celecoxib, cyclobenzaprine, and oxycodone for pain on discharge
  – Developed cough during admission—discharged on guaifenesin and cefdinir
  – Follow-up arranged in Hematology clinic
**Return to Play**

- On discharge, the athlete was instructed to rest until complete resolution of symptoms
- Two weeks later, he continued to have a cough and was placed on additional antibiotics
- Two weeks later, the cough resolved and the athlete was cleared to gradually progress activities, starting with light conditioning
- He progressed over the course of four weeks to full participation.

**Return to Play**

- Two weeks later, he decided to retire from football and move back home to Amsterdam
- The athlete cited difficulty with spring workouts, expense of school, and homesickness as major factors in this decision

**Questions**

- What is the difference between sickle cell disease (SCD) and sickle cell trait (SCT)?
- What can go wrong with these athletes?
- How are athletes with SCD or SCT identified?
- What prevention strategies are in place?
Sickle Cell Disease

• Terminology
• Epidemiology
• Complications
• Screening/Diagnosis
• Management
• Return to play

Sickle Cell Disease

• Normal adult hemoglobin
  – $2\alpha + 2\beta = \text{Hb A tetramer}$
• Hemoglobin S
  – Mutation in the beta-globin chain → Poorly soluble hemoglobin, which forms long, inflexible chains when deoxygenated
  – Inflexible hemoglobin chains → Stiff & sticky (sickle) red blood cells
  – Sickle cells logjam in small vessels → Compromise blood supply

Question

• What is the difference between SCD and SCT?
Question

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Genotype

• Sickle cell disease
  – All conditions associated with sickling
• Sickle cell anemia (Hb SS)
  – Homozygous for hemoglobin S
• Hemoglobin SC disease (Hb SC)
  – Hemoglobin S and hemoglobin C (typically 50:50)
• Sickle cell trait (Hb AS)
  – Hemoglobin A and hemoglobin S (typically 60:40)

Phenotype

• Sickle cell anemia (SCA)
  – Numerous complications; rarely compete in sports
    • Most common complication is pain crisis (0.8 per year)
    • Anemia, infection, stroke, CVD, renal disease, leg ulcers, priapism
    • Life expectancy: 45 years
  – No reported cases in NCAA athletes
• Hemoglobin SC disease
  – Less severe than SCA; more severe than SCT
    • Most common complication is pain crisis (0.4 per year)
    • At risk for same complications above—much less common
    • Life expectancy: 64 years
  – Four reported cases in NCAA athletes
  – All eventually retired due to complications
• Sickle cell trait
  – “Not a disease;” athletes compete in sports with few complications
  – Roughly 2,000 current NCAA athletes
Epidemiology

• Sickle cell gene is most common in Africa, India, the Middle East, and Mediterranean countries
  – Malarial distribution
  – Frequency of sickle cell gene: 4%
  – SCA = 0.2%; SCT = 8%
• SCT: 300 million people worldwide, 3 million U.S.
  – 8-10% of African Americans
  – 0.5% of Hispanics
  – 0.2% of Whites
• SCT does not alter life expectancy

Question

• What can go wrong with these athletes?

Complications of SCT

• Gross hematuria
• Venous thromboembolism
• Splenic infarction
• Exertional collapse
Gross hematuria

- Results from sickling deep in the renal medulla
  - Initial therapy is relative rest and hydration
    - Typically resolves within two weeks

Venous thromboembolism

- Studies conflict on the relative risk of VTE in athletes with SCT compared to those without
  - Range from 1.5-4 times relative risk
  - Monitor athletes with immobilizing injuries for deep venous thrombosis
    - Especially those taking oral contraceptives

Splenic infarction

- Hypoxic splenic sickling → infarct, typically at altitude
  - Ryan Clark
    - Splenic infarction in Denver in 2007
    - Splenectomy and cholecystectomy were done
    - Out for the rest of the season
    - Held out of games in Denver thereafter
  - Most cases occur with mild to moderate activity
    - Consider oxygen for long flights/road trips to altitude
  - One case series documented 30 of 50 cases occurred in non-black persons
    - Think of SCT splenic infarction in anyone who develops left lower chest pain while at altitude
    - Diagnosed early, it responds to conservative therapy, including descent
Exertional collapse

• NCAA Division-1 football
  – 16 deaths from 2000-2010
    • All from conditioning; zero from practice/play
    • 10 (63%) attributed to exertional sickling
  – SCT independent risk factor
    • Black athletes with SCT 37 times more likely to experience exertional death than those without SCT
• Military recruits
  – SCT independent risk factor
  • Black recruits with SCT 30 times more likely to experience exertional death than those without SCT

Exertional collapse

• Perfect storm of undue exercise intensity, sustained for at least a few minutes, and a heroic effort beyond the physical limits of an athlete on any given day.
  – Intense exertion → Hypoxemia → Sickling
  – Sickle cells → Muscular ischemia → Rhabdomyolysis
• Deaths are largely due to rhabdomyolysis
  – Acute renal failure
  – Hyperkalemia
  – Fatal arrhythmias

Exertional collapse

• Dale Lloyd
  – Freshman football athlete
  – Collapsed after a conditioning run
    • 16 successive 100 yard sprints
    • Lagged behind on final sprints
    • Shortness of breath and weakness after work-out
    • Initially alert; lethargic within 10 minutes
  – Received IV fluids in training room, then lost consciousness and was rushed to the hospital
  – Profound lactic acidosis and rhabdomyolysis
  – Died 15 hours after collapse from hyperkalemia and fatal arrhythmia
Exertional collapse

• Typical Presentation
  – Unlike cardiac arrest
    • Able to talk at first
  – Unlike heat illness
    • Slumps to the ground
    • Weakness > Pain
    • Muscles “normal”—not tight or cramping
    • Normal temperature
  – Unlike asthma
    • Tachypnea due to lactic acidosis; no wheezing

Question

• How are athletes with SCD or SCT identified?

Screening/Diagnosis

• NCAA Mandate
  – All NCAA athletes are required to be screened
    • May provide records or opt out/sign a release
• Tests
  – Solubility test (Sickledex)
    • 98.4 - 98.9% sensitive, 100% specific
    • If positive, proceed to confirmatory test
  – Hemoglobin electrophoresis
    • Gold standard
Questions

• What prevention strategies are in place?

Prevention

• Athletes with SCT should train *consciously*...
  – Set their own pace
  – Engage in a slow and gradual preseason conditioning regimen
  – Build up slowly while training, allowing adequate rest and recovery between repetitions
  – Be excused from performance tests such as serial sprints or timed mile runs, avoiding all-out exertion beyond 2-3 minutes without a break
  – Access supplemental oxygen at altitude as needed

Prevention

• Athletes with SCT should train *cautiously*...
  – Stay well hydrated at all times, especially in hot and humid conditions
  – Maintain proper asthma management
  – Refrain from extreme exercise during acute illness
  – Stop activity immediately upon struggling or experiencing symptoms such as muscle pain, weakness, undue fatigue, or breathlessness
Management

• In the event of a sickling collapse...
  – Be prepared with an Emergency Action Plan
  – Check vital signs
  – Administer oxygen
  – Cool the athlete if necessary
  – If obtunded, call 911, attach AED, start IV, and transport the athlete to the ED
  – Tell receiving hospital to expect rhabdomyolysis

Return to play

• Limited evidence supports recommendations
  – Once the athlete is asymptomatic at rest and has normal end-organ function, re-visit precautions for safe participation.
  – If the athlete desires to resume activity, allow a gradual supervised return to activity as tolerated.
Conclusions

• What is the difference between SCD and SCT?
  – SCT is the most common form of SCD we will encounter (300 million worldwide; 3 million in the U.S.)

• What can go wrong with these athletes?
  – Most common complication is exertional rhabdomyolysis

• How are athletes with SCD or SCT identified?
  – Screening is mandatory at all NCAA levels
  – If positive, confirmatory testing is required

• What prevention strategies are in place?
  – Educate athletes to train consciously and cautiously
  – Be prepared with Emergency Action Plan for complications

References

7. UpToDate. Variant sickle cell syndromes.

Questions?