Sickle Cell Trait in Athletes

See also Exertional Heat Illness in Athletes
See also Cardiac Disorders in Athletes

Background

1. General information
   - Hemoglobin consists of a tetramer of globin polypeptide chains
     - Alpha (2 chains)
     - Beta (2 chains)
   - Globin chains folded to allow covalent linkage of 4 heme iron elements
   - Hemoglobin transports oxygen via conversion/restoration of 4 heme elements
   - Process relies upon precise movement of globin chains in association with oxygenation/deoxygenation
     - Compositional changes of globin chains results in considerable distortion of this movement
2. Implications in athletes
   - Activities which involve high levels of vigorous cardiovascular activity of particular concern
     - Football
     - Basketball
     - Soccer
     - Distance Running
     - Military Training
   - Activity in specific conditions intensify the risk
     - Altitude-Hypoxia
     - High Heat-Dehydration
3. Web sites for physicians
   - National Athletic Trainers Association (NATA) Consensus Statement
     - http://www.nata.org/statements/consensus/sicklecell.pdf
   - National Collegiate Athletic Association (NCAA) Sports Medicine Handbook
     - http://www.ncaa.org/wps/ncaa?key=/ncaa/ncaa/academics+and+athletes/personal+welfare

Pathophysiology

1. Hemoglobin S
   - Evolved as a protective element against malaria
   - Substitution of Valine for Glutamic Acid as 6th amino acid of beta globin chain
   - Beta S chains are poorly soluble when deoxygenated
   - Distorts red blood cells into crescent or "sickle" shape when in presence of other abnormal chains
   - Sickling obstructs blood vessels
     - Decreased perfusion of blood
     - Decreased removal of metabolites

- Precipitated by physiologic stress/strenuous exercise leading to
  - Severe hypoxemia
  - Metabolic acidosis
  - Hyperthermia of the musculature
  - Red-cell dehydration
  - Ischemic rhabdomyolysis secondary to micro-infarctions
- In exercise, precipitating factors include lowering of blood oxygen saturation and acidosis resulting in
  - Right shift of oxygen-dissociation curve and subsequent displacement of oxygen from Hemoglobin S
  - Complete sickling of all 4 tetramers from continued lowering of oxygen saturation
- Typically sickling presents following 2 to 3 minutes of sustained strenuous activity

2. Sickle cell trait
   - Benign, heterozygous condition
   - Ratio of Hemoglobin A to Hemoglobin S 60:40
   - No hematologic manifestations
   - Abnormalities of red cell parameters may influence exercise tolerance
   - Underlying renal damage impairs ability to concentrate urine and conserve water
3. Incidence, prevalence
   - 8-10% of African-Americans (one in 12), rarer in all other races
     - Caucasians: one in 2000 to one in 10,000
   - Estimated 3 million Americans possess the trait
   - Found in all levels of sports competition
   - Both genders equally affected
4. Risk factors
   - Morbidity increased by the following risk factors
     - Dehydration
     - Extreme heat
     - Exercise at high altitude
     - Deconditioning
     - Repetitive running of hills or stairs
     - End of practice burnout drills often referred to as "Gassers"
     - Sustained high-exertional activity
     - Asthma
     - Illness
5. Morbidity / mortality
   - Case reports exist of sudden death after extreme exertion, overall rare and controversial
     - First known sickle death in 1974 in college football player
     - Most recent case occurring in 2006 in college football player
     - 13-15 reported college football deaths over past four decades

        - Many more reports of fatalities that occurred during military training, no specific numbers currently available
            - Recruits with sickle cell trait 30 times more likely to die from this during basic training
            - Risk of exertional rhabdomyolysis was 200 times greater in recruits with sickle cell trait
        - Several non-fatal cases reports
            - Majority occur in college football followed by high school football
        - Exertional sickling responsible for 5% of sudden, non-traumatic sports deaths over past decade
    - Causes of death
        - Rhabdomyolysis
        - Exertional heat stroke
        - Cardiac Arrhythmia, often 2° to hyperkalemia
        - Myoglobinuric acute renal failure
        - Profound metabolic acidosis
        - Multiple-organ system failure

Diagnostics

1. History
    - Sickling athletes often found weak on the field
        - No prodrome of symptoms
            - No twitching or twinging of the muscles occurs prior to sickling (unlike heat stroke, heat exhaustion, and heat cramps)
        - Typically during first half hour of play
    - Patients report a mild "cramping" sensation and profound weakness
    - Athletes often "slump" over from weakness and lie still
    - Pain and weakness often progressive and commonly involves lower back, buttocks, and/or legs
2. Physical exam
    - Core temperature not elevated
    - Vital signs may demonstrate signs of shock
3. No visible or palpatory abnormality of the muscles
    - No hypertonicity as seen with muscle cramping
4. Diagnostic testing
    - Laboratory evaluation
    - Screening
        - Prenatal Diagnosis
            - All states currently screen for this trait at birth
            - DNA based testing for prenatal diagnosis
    - Childhood/adulthood diagnosis
        - Hemoglobin Electrophoresis positive
        - Solubility tests positive
        - Red cell morphology normal
        - Red cell indices normal
        - Reticulocyte index normal
        - Peripheral blood smear does not show irreversibly sickled cells

Differential Diagnosis

1. Cardiac collapse
2. Heat exhaustion
3. Heat cramps
4. Heat stroke

Sports Participation Considerations

1. Eligible to participate in sports, according to
    - The American Academy of Pediatrics Committee on Sports Medicine and Fitness
    - The National Athletic Trainers' Association
    - The National College Athletic Association
    - The National Institute of Health
2. Sickle cell athletes should refrain from performance tests, such as
    - Distance Runs
    - Serial Sprints
    - "Suicide Sprints"
    - "Gassers"
3. Preparticipation Clearance
    - The NCAA Committee on Competitive Safeguards and Medical Aspects of Sports recommends
    - Confirmation of known sickle cell trait
        - Document results of newborn screen and confirm with follow-up testing
    - Testing of all unknown athletes prior to sports participation
4. Athletes must be removed from play if they experience any of these symptoms
    - Muscle pain
    - Muscle weakness
    - Fatigue
    - Dyspnea

Therapeutics

1. Prevention
    - Have an Emergency Action Plan readily available
    - Encourage preseason sports-specific conditioning programs
        - Avoid off-season conditioning tests
    - Acclimate to increased physical activity gradually with paced progressions
    - Maximize periods of rest and recovery between repetitions
    - Athletes should concentrate on sports-specific strength and conditioning programs that are custom tailored to their individual needs
    - Engage in year-round training
    - Avoid exertion to the point of muscle pain
    - Minimize effects of heat, humidity, and dehydration
    - Monitor closely any athlete new to higher altitudes, especially >5,000 feet
    - Avoid use of diuretics
    - Patients should immediately report any fatigue, dyspnea, muscle weakness or cramping
        - Activity should stop at the first sign of such symptoms

- Control asthma
- Avoid workouts when sickle cell athletes have illnesses, especially nausea, vomiting, and diarrhea
- Avoid training after periods of sleep loss
- Encourage regular hydration prior to, during, and following activity
- Have oxygen supply readily available
- Prepare exercise programs with adequate rest
  - Known sickle cell patients should be afforded extended recovery times during exercises that create high levels of lactic acid
  - Allow sick cell patients to set their own pace

2. Acute treatment
   - Treatment aimed at rehydration and correction of complicating pathology
   - Monitor vital signs closely
   - Administer high-flow oxygen with a non-rebreather face mask
   - Cool the athlete if core temperature is elevated
   - If patient becomes obtunded
     - Attach AED
     - Start IV
     - Transfer to nearest emergency department
3. Return to play
   - Highly individualized
   - Dependent on additional diagnoses/response to treatments
     - Mild Sickling
       - An athlete who is asymptomatic after 15-30 minutes of cooling and hydration may return the following day
     - Moderate Sickling
       - An athlete who has residual muscle soreness or weakness should receive daily assessment and gradual return to play
     - Severe Sickling
       - An athlete who is hospitalized with rhabdomyolysis or renal failure secondary to exertional sickling may not return to play

Patient Information

1. Sickle Cell Information Center
   - http://www.scinfo.org/sicklept.htm
2. Sickle Cell Disease Association of America
   - http://www.sicklecelldisease.org/

References

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