Sickle Cell Disease and the Competitive Athlete
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Learning Objectives
- Understand the impact of Sickle Cell Disease and Sickle Cell Trait (SCT) on sports participation
- Be aware of NCAA policy regarding SCT
- Recognize the clinical presentation of exercise collapse associated with SCT (ECAST)
- Identify the risk factors for SCT complications
- Develop strategies to prevent exercise related complications associated with SCT

Sickle Cell Disease vs. Trait
- Genetic disorder of hemoglobin production
  - 1st clinically identified in 1910
  - Reported as genetic condition 1949
  - Hemoglobin abnormality in 1951
- Sickle Cell Disease – inherit two sickle cell genes – one from each parent
- Sickle Cell Trait – inherit one sickle cell gene
Molecular Pathology of Sickle Syndromes

- Normal Hb (HbA) – 2 alpha and 2 beta globin proteins
- Sickle Hb (HbS) – 2 alpha and 2 sickle beta globin
- Each RBC has many Hb molecules to deliver oxygen from the lungs to the tissues where it is needed
- SCD = 85+% of Hb is HbS
- SCT = 35–55% of Hb is HbS
- There are actually multiple genes for globin proteins – so manifestations of SCD/SCT can vary

Molecular Pathology of Sickle Syndromes

- Deoxygenated HbS forms hydrophobic bonds that deform the RBC into a crescent
- These "sickle" cells that are "sticky" and rigid together with proinflammatory mediators clog vessels resulting in vaso-occlusive events
- Results in acute ischemia (crisis), chronic end organ damage and hemolysis

Sickle Physiology – Additional Factors

- Level of oxygen in the cell – Lower O2 results in more deoxyHbS
  - high altitudes worse
  - deconditioned pt without enhanced cardiac output
- pH level – Low ph promotes deoxygenation
  - Exercise induced acidosis worse
- Tissue temperature – higher temps promote deoxygenation
Sickle Physiology – Additional Factors

- **Hydration –** Dehydration increases viscosity
  - promotes hypercoagulable state

- **Age**
  - Death rate in SCT 8x higher for 28–29yo vs. 17–18yo
  - Etiol?...may be from chronic renal papillary necrosis and resultant inability to concentrate urine

- **How much HbA or other hemoglobinopathy –** may reduce sickling
  - SCT carriers may vary in the amounts of HbS

SCD/SCT and Sports

- SCD typically unable to participate as over-exertion and competitive sports involve factors that promote sickling/crisis

- With the Dx of SCD in the 1950’s – SCT was initially believed to be a benign condition with little to no health consequence

- 1975 – NCAA statement –SCT not a barrier to achieving the highest levels of athletic performance

SCT and Exercise Concerns

- 1970 (NEJM, JonesSR, et al) US Army reports 4 deaths over 1 year during basic training at 4,050 ft altitude

- 1987 (NEJM, Kark JA et al) Army retrospective review of all deaths from 1977–1981 showed Black recruits with SCT had 30 fold higher risk of sudden death

- 1995 (MSSE, Van Camp et al) – ten year review of nontraumatic sports-related deaths includes 7 caused by exertional rhabdomyolysis associated with SCT
Study of Ivory Coast Athletes – 1998
- Intl J Sport Med – Bile et al –
- Large epidemiologic study of track and field athletes 1956–1995
- Higher % SCT in field throw and jump champions
  - ? Does SCT benefit in brief explosive events
    - How? – Vincent et al showed SCT has greater type II muscle fibers
- SCT may limit performance in activities requiring sustained aerobic metabolism
  - lower cytochrome C oxidase activity – so lower oxidative energy metabolism at the tissue level.

SCT Concerns and the NCAA
- 2000–2010 – 9 of 21 deaths of collegiate football players linked to SCT
- Sept 2006 – Dale Lloyd II dies at Rice University after sprinting 100 yds. for the 16th consecutive time
- Wrongful death suit – led to NCAA policy change
  - 2009 – recommend determining SCT status
  - April 2010 – All Division 1 athletes MUST be tested for SCT, have proof of prior test or sign waiver of liability if they decline testing

SCT – Screening
- US – all newborns are screened for SCD
- Solubility test – “Sickledex”
  - 2009 CDC consensus group (Grant et al–Am J Prevent Med 2011) –recommended against this test in favor or more reliable screens
- Hemoglobin electrophoresis
- Other –
  - Liquid chromatography
  - DNA testing
SCT – Epidemiology

- Seen highest frequency in persons of African American and Middle Eastern descent – but also among those of Mediterranean or Indian origin. (Jordan et al – Am J of Prev Med 2011)
- 300 million carriers of SCT worldwide
- 3–4 million SCT in US,
  - 8–9% of the African Americans in US

Serious Complications of SCT in Athletes

- Splenic infarction
  - Ryan Clark – Steelers safety Nov 2007 playing game in Denver
- Renal papillary necrosis
- Hematuria
- Exertional Rhabdomyolysis (ER)
- Exercise-related sudden death

Case Presentation
(MSSE – Lanzalone ML et al 2009)

- 19 yo African American college FB player
  - apparently healthy
  - PMH of seasonal allergies and ?EIA at age 13 (SOB and fatigue when started baseball)
- Late September workout – turf temp 76º with mild wind
Case Presentation (MSSE – Lanzalone ML et al 2009)

- 4:00PM – weight training indoors
- 4:30PM – outdoors for 16–100 yard sprints
  - Breaks of 1–2 min between each sprint
- 4:55PM – completes sprints but c/o SOB and leg pain – is alert
- 5:05PM – becoming lethargic but still conscious; +SOB – legs too weak to support weight – University EMS contacted – taken indoors – O\textsubscript{2} begun
- 5:12PM – University EMS arrives – IVF started – O\textsubscript{2} 100% via bag valve mask – Fire Dept EMS called
- 5:28PM – Fire Dept EMS arrives

Case Presentation (MSSE – Lanzalone ML et al 2009)

- 5:28PM – FD EMS Assessment: pt unconscious with shallow respirations –
  - Glasgow Coma score of 3
  - POx on room air 62% – 100% with high flow O\textsubscript{2}
  - EKG = sinus tach with peaked t waves in V2–V3
- Nasally intubated
- Rushed to ED – arrives 5:52PM
Case Presentation
(MSSE – Lanzalone ML et al 2009)

Emergency Department findings
- BP 151/49, P 126, R 30, T 97

7PM Lab results
- ABG = pH 7.05, PCO2 45mmHg, PO2 540mmHg
- Lactic acid 33mmoll (ULN = 2.2)
- Serum bicarbonate 8mEq (LLN = 24)
- Serum Creat = 2.3
- Phosphorus = 12.8 (ULN = 4.5)
- Potassium = 5.2

7PM Labs (cont.)
- Creatine Kinase = 536 (ULN=220)
- Myoglobin = 7485 (ULN = 72)
- CSF = nml
- Drug Screen = neg
- CBC nml (Hb = 14.5)
- PT = 23, PTT = 84, Fibrinogen = 87, Fibrin Sp Prod > 20
- EKG = peaked T waves
- CXR = Nml

Through the night the patient was given:
- IVF, IV antibiotics, renal dialysis,
- 20UFFP, 10U RBC, 4U Platelets

- Hb dropped to 4.3
- CK climbed to > 41,000
- Potassium climbed to over 9

Pt died 15 hours after admission
Summit on SCT and Strenuous Exercise

- Consortium for Health and Military Performance (CHAMP) – September 2011 – Bethesda
- Experts from the DOD, ACSM, AMSSM, NCAA, ASH and others
- Charge
  - Training recommendations to mitigate risk of strenuous exercise with SCT
  - Develop to identify, treat, and RTDP for nonfatal collapse

Exercise Collapse Associated with SCT (ECAST) – Setting

- Repeated high intensity exercise w/ little or no rest in between
  - Serial sprints
  - Fast-tempo multi-station drills
- Near maximal exertion – “all out / heroic” effort sustained for several minutes
- Early in training (deconditioned)
- Hot temperatures
- High altitudes

ECAST – Clinical features

- Athlete reports muscle pain AND weakness
- Muscles look and feel normal to examiner
  - Differs from heat cramps – no locked up muscles
- Athlete slumps to ground but typically can talk at first
  - Differs from cardiac arrest
- Rapid tachypnea from lactic acidosis – but moving air well
  - Differs from acute asthma attack
- Rectal temp <103
  - Differs from Heat stroke
**ECAST Treatment – “Chain of Survival”**

- Athlete collapses and unresponsive
  - EMS/CPR/AED/Tx for shock/Vs incl temp and cool if appropriate/IV access/Oxygen/ED transport

- Athlete collapses and responsive
  - Brief Hx/Vs incl temp and cool if appropriate/Attach AED/IV access/Oxygen
  - If no immed improvement – Transport to ED
  - If immediate improvement – Rest/Rehydrate and consult with physician for graded RTP

**Likely Pathophysiology of SCD in SCT**

- Widespread intramuscular and intravascular sickling leads to vascular occlusion, endothelial damage and impaired blood flow to muscles.
- Ischemic rhabdomyolysis
- Severe Hyperkalemia/acidosis
- Lethal cardiac arrhythmia
- May also lead to DIC

**ECAST – PREVENTION**

- Appropriate progression in exercise intensity
  - NCAA recommends that athletes with SCT should “set their own pace”

- Avoid repeated high intensity drills with limited to no recovery

- Avoid some timed performance tests
ECAST – PREVENTION

- Prevent heat illness
  - Strict adherence to heat acclimatization
  - Liberal hydration
  - Allow “heat dumping” – A/c, shade, removal of layers
  - Do not exercise when ill
  - Provide supplemental oxygen when needed
- Identify SCT status

References