Sickle-Cell Management

Objectives:
After reading this lecture the participant should be able to:

1. Explain the basic disease process of Sickle Cell Anemia
2. Have an understanding of the precipitants of sickle cell emergencies
3. Recognize life and limb threatening emergencies in the sickle cell patient
4. List effective methods of treating sickle cell patients in the field as well as in the hospital

Gaining perspective on the spectrum of sickle cell anemia:
Question: What do all these real life presentations have in common?

a) A 35 year old man who comes in complaining of chronic back pain
b) A 8 year old boy with tachycardia, thready pulses and very difficult to arouse
c) A 45 year old man who presents with shortness of breath, chest pain and tachycardia
d) An 18 year old male who complains of new onset of right hip pain
e) A 27 year old male who complains of a painful erection lasting all day

Answer:
These are all common or life threatening emergencies directly related to sickle cell anemia

What is Sickle Cell Disease?

- Sickle cell disease is a disease of the red blood cells
- Red cells function to carry and provide oxygen to the body
- Normal red blood cells are shaped like inner tubes and are extremely flexible in order to fit through the microscopic capillaries which connect arteries to veins
- In short, sickle cell disease is a process that makes the red blood cells too stiff to fit through the capillaries causing them to block blood flow to vitals organs and extremities

References
What Causes Sickle Cell Anemia?

- Hemoglobin is the actual molecule that transports oxygen in the red blood cell
- Sickle cell anemia is a genetically acquired abnormality in the molecule hemoglobin
- The disease is a recessive gene meaning you have to get one sickle gene from each parent to have the disease
- A normal hemoglobin molecule is referred to as hemoglobin A(adult)-Hb A
- A genetic mutation in the hemoglobin molecule exchanges only a tiny part of the entire molecule and creates hemoglobin S (sickle) or Hb S
- This small change is enough to affect the whole function of the hemoglobin molecule

References

Epidemiology: Who Gets Sickle Cell Anemia

- 70-80,000 patients in the U.S.
- Most common inherited blood condition in America
- People who get Sickle Cell Anemia (SSA) are descendants of people who come from parts of the world where malaria is common (Africa and South East Asia)
- The sickle mutation an adaptive benefit to those exposed to malaria
- Red blood cells with the HB S mutation are resistant to the often deadly disease of malaria

References

What are the physiologic changes in the sickle cell disease?

- When exposed to adverse conditions the hemoglobin molecules form a sort of polymer and crystallize into inflexible crescent or sickle shape
- The sickle shape makes it difficult for the blood to pass through the microscopic capillaries
- The sickled blood cells block passage of other blood cells and deprives tissue of oxygen and nutrients
- In addition, the SC RBC does not bind and carry oxygen very well
- The lack of oxygen creates a cascading cycle of sickling, blockage of blood flow and inadequate oxygen delivery
- The lack of oxygen causes tissue/bone ischemia which leads to the pain the patients feel
References

Factors that cause sickling
1. Dehydration: even a mild amount dehydration can cause sickling
2. Cold Weather
3. Hypoxia: Tissue hypoxia created from even a short sprint can lead to occlusion
4. High altitude: this is related to decreased pressure of oxygen at altitude
5. Acidosis from any cause
6. Infections

Pathophysiology
- Once the hemoglobin has polymerized and changed the form of the red blood cell to the sickle shape major changes in physiology take place
- The following are the physiologic changes that occur:
  1. Flow of oxygen and nutrients in RBC's through small capillaries is slowed down because of congestion
  2. The sickled cells are destroyed at a rapid rate because of their inflexibility
- Normal RBC's have a life span of 90-120 days
- Sickled RBC's have a life span of 10-20 days
- The bone marrow increases production of RBC's to replace those destroyed
- Eventually the rate of destruction is so great that the body cannot keep up
- The red cell count or hematocrit drops
- Thus the name sickle cell anemia

The Life Cycle of a sickle cell patient
- All newborn children have a different type of hemoglobin than adults
- This hemoglobin is residual and adapted to living in the uterus
- This hemoglobin is referred to as hemoglobin F
- At the age of about 6 months adult hemoglobin is manufactured
- The adult hemoglobin is the one that contains the SC gene mutation
- Thus, at the age of six months the infant is prone to all the disease processes of SC
- Some patients with sickle cell anemia have persistent fetal hemoglobin in their RBC’s
- Those with persistently elevated Hemoglobin F levels tend to have minor symptoms
Emergencies in Sickle cell anemia can be broken up into Clinical presentations

- Constitutional
  - Impaired growth
  - Increased susceptibility to infection
- Vasoocclusive
  - Micro-infarcts
  - Macro-infarcts
  - Sequestration (RBC trapping) Crisis
- Anemia
  - Severe hemolysis
  - Aplastic crisis

Constitutional Symptoms: Impaired Growth

- Pt's with SC often have impaired growth and physical development
- They tend to be smaller than their non-SC siblings
- This also leads to the observation that they preserve a youthful look longer
- Recurrent infections and marked increase in RBC marrow products steal nutrients from growing tissues and cells
- The body prioritizes marrow production over height and weight growth
- Thus the impaired growth

Increased Susceptibility to infection

- The normal spleen is an important part of the immune system
- It serves as a filter for the blood system
- Importantly the spleen helps to destroy certain types of bacteria such as Strep. Pneumonia and neisseria (both common agents in meningitis and sepsis)
- The spleen also destroys old or abnormally shaped blood cells
- The spleen senses that the sickled cells are abnormal and traps or sequesters them for destruction
- As a result of chronic vascular stasis and red blood cell congestion in the spleen becomes enlarged in childhood
- Recurrent ischemia from poor blood flow leads to multiple infarctions in the spleen
- The spleen is eventually reduced to a small functionless bit of lymph tissue
• Thus patients with sickle cell disease are functionally without a spleen
• This makes them immune compromised and susceptible to sepsis from Streptococcus Pneumonia or Neisseria species.

References

Microinfarcts and Vasooocclusive (trapping of RBC's in small blood vessels) crisis
• As mentioned before these are caused by trapped sickled cells
• These trapped cells cause small local areas of cell death (infarcts)
• These tiny infarcts are responsible for the pain
• These areas of pain should NOT be tender or inhibit range of motion
• Pain crisis is the major reason for ER visits by SC
• 1/3 of pain crisis are caused by viral or bacterial infection
• Thus, an important part of history is recent infection (even a cold)

References

Priapism (a painful prolonged erection)
• Is caused by RBC trapping in the penis.
• Is considered a Vasooocclusive crisis
• If the priapism is prolonged it can lead to impotence or necrosis of the penis
• Urgent and aggressive hydration, treatment with intravenous beta agonists (terbutaline) and surgical decompression are necessary to treat this emergency

References

Macro-Infarcts-When large amounts of Sickled RBC form clots
• SC patients are susceptible to strokes, even in childhood
• SC patients have a 25% lifetime risk of cerebral vascular accidents
• These strokes often present with hemiparesis
• They often improve from these ischemic strokes
• For an unknown reason SC patients are also at increased risk for having subarachnoid bleeds
• For this reason any SC patient complaining of sudden onset of severe headache should raise concerns about a intracranial bleed.
• The kidneys in SC patients are not spared from damage.
• Infarcts in the kidneys do not allow them to reabsorb water normally
• This leads to an increasing incidence of dehydration and more sickling

References

Acute Chest Syndrome

• Caused by a clot that forms in the lungs
• This clot then becomes infected
• Presents with fever, pleuritic (sharp) chest pain
• Patients are hypoxic and with increased respiratory rate
• Clot and infection are not always seen by Chest X-ray
• Sometimes a nuclear lung scan can be diagnostically helpful (V/Q scan)
• Patients are treated with antibiotics
• Occurs in 30% of SC pt's
• Accounts for 15% of deaths over ten years of age

References

Severe hemolysis and Sequestration Crisis

• Severe Hemolysis and Sequestration are two emergencies that may present with near shock or shock
• Both of them represent a very large and rapid drop of circulating red cells
• Sequestration Crisis is when all of the red cells are trapped inside of the spleen
• This is because the spleen sees the sickled cells as abnormal
• Sequestration crisis is usually seen in children under 5 years old
• When a large proportion of the SC patient’s cells become sickled massive destruction (hemolysis) can occur
• This causes a rapid drop in the amount of circulating cells
• These patients will present with tachycardia and sometimes hypotension from low circulating blood volume
• They may note an increase in the yellowness of their eyes (icterus) or skin jaundice
• These patients can die very rapidly if not managed properly
Aplastic Crisis

- Aplastic crisis, or complete bone marrow production failure is a life threatening emergency
- Frequently occurs after a viral illness
- Infection suppresses bone marrow production temporarily
- The normal destruction of sickled cells combined with no new production leads to a rapid fall in RBC levels and hematocrit.
- Patients are tachycardic and sometimes hypotensive
- These patients can also die quickly if the process is not recognized

Clinical Pearls for Evaluation of the sickle cell patient

Important Elements of History

- Triggers:
  1. Recent Infection (even a mild cold virus),
  2. Fever
  3. Poor oral intake
  4. Exposure to Cold
- Weakness or dizziness when standing also known as orthostatic hypotension means that the patient may be missing circulating red blood cells.
- Chest Pain
  o Sharp: Think acute chest syndrome, pneumonia or P.E (pulmonary embolus).
  o Dull: does it sound cardiac
- Cough- Productive ➔ More Likely URI (upper respiratory infection) or Pneumonia
- Non Productive ➔ P.E or acute chest syndrome
- Abdominal Pain: Important key is: is it THEIR USUAL PAIN or different
- Joint Pain: Is it different joint pain, is there fever--if yes think joint infection

Initial evaluation

As always the ABC need to be considered as well as your local protocols

- Sickle Cells anemia typically does not present with problems related to airway
- Breathing problems can be caused by acute chest syndrome
- Tachycardia and bradycardia can be due to dehydration, loss of circulating red cells (sequestration, hemolysis) or sepsis
- Fever may be due local or systemic (sepsis) infections
Physical Exam

- Neuro: limb weakness, vision changes, indicate thrombotic (clot) stroke
- Decreased mental status or asymmetric pupils may indicate an intracranial bleed such as subarachnoid hemorrhage
- Skin: increased jaundice may indicate rapid destruction of red cells
- Eyes: yellow eyes (icterus) may also be a sign of increased RBC destruction
- Lungs: listen for signs of pneumonia (rhonchi or decreased aeration)
- CV: Tachycardia and weak pulse may indicate shock
- Abdomen: enlarged liver or spleen may indicate massive trapping of RBC's
- Right Upper quadrant pain may indicate symptomatic cholelithiasis (trapped gallstones) as SC pt's are prone to formation of gallstones
- Musculoskeletal: Severe Pain with moving a limb suggests severe infection in the joint (osteomyelitis)

Treatment

- Establish IV and give fluids
- This decreases the viscosity and concentration of the sickled cells
- Helps to reverse sickling process
- Eventually helps to alleviate pain
- Absolutely indicated in the patient you suspect shock from sequestration, hemolysis or sepsis.

Oxygen

- Recall that SC RBC's do not hold/bind oxygen very well
- This causes decreased oxygen delivery to the peripheral tissues
- Raise the available oxygen level by saturating available hemoglobin and plasma with oxygen
- Can be given either by facemask or nasal canula
- RBC's are less prone to sickling in environments with adequate oxygen
- It is easy to do!

Exposure

- Cold increases the sickling rate of red blood cells
- Pt's in cold environment require transport in a warm ambulance with adequate blankets to cover extremities
- Warmed IV fluids are helpful if available

References
2. Stoy, W.A. Bleeding and Shock. Mosby's EMT- Basic Textbook, Chapter 25
A note on sickle cell anemia

- A very difficult disease to deal with if you are the patient
- Continuous pain crisis caused from infarction of tissue makes pain an every day reality
- The severity of their sickle cell disease determines the amount of tissue infarctions and complications they experience
- SC patients are dependent and require pain medicine to live as normal of life as possible with this disabling disease
- Care providers should be empathetic to the amount and frequency of their pain and other related complications

References

Summary of pre-hospital issues:

1. Care is primarily supportive.
2. Begin high flow oxygen to saturate hemoglobin.
3. Start IV fluids with isotonic crystalloid solution. Hydration will help the vasoocclusive process.
4. IV access may be different especially in older patients, as these patients have had recumbent hospitalizations and IV’s.
5. Pain management should begin as soon as possible.
6. Consult local protocol and medical control.
7. Transport the patient.