Perioperative Management of Patients with Sickle Cell Disease

November 29th, 2012

David Vivas, MD
Case - History

• CC: RLQ pain

• HPI: 14 y/o female with h/o Hg SC presented to ED with 4 days h/o abdominal pain, initially diffuse but later locating to RLQ, associated with nausea, vomiting x 4 (nonbilious/nonbloody) and back pain. Patient denied fevers, diarrhea.
Case - History

- **PMH:** SCD, multiple hospital admissions for pain crises in Jamaica

- **PSH:** None

- **SHx:** Patient recently emigrated to the US from Jamaica (2 weeks prior to presentation)

- **FHx:** Father, mother, brother with SCD

- **NKDA**
Case - PE

- VS: T 102.0, HR: 125, BP: 111/69, RR: 30, SaO2: 99%
- AAOx3, In mod. distress
- Scleral icterus
- CV: RRR, tachycardic
- Chest: CTA, b/l
- Abdomen: Mod. distension, + BS, soft, diffusely TTP. + guarding on RLQ
- Ext: No edema
Labs

- CBC: 32.4>11.7/33.8<226  Ret: 2.41
- BMP: 137/3.3/101/24/9/0.65<107
- LFT: 15/13/7.2/4.4/85/4.9

Abdominal US

- Splenomegaly, mild enlargement of the liver, normal appearing gall bladder
Case

- Patient was admitted to Pediatrics
  - IV fluids
  - IV Abx
  - Pain control
- Pediatric Surgery Consult:
  - Recommend CT abdomen/pelvis IV/PO contrast
Case – CT scan

- Acute appendicitis, suspected perforation. No discrete abscess

- Moderate splenomegaly. No splenic lesions
F/u Labs

• CBC: 13.7>8.8/24.6<162  Ret 1.15

• LFT: 4/27/5.6/3.3/70/8.3
Pediatric Hematology Consultation:

- Hb SC patient with unusually difficult course in Jamaica (No ACS reported) with urgent need for laparotomy
- Concern for some sequestration due to drop in Hb, tender liver and spleen, rising Tbili
Case – Hematology Evaluation

- Pediatric Heme Consultation Recommendations:
  - Exchange would be invasive and delay surgery
  - Transfuse 2 units RBC’s over 2-3 hrs
  - Avoid over-hydration
  - Aggressive pulmonary toilet, IS
  - PICU admission
Case – Operative Course

- 2 units of PRBC’s were ordered

- Patient was taken to OR for emergent appendectomy after 1st unit PRBC was being administered
Case – Operative Course

- Open Appendectomy
- 200 ml pus drained upon entering peritoneal cavity
- Appendix was necrotic, covered with fibrin, perforated
- Wound was left open
Case – Post op Course

• Patient was extubated and transferred to PICU
  • NGT
  • IV Abx (meropenem)
  • Incentive spirometry
  • Pain control
Case – Post op Course

POD # 1- 6 patient improving

• Pain well controlled
• Febrile on POD # 1
• Low grade fever on POD # 3
• Afebrile after POD # 3
• Bowel function returned POD # 2
• Diet advanced to regular by POD # 4
• Wound was closed on POD # 4 (delayed primary closure)
Case – Post op Course

• POD # 7 patient was transferred to regular pediatric floor
• POD # 8 – 10 WBC noted to rise from 6.7 to 13.4
• POD # 10 surgical wound was opened
• POD # 11
  • WBC 13.8
  • CT Abd/Pel: 3.3 x 3.3 cm abscess in LLQ anterior to psoas muscle
Case – Post op Course

- Patient underwent IR drainage of intra-abdominal collection.
- By POD #18 patient had finished course of Abx and remained afebrile, tolerating a diet, with a clean surgical wound. WBC remained WNL.
- Patient was D/C home on POD #19.
Questions?
1. Background
   1. Basic Science/Genetics
   2. Epidemiology
   3. SC Syndromes Overview
   4. Major clinical manifestations

2. Implications for surgical treatment
   1. General Considerations
   2. Management Principles
Sickle Cell Dz: Basic Science

- Hemoglobin is a tetrameric protein consisting of 2 alpha (α) and 2 nonalpha polypeptide chains (ε, γ, β, δ) attached to 4 iron-containing heme complexes.

- Sickle cell anemia is a genetic disorder caused by an autosomal co-dominant single gene defect in the β-globin chain of HbA, which produces HbS.

- HbS is formed by the substitution of glutamic acid (negatively charged) by valine (nonpolar) in position 6 of the β-globin chain of hemoglobin.
This has 2 interrelated effects:

- The hemoglobin S molecule is unstable and degrades more rapidly

- The deoxygenated form is insoluble and precipitates out of solution in the cytosol
HbS becomes insoluble at O2 tension in venous range 5-5.5 kPa

Upon deoxygenation, HbS tends to crystallize and precipitate

The precipitation and polymerization of hemoglobin deforms the cell

The distortions include the characteristic “sickle” shape that gives the disease its name
Sickle Cell Dz: Basic Science

A Normal red blood cells

1. Normal red blood cell (RBC)
2. RBCs flow freely within blood vessel

B Abnormal, sickled, red blood cells (sickle cells)

1. Sickle cells blocking blood flow
2. Sticky sickle cells
3. Cross-section of sickle cell
   - Abnormal hemoglobin form strands that cause sickle shape
• The term sickle cell anemia (SCA) refers to HbSS disease

• SCA occurs if HbS is inherited from both parents (HbSS genotype)
Other forms of sickle cell disease may occur if HbS is inherited from one parent and another abnormal hemoglobin, is inherited from the other parent:

- Hemoglobin C (HbSC)
- β-thalassemia (HbSβ-thalassemia)
Hemoglobin C is a β-chain variant, most common in people of West Africa.

The combination with another mutation (ex HbSC disease) produces symptoms of sickle cell disease.

The term sickle cell disease (SCD) refers to all of the genotypes (HbSS, HbSC, HbSβ-thalassemia).
Epidemiology

- SCD is the most common inherited blood disorder in the United States, occurring in 1 : 2,647 births
- SCA accounts for 60% to 70% of SCD in the U.S.
- SCD occurs in 1 in every 500 African Americans
- About 8% of African Americans are carriers SCD
In sickle cell trait (SCT), there is inheritance of one Hb S allele (Hb AS)

25% to 30% of neonates in western Africa are carriers of the SCT

Approximately 8% of African Americans have SCT
Sickle cell disease is characterized clinically by a shortened life span.

- Median age at death is approximately 42 years for men and 48 years for women.

- Affected patients characteristically are asymptomatic until approximately 4 to 6 months of age.
Sickle Cell Syndromes

Overview

• Disease manifestations are most severe in patients with homozygous Hb SS

• SCT (Hb AS) is often asymptomatic but sickling can occur at very low oxygen tensions (below 3 kPa)
Anemia

- Chronic, reasonably well-compensated hemolytic anemia, reticulocytosis
- Erythrocytes are destroyed randomly, with a mean life span of 17 d (normal: 110 to 120 d)

Acute severe anemia:

- Splenic sequestration crisis
- Aplastic crisis
- Hyperhemolytic crisis
Sickle Cell Syndromes
Major Clinical Manifestations

Acute painful episodes (sickle cell crisis)

- Most common
- May be precipitated by weather conditions, dehydration, infection, stress, exercise, alcohol consumption, obstructive sleep apnea
- Up to half of episodes have no identifiable cause
- Can affect any area of the body, with the back, chest, extremities, and abdomen being most commonly affected
- Can range from trivial to excruciating
Acute chest syndrome (ACS)

- Most common form of acute pulmonary disease
- Second most common cause of hospitalization in SCD and the leading cause of death
- Defined as the new appearance of an infiltrate with pulmonary symptoms in a patient with SCD
Sickle Cell Syndromes
Major Clinical Manifestations

Acute chest syndrome (ACS)

• Fever, chest pain, and cough
• The etiology of ACS is multi-factorial
• ACS is a frequent postoperative problem
• Typically detected 2–3 days postoperatively and last for 8 days
Sickle Cell Syndromes
Major Clinical Manifestations

Hyposplenism or functional asplenia
Infections
Osteomyelitis
Cerebrovascular events
Osteonecrosis (also called avascular necrosis)
Renal complications
• Renal failure in up to 18 percent of patients
Hepatobiliary complications

- Acute hepatic ischemia, benign cholestasis, hepatic sequestration crisis, acute and chronic cholelithiasis secondary to pigmented gallstones

Priapism
SCD patients undergo certain procedures at a higher rate than the general population:

- Cholecystectomy
- Splenectomy
- Femoral head reconstruction due to avascular necrosis
- Joint replacement
- Craniotomy due to sub-arachnoid hemorrhage
• Surgery requiring GA may increase risk of perioperative sickling and vaso-occlusive events in SCD

• Sickle cell crises may be precipitated by:
  • Surgical trauma and inflammatory response to tissue injury
  • Hypoxia associated with ventilatory depression (e.g. pain, opioids etc)
  • Dehydration induced by reduced oral fluid intake
Sickling Triggers

- Hypoxemia
- Acidosis
- Hypothermia
- Dehydration
- Low perfusion states
- Infections
- The perioperative period is critical for the patient with SCD

- Factors increasing perioperative risk specifically for SCD patients include:
  - Expected decrease in PaO₂
  - Pre-operative opioid tolerance
  - Fluid compartmental shifts
  - Disruption in thermoregulation
Perioperative complications in SCD

- Painful crisis
- Acute chest syndrome (ACS)
- Hyperhemolytic crisis
- Aplastic crisis
- Renal complications
Perioperative complications in SCD

Incidence of acute sickle cell exacerbations (n=1079 procedures)

- 0% for tonsillectomy
- 2.9% for hip surgery
- 3.9% for myringotomoy
- 7.8% for intra-abdominal nonobstetric surgery
- 16.9% for cesarean section and hysterectomy
- 18.6% for dilation and curettage
• Reversal of the sickling process is difficult

• Focus is on prevention of vaso-occlusive crisis
Sickle Cell and Surgery
Management Principles

1. Pre-operative assessment

2. Perioperative strategies
   1. Hydration
   2. Pain Control
   3. Oxygenation/Ventilation
   4. Temperature regulation
   5. Infection Control
   6. Peri-operative Blood Transfusions
Preoperative Assessment and Workup

• Identify the frequency, pattern, and severity of recent sickle exacerbations, and the presence and extent of organ damage

• Hemoglobin level, WBC w/diff, reticulocites, LDH, LFT

• CXR, Pulmonary function tests, ABG

• EKG, or neurologic imaging may be indicated
Hydration

• Dehydration is a recognized cause of sickle cell–related complications
• Patients should be encouraged to drink clear fluids freely until as close to surgery as possible
• Preoperative fasting guidelines have been shortened to allow for oral intake of clear fluid up to 2 hours preoperatively
• There is a lack of evidence to support admission for intravenous hydration preoperatively beyond that appropriate for the surgical procedure and the degree of renal dysfunction
Pain

• In SCD patients pain control is of utmost importance for two reasons
  • Painful crisis is a common complication of SCD that can be brought on as a result of the physiologic stress of surgery
  • Patients with SCD often experience some degree of chronic pain and may be on a regular analgesia regimen before having an operation
Pain continued..

- Increasingly, patients with SCD who experience acute pain crisis are treated with a PCA pump delivery system for opiates.
- It is recommended to use a recognized pain assessment scale, such as the visual analogue scale. Pain should be regularly assessed.
- Remember that patients with SCD may have developed tolerance to some analgesia and may require greater doses than other patients.
Oxygenation

- A decrease in oxygenation as well as V/Q mismatching can increase the risk of pulmonary infarction or infection in patients with SCD, increasing the risk of ACS
- Patients should be well oxygenated before and throughout surgery, and until fully awake
- Respiratory therapy is indicated for all patients undergoing general anesthesia
Oxygenation continued…

- Hyperoxegenation is recommended at induction of anesthesia
- Careful monitoring of perioperative oxygen saturation is crucial
- Decreasing oxygen saturations should be promptly assessed by the physician to detect mucous plugging, evolution of the acute chest syndrome, or pulmonary embolism
Temperature

• Hypothermia can cause vasoconstriction and red blood cell sludging, leading to an increase in capillary transit time and the risk of vaso-occlusion

• During most surgical procedures, patients should be kept warm

• The operative ambient temperature should also be maintained
Infection Control

- Patients with SCD are generally immunocompromised at a young age
- Prevention of infections in perioperative patients with SCD is extremely important because infection is often a precursor to sickle cell complications
- Good hydration, early mobilization, and meticulous hand washing are important and relatively easy to implement
- Prophylactic antibiotics should be commenced intraoperatively and continued until after discharge from the hospital
Preoperative Blood Transfusions

• Erythrocyte transfusion may be indicated:
  • To augment oxygen-carrying capacity
  • To prevent acute exacerbations of sickle cell disease

• Exchange transfusion
  • To lower the level of HbS, usually to around 30%

• Simple transfusion of 1 or 2 units of blood
  • To raise the overall hemoglobin level to approximately 10 g/dL
Preoperative Blood Transfusions

• The case for preoperative transfusion
  • Improving oxygen delivery
  • Reduced whole blood viscosity, reducing the risk of vaso-occlusion

• The case against preoperative blood transfusion focuses on the risks
  • Transmission of bloodborne infectious agents
  • Incidence of red blood cell alloimmunization (8% to 50%) and increases with the number of transfusions
Preoperative Blood Transfusions

• Individualized approach to preoperative blood transfusion:
  • Assess every case individually
  • If absolutely necessary to transfuse
    • Patient understands the risks of blood transfusion
  • Use of leukocyte-depleted blood
Preoperative Blood Transfusions
Individualized approach to preoperative blood transfusion:

- Assess the need for transfusion based on the type of surgery
  - Low, moderate, high risk
  - Length of time of surgery
  - Transfusion history
  - History of sickle cell–related complications
  - General health state of the patient
RCT involving 604 patients compared:

- Aggressive transfusion protocol
  - To reduce the proportion of hemoglobin S to less than 30%
- Conservative transfusion protocol
  - To achieve a hematocrits of 30%

No significant difference in postoperative sickle cell exacerbations

- The group in the aggressive protocol had a higher incidence of transfusion complications such as alloimmunization
- Study suggested that aggressive transfusion protocols to dilute hemoglobin S were no more effective than the correction of anemia in preventing complications

Cochrane Cystic Fibrosis and Genetic Disorders Group Trials
(Most recent search: 06 October 2011)

• Selection criteria
  • RCT comparing preoperative blood transfusion regimens to different regimens or no transfusion in people with SCD undergoing surgery

Results

• 2 studies were identified
• Total of 920 participants
• First study compared an aggressive transfusion regimen to a conservative transfusion regimen in 604 elective operations in people with sickle cell disease
• The conservative regimen was found to be as effective as the aggressive regimen in preventing perioperative complications, and was associated with fewer transfusion related adverse events
Sickle Cell and Surgery
Blood Transfusions

• Results
  • The second study compared a preoperative transfusion group to a group receiving standard care, and did not show an advantage to preoperative transfusion

• Conclusions
  • Conservative therapy appears to be as effective as aggressive therapy in preparation for surgery
  • Further research is needed to examine the optimal regimen for different surgical types, and to address whether preoperative transfusion is needed in all surgical situations
In Summary

• Sickle Cell Disease is a common genetic disorder in the US especially among African-Americans

• SCD has multiple major clinical manifestations that can impact the surgical patient, both by increasing the need for specific surgeries, and by increasing the overall risk for all surgeries

• In the SCD surgical patient, specific attention should be paid to select clinical parameters, such as peri-operative oxygenation, infection control, and Hb levels, to most effectively reduce peri-operative risk
References

Acute chest syndrome

a. Is a major cause of death in sickle cell patients

b. Affects only those sickle cell patients with asthma

c. Is associated with sinus surgery

d. Occurs after a blood transfusion
Question 1

Acute chest syndrome

a. Is a major cause of death in sickle cell patients
b. Affects only those sickle cell patients with asthma
c. Is associated with sinus surgery
d. Occurs after a blood transfusion
Individuals with sickle cell disease require a daily regimen of penicillin because:

• a. They are at risk for infection from encapsulated bacterium
• b. They are at an increased risk for bacterial endocarditis
• c. They are at increased risk for viral infections
• d. Penicillin reduces the incidence of renal dysfunction
Individuals with sickle cell disease require a daily regimen of penicillin because:

• a. They are at risk for infection from encapsulated bacterium
• b. They are at an increased risk for bacterial endocarditis
• c. They are at increased risk for viral infections
• d. Penicillin reduces the incidence of renal dysfunction
The most severe sequelae from a sickle cell crisis is:

A. Acute chest syndrome, osteomyelitis, cholecystitis
B. Cerebrovascular accident, nephrocalcinosis, osteomyelitis
C. Acute chest syndrome, cerebrovascular accident, priapism
D. Acute chest syndrome, cerebrovascular accident, cholelithiasis
Question 3

- The most severe sequelae from a sickle cell crisis is:
  - A. Acute chest syndrome, osteomyelitis, cholecystitis
  - B. Cerebrovascular accident, nephrocalcinosis, osteomyelitis
  - C. Acute chest syndrome, cerebrovascular accident, priapism
  - D. Acute chest syndrome, cerebrovascular accident, cholelithiasis