Jennifer Krauland, DO
Internal Medicine/Pediatrics PGY 3
Grand Rounds September 24, 2014

CASE OF A 14 MONTH OLD WITH SICKLE CELL AND ACUTE SPLENIC SEQUESTRATION

Objectives

- Case presentation
- Brief overview of Sickle cell disease
- Identification and management of acute splenic sequestration
- Management of severe anemia
- Identify and manage DIC

CASE PRESENTATION

HPI

- 14 month old female presented to an outside hospital after “seizure like activity”. Patient was brought in by parents and said that she made a strange face then was stiff and making jerking motions in dad’s arms and then became limp.
- Parents stated that she had had a fever of 101 that day with vomiting, rhinorrhea and decreased PO intake

History

- PMHx: HbSS (baseline Hgb 7), recently treated for scabies
- Surgical Hx: None
- Meds: Folic acid 1mg daily, Pen VK 125mg BID
- Allergies: Augmentin, causes rash
- FamHx: siblings with sickle cell trait

Outside hospital exam

- Records indicate that she arrived unresponsive, pale, tachypneic with agonal respirations and rigid abdomen
- Vitals on admission: HR 168, RR 64, Temp 98.1
- BP throughout her time at the outside hospital 97-109/32-38

OSH initial labs

- VBG: pH 6.5, pCO2 22.1, pO2 51.7, HCO3 1.7
- WBC 34.5, Hgb 1.5, Hct 4.6, plt 57K
- Na 148, K 7.7, Cl 104, CO2 <5, BUN 18, Cr 1.3, glucose 187, Ca 9.7

- She was given a 20cc/kg bolus, intubated and placed on a vent,
- Transfused **2 units** of PRBCs (approx 50ml/kg over 2 hours), and given a dose of solumedrol.
- Given kayexalate, albuterol, calcium chloride, insulin/D25 for the hyperkalemia.
- Was also given Rocephin 50mg/kg
- Patient promptly transferred to CHNOLA PICU

Arrival to CHNOLA PICU

- Physical exam
  - Vitals: BP 133/62, pulse 176, RR 67, pulse ox 95% on FiO2 100%, temp 102.4, weight 10.1 kg
  - Gen: agitated and combative
  - HEENT: intubated, **ETT with pink secretions, NGT with dark/frank blood**, TM clear
  - CV: **tachycardia**
  - Resp: coarse breath sounds bilaterally with **inspiratory stridor due to air leak, + retractions**
  - Abd: absent bowel sounds, **spleen palpable with tip felt in pelvis, hepatomegaly**
  - Ext: right hand swelling, dark purple in color, **cap refill >3-4 secs**, pulses 2+

CHNOLA admission labs

- Hgb 17.9
- Hct 52
- Platelets 22K
- PT 22
- INR 1.98
- PTT 44
- Fibrinogen 141
- D. dimer >20
- pH 7.16
- pCO2 46
- pO2 45
- Na 144
- K 4.1
- Cl 113
- CO2 20
- BUN 25
- Cr 0.4
- Glucose 279
- Ca 7.5
- Phos 4.9
- Mag 2.2
- AST >1000
- ALT 270
- Tbili 1.8

Labs con't

- Viral panel: +rhino/enterovirus
- UA
  - Color brown
  - SG 1.025
  - pH 6
  - LE negative
  - + nitrite
  - 1+ protein
  - 3+ blood
  - 1+ bili
  - 3+ bacteria
  - 0-2 granular casts
- BCx: pending
- UCx: pending

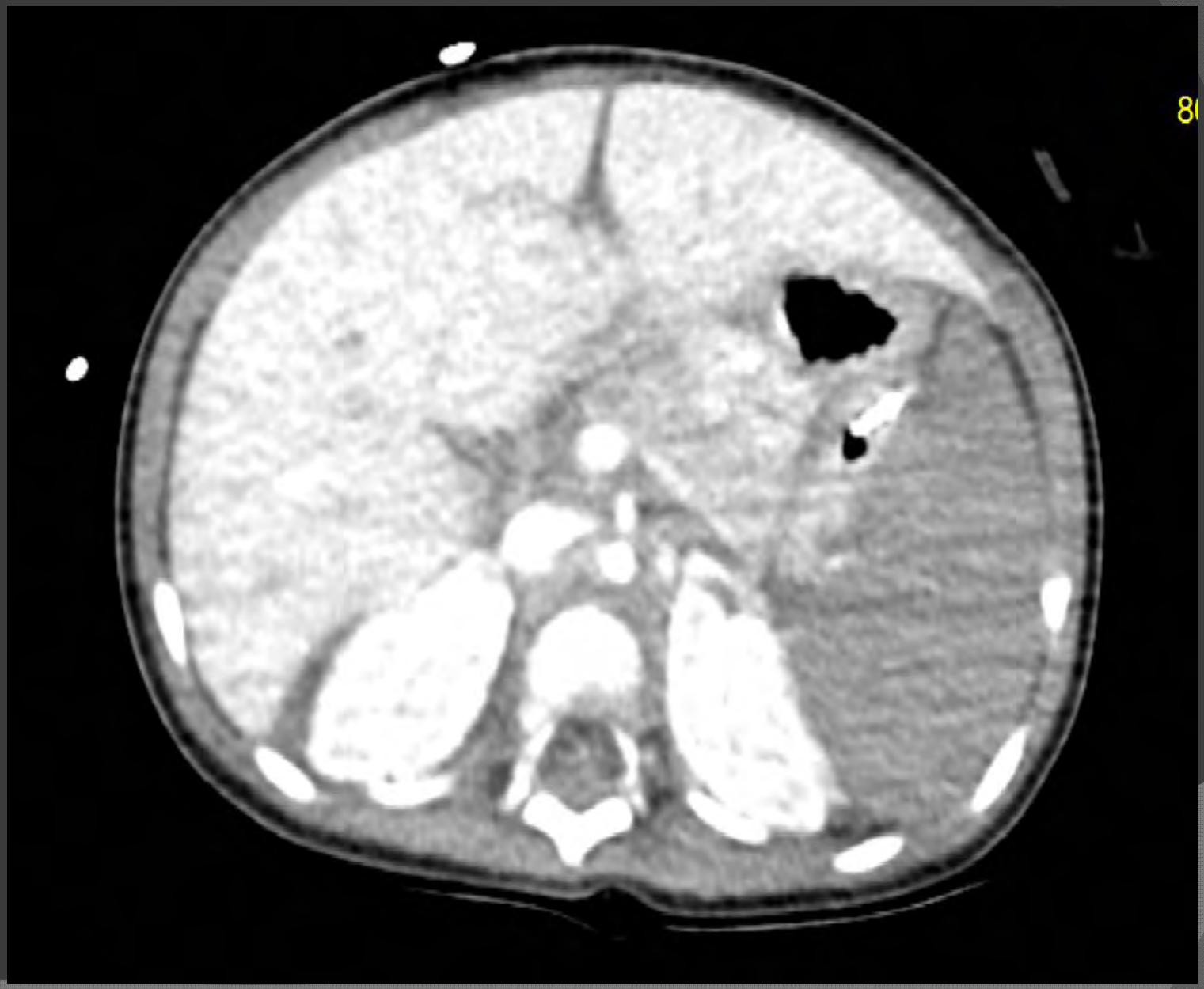
Early hospital course

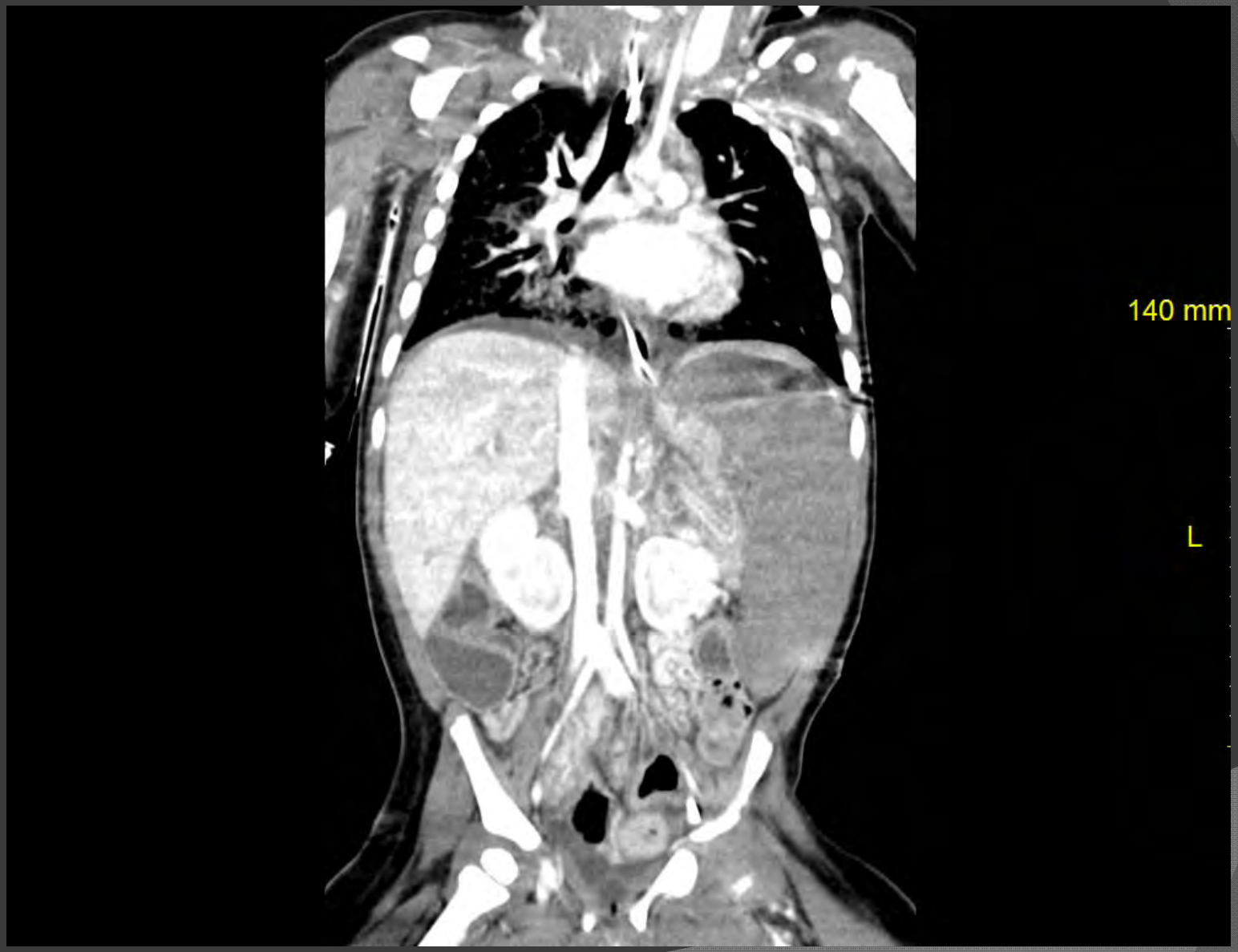
- Patient presented in DIC and was transfused 150ml (15cc/kg) of FFP and then 100ml of platelets (10cc/kg) with a goal platelet count of 50K
- She was started on versed, fentanyl and vecuronium for sedation and to chemically paralyze

- Also started on Rocephin (75mg/kg) and Vancomycin (15mg/kg/dose) for suspected sepsis
- Once stable she was sent for CT of head, chest, abdomen and pelvis

Head CT

- Normal head CT scan of the brain. Inflammatory changes of the paranasal sinuses and mastoids




140 mm
L

CT chest/abd/pelvis

- Severely enlarged hypoperfused spleen. Hepatomegaly with small ascites. Pulmonary edema with small bilateral pleural effusions. Low attenuation fullness at the root of the mesentery likely representing edema

Echo

- Normal cardiac anatomy, no septal defects, no outflow obstructions. Unobstructed aortic arch. No PDA. Normal proximal coronary artery anatomy. Cardiac dimensions within normal limits. Normal RV and LV contractile function. Competent valves. No vegetations or clots. No pericardial effusion

Sickle Cell Disease overview

Sickle Cell Disease

- Autosomal recessive inheritance
- Glutamic acid is susbstituted for valine which allows for the polymerization of hemoglobin when deoxygenated
- Sickled RBCs have a life span of about 20 days and are more rigid than normal RBCs

- The anemia seen with SCD is caused by the destruction of the RBCs
  - Degree of anemia varies patient to patient
  - There is increased bone marrow production of RBCs but it is unable to keep up with the hemolysis
- Vaso-occlusion is a result of the sickled cells blocking blood flow to the tissue as they are unable to move in the vessels

Genotypes

- Sickle cell anemia (Hb SS)
- Sickle Hb SC
- Sickle S beta plus ($S\beta^+$ thalassemia)
- Sickle beta zero ($S\beta^\circ$ thalassemia)

- 65%
- 25%
- 8%
- 2%

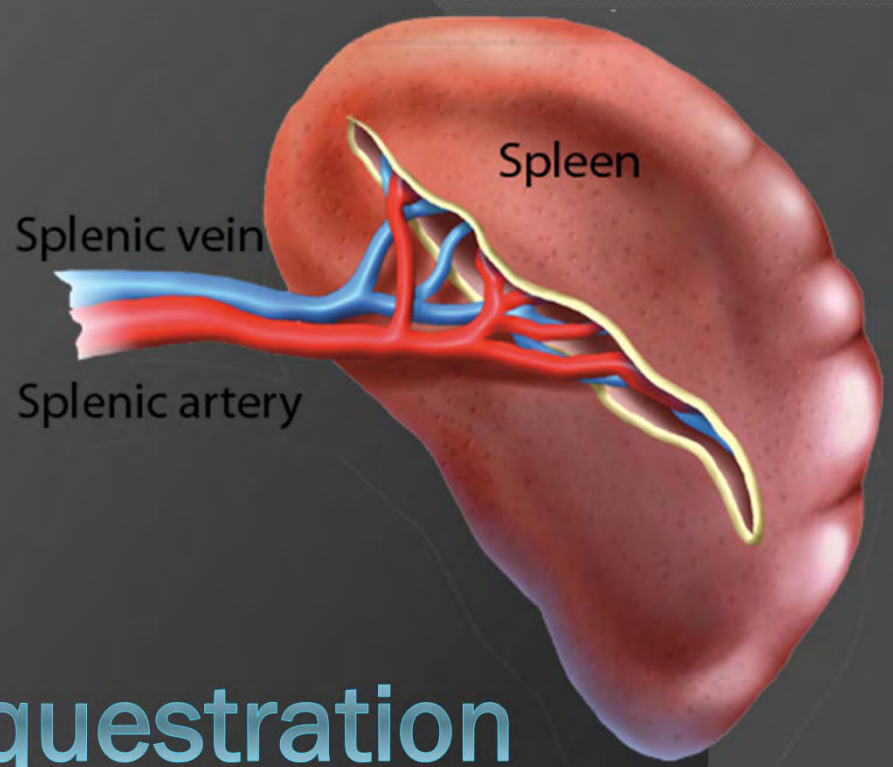
Health Maintenance

- Mandated testing in all 50 states and Washington DC on the newborn screen
- PCN prophylaxis should begin no later than 2 months of age
- Immunizations: routine except that these children should receive 23 valent PPSV at 2 and 5 years of age

SCD emergencies…

- Fever
- Pain crisis
- Acute chest syndrome
- Acute splenic sequestration
- Stroke

Acute splenic sequestration crisis (ASSC)



Some basics

- Vaso-occlusion within the spleen and pooling of RBCs causes a drastic fall in Hgb with persistent reticulocytosis and enlarging spleen
- Associated with 10-15% mortality
- Recurrent in about 50% of survivors

Characterized by:

- Splenic enlargement
- Drop in Hgb of at least 2 grams from baseline
- Thrombocytopenia
- Reticulocytosis

Signs and symptoms

- Weakness
- Pallor
- Tachycardia
- Tachypnea
- Abdominal swelling and tenderness

- Parents are instructed to examine their child's abdomen to help catch an enlarging spleen early
- Most commonly seen in infancy and early childhood in HbSS
- Those with SC disease tend to have sequestration at an older age
  - Most frequently seen in children from 2-17 years old
  - Overall incidence about 5%

- Most drastic complication is hypovolemic shock
  - Cardiovascular collapse and death can occur within 30 minutes

Acute Treatment

- IV fluids to maintain the vascular volume
- Blood transfusion to treat anemia and allow release of pooled RBCs

Chronic Treatment

- Frequent transfusions every few months to maintain Hgb close to 10
- Splenectomy if indicated, after age 2
  - Should also receive menactra and PSSV23 prior to splenectomy

Management of severe anemia

Severe anemia

- At the outside hospital she presented with a Hgb of 1.5 due to splenic sequestration and was transfused 500ml of blood over 2 hours
  - Her normal entire blood volume is about 600cc

- In general, guidelines support using the gram of hemoglobin as the amount per cc for transfusion when Hgb is this low

- This volume of blood likely led to her volume overload as her Hgb was 17.9 on admission
- The patient actually required phlebotomy of 150cc, with a goal to reduce Hgb to 10

Management of Disseminated intravascular coagulation (DIC)

Our patient

- She presented with
  - PT 22
  - PTT 44
  - INR 1.98
  - Fibrinogen 141
  - D. dimer >20

Some basics

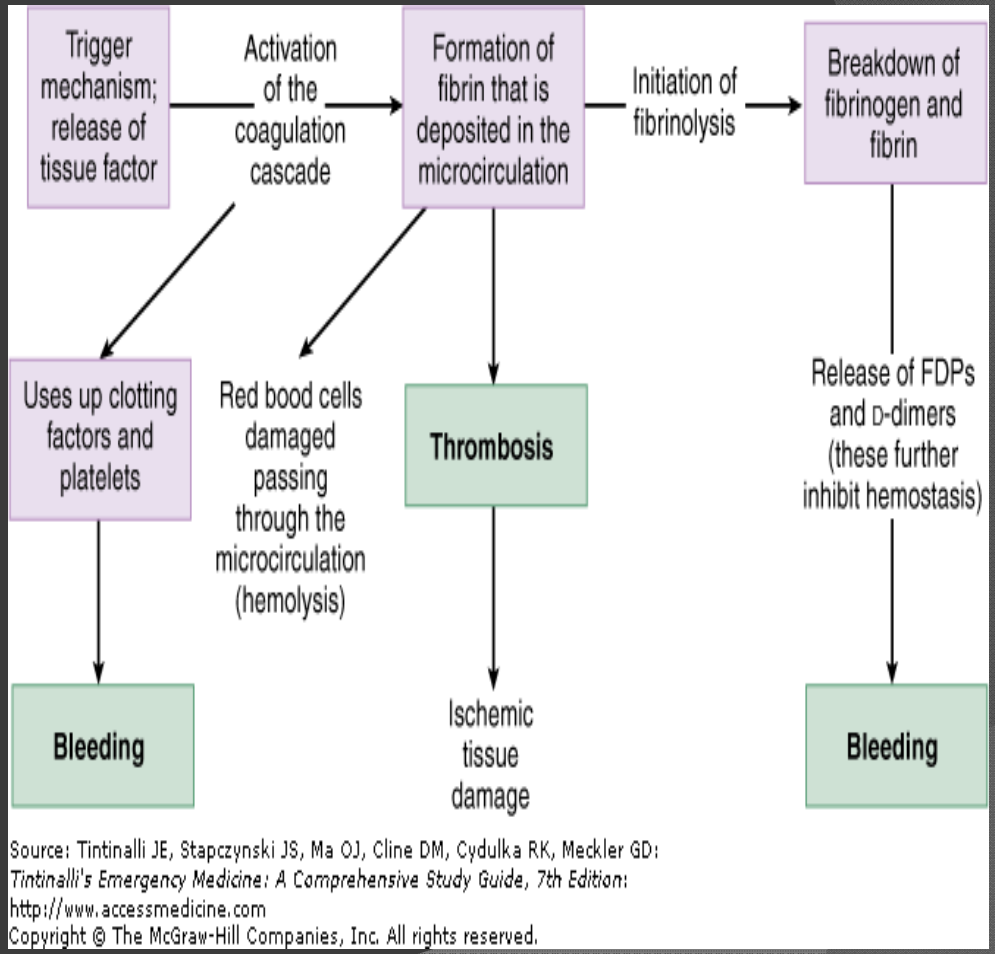
- Systemic activation of pathways leading to and regulating coagulation, which can cause the production of fibrin clots that may cause organ failure with simultaneous consumption of platelets and coagulation factors that may result in bleeding

Causes

- May be caused by a wide array of clinical disorders including sepsis, trauma, liver disease, vascular anomalies, malignancy

Pathway

- Derangement of the fibrinolytic system contributes to intravascular clot formation
- Accelerated fibrinolysis may also cause severe bleeding



Presentation

- Hemorrhage
- Diffuse/localized thrombosis
- AMS
- Hypotension
- Tachycardia
- Friction rub
- ARDS
- Hematemesis
- Azotemia/renal failure
- Acidosis
- Petechiae, purpura
- Wound bleeding

Diagnosis

- Thrombocytopenia
- Elevated FDP
- Increased clotting time (PT and PTT)
- Low fibrinogen
  - ISTH scoring system for overt DIC

DIC scoring system

Laboratory Test	Result	Score
Platelet count (cells/uL)	>100,000 50,000 – 100,000 <50,000	0 1 2
Increase in fibrinogen and fibrin-related markers (eg, FDP's)	None Moderately Increased Strongly increased	0 2 3
Prolonged prothrombin time	<3 3-5.9 >6	0 1 2
Fibrinogen	>1 g/dL < 1 g/dL	0 1

Treatment

- Key to treatment is treating the underlying cause
- Transfusion of blood products should not be based on lab values alone

- Our patient’s DIC score was 6 on admission
- She received FFP on arrival and also received vitamin K 3mg daily for 3 days
- She also required multiple platelet transfusions during her hospital course to maintain her count >50K

Other complications of Sickle cell in our patient

Our patient

- On hospital day 3, a repeat head CT was done that showed multifocal areas of edema that could be related to infection or infarction
- On hospital day 4, she was noted to have seizure like activity and was loaded with keppra and then started on a maintenance dose
- STAT head CT and MRI were done at this time

Head CT

- Improved multifocal areas of edema, compared to the head CT from 1 day prior. Inflammatory fluid in middle ears and mastoids

MRI

- Restricted diffusion in the frontal and parietal occipital regions bilaterally without associated spin echo abnormality or abnormal contrast enhancement. Findings which could be related to hypoxia/ischemia, hypoglycemia and/or status epilepticus

EEG

- Diffuse severe background slowing with loss of regional differentiation. Abnormal sleep forms with loss of K complexes, sleep spindle asymmetry with relatively less well sustained spindles over the left central head region
- These findings are consistent with diffuse bihemispheric cerebral dysfunction as well as suggestive of more pronounced dysfunction over the left parasagital area

Stroke

- One of the leading causes of death in both children and adults with SCD
- More common in HbSS
- Type of stroke varied with age
  - More likely to be ischemic in younger patients
- “Silent infarcts”

Risk factors

- Higher cerebral blood flow in younger children
- Sludging and occlusion of blood vessels that causes ischemia
- Chronic anemia that may reduce cerebrovascular reserve
- Increased adherence of sickle cells to endothelium that may cause further endothelial injury
- Hypercoagulable state

Treatment

- Chronic transfusions to maintain sickled hemoglobin 30% or lower
  - Stroke Prevention Trial in SCD (STOP trial)
    - Iron overload
    - Alloimmunization

Our patient's hospital course

- Extubated after 9 days, had some post extubation stridor that resolved with decadron and weaned to room air
- Treated with both vancomycin and claforan at meningtic doses for full 7 days, all cultures were no growth during stay. She was also placed on acyclovir for concern for HSV but was stopped when the PCR came back negative
- DIC resolved prior to transfer to floor from PICU

- After her seizure on hospital day 4 keppra was added. She did not have any further seizure activity while in patient and was discharged home to continue the keppra.
- She had no lasting neurological deficits from her global hypoxic injury and did not have a true stroke.
- She was continued on her home medications of Pen VK and folic acid

References

- Vichinsky, Elliot. Overview of the clinical manifestations of sickle cell disease. UpToDate. Sept 25, 2013. http://www.uptodate.com/contents/overview-of-the-clinical-manifestations-of-sickle-cell-disease?source=search_result&search=splenic+sequestration&selectedTitle=2%7E150
- McClain, Kenneth and Landaw, Stephen. Approach to the child with an enlarged spleen. UpToDate. Nov 20, 2013. http://www.uptodate.com/contents/approach-to-the-child-with-an-enlarged-spleen?source=search_result&search=splenic+sequestration&selectedTitle=3%7E150
- Management of Sickle Cell Disease. NIH Division of Blood Disease and Resources. 2002. http://www.nhlbi.nih.gov/health/prof/blood/sickle/sc_mngt.pdf
- Thachil, J. and Watson, HG. Guidelines for the Diagnosis and Management of Disseminated Intravascular Coagulation. *British Journal of Haematology*, 145, 24–33. 2009. http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2141.2009.07600.x/pdf
- Wong,, Wendy and Glader, Bertil. Disseminated intravascular coagulation in infants and children. UpToDate. May 2, 2014. http://www.uptodate.com/contents/disseminated-intravascular-coagulation-in-infants-and-children?source=search_result&search=dic&selectedTitle=4%7E150
- Splenic sequestration http://www.ihtc.org/patient/blood-disorders/sickle-cell-disease/splenic-sequestration/
- Splenic Sequestration in Sickle Cell Disease. NEPSSC.org
- Velez, Maria, MD. Heme-onc Emergencies. http://www.medschool.lsuhsc.edu/pediatrics/residents/docs/Emergencies%20PHO%20for%20Interns%202011.pptx
- CDC: sickle cell disease complications and treatment. http://www.cdc.gov/ncbddd/sicklecell/treatments.html
- CDC: sickle cell disease date and statistics: http://www.cdc.gov/ncbddd/sicklecell/data.html
- DIC: Medscape http://emedicine.medscape.com/article/199627-overview
- Management of Sickle Cell Disease, 4th ed. Chapter 18: Acute splenic sequestration
- Lee, Margret T. et al. Stroke Prevention Trial in Sickle Cell Anemia: extended follow-up and final results. *Blood.* Aug 1, 2006: 108(3): 847–852.
- Powell, RW, et al. Acute splenic sequestration crisis in sickle cell disease: early detection and treatment. *Journal Pediatric Surgery* 1992 Feb;27(2):215-8.