Acute Complications of Sickle Cell Disease – Case Study
5 year old girl with Hemoglobin SS, weakness and slurred speech

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Objectives

To discuss the diagnosis and treatment of acute neurologic symptoms in a child with sickle cell disease
5 year old girl with Hemoglobin SS

- **Mother calls clinic:**
  “My daughter has been having R arm and leg pain for the past 2 days. She hasn’t been moving her arm and leg much, but they’ve been hurting. Now her speech is slurred. What should I do?"

- **PMH:** diagnosed with Hemoglobin SS by newborn screen. Baseline Hb 7 g/dl, history of asthma, splenic sequestration, UTI, allergic to cephalosporins, hospitalized for acute chest syndrome one month ago
ED evaluation

Exam:
• Afebrile, alert and oriented
• R extremities: 0/5 strength
• Asymmetric smile
• Hemoglobin 7.5 g/dl

Diagnosis: R hemiparesis, acute stroke

Transfer to PICU
Asymmetric smile

Bells Palsy
Facial nerve lesion

Stroke
Supranuclear lesion

http://www.newhealthadvisor.com/images/1HT07504/bells%20palsy%20vs%20stroke.png
Recent events

• 2 weeks ago: TCD “Normal”
• 1 month ago: Hospitalized for RLL acute chest syndrome, spleen 3 cm. Treated with meropenem, azithromycin, Tamiflu, blood transfusion after hemoglobin fell to 6.1.
• 2 months ago: ED visit for crying, fell down, “looked like she was having a seizure,” “transient RLE weakness.” Head CT was normal. Symptoms resolved, discharged home.
CT scan 2 months ago

**INDICATION:** Status post fall and transient right lower extremity numbness. History of Hgb SS.

**FINDINGS:** There is no acute intracranial hemorrhage, abnormal parenchymal density, mass or mass effect, or abnormal extra-axial fluid collection. Specifically, no definite acute cortical based (large) cerebral artery territory infarct is noted.

**IMPRESSION:** No evidence of acute intracranial abnormality.
Past neurologic evaluation

- 2 years ago: history of seizures
  Brain MRI/MRA normal
**Current Brain MRI/MRA**

1. Acute left anterior cerebral artery/middle cerebral artery territory infarctions
2. Severe attenuation of the upper cervical, petrous, and cavernous internal carotid artery, with reconstitution via right sided and posterior circulation, new when compared with the prior exam. Compatible with a moya-moya type pattern in this patient with sickle cell disease.
Recent TCD

Left:
• Left middle cerebral artery ranges from 86 to 149 cm/sec.
• **Left anterior cerebral artery 60 cm/sec.**
• Distal left internal carotid artery ranges from 124 to 136 cm/sec.
• Left posterior cerebral artery ranges from 22 to 59 cm/sec.

Right:
• Right middle cerebral artery ranges from 130 to 135 cm/sec.
• Right anterior cerebral artery ranges from 125 to 129 cm/sec.
• Distal right internal carotid artery ranges from 77 to 139 cm/sec.
• Right posterior cerebral artery ranges from 28 to 40 cm/sec.
• Basilar artery ranges from 86 to 96 cm/sec.

**IMPRESSION:** Normal transcranial Doppler evaluation according to the STOP criteria.
Stroke in Sickle Cell Disease

- ~ 1/10 children with Hemoglobin SS or Sβ0thal may have a stroke
- Strokes can occur in children as young as 2 -3 years
  - Children < 15 years: ischemic
  - Adolescents and adults: can be hemorrhagic
- Silent (asymptomatic) infarcts may occur in an additional 15 – 20% children
- Symptoms
  - Severe headache, visual problems, weakness (usually unilateral), slurred speech, behavioral changes, seizures
  - Stroke onset can coincide with other complications (ACS, pain episodes, post-op)
- Evaluate and act immediately!!!! Restoring cerebral perfusion preserves neurons.
Cerebral Artery Stenosis

- **Intimal proliferation**
  Excessive thickening of the inner layer of the artery results in narrowing of the lumen


Gee, BE unpublished
Risk factors for stroke in SCD

- High white blood count
- High reticulocytes
- Low hemoglobin
- Low fetal hemoglobin
- HLA-DRB1 locus
- High blood flow in cerebral arteries

- No associations found with hypercoagulability gene polymorphisms
Stroke: Evaluation and Treatment

• Stabilization: A, B, C’s, evaluate for increased ICP
• Brain Imaging
  – CT scan may not show early changes of infarct, but can show hemorrhage, midline shift, cerebral edema
  – MRI is study of choice, if available
• RBC Exchange Transfusion ASAP
  – For any patient with neurologic deficits > 24 hours or if deficits are severe
  – Single volume exchange (70-80 cc/kg) will reduce Hb S to about 30%
• Do not use anti-coagulant or fibrinolytic therapy acutely
Stroke: Follow-up

- Rehab evaluation and intensive therapy as needed
- Neuro-psychologic evaluation of cognitive abilities and behavior
- Chronic transfusion program to prevent recurrent ischemic strokes
- Evaluation for hyper-coagulability
- Minor antigen-matched RBCs to prevent allo-immunization
- Family support
After effects of stroke

• Stroke in young children interrupts normal brain development
• Long-term disabilities
  – problems with movement (gait, fine motor, oral)
  – difficulty learning
  – changes in personality
  – inability to control bowel or bladder
• Hemiparesis can result in musculoskeletal asymmetry: muscle atrophy, shortened extremities, scoliosis
Longterm management

• After a first stroke, a person with SCD has a 50-75% chance of recurrence if no further treatment is given
• Repeated strokes can usually be prevented by red blood cell transfusions every month
• Even with regular transfusions, 20-30% of people may have more strokes
  – Add Aspirin or other anti-coagulants
  – Intensify transfusions
  – Cerebral revascularization
  – Bone marrow transplantation
Advanced cerebrovascular disease

• *Moya-moya* disease
  – Abnormal netlike vessels and transdural anastomoses

• Aneurysms
  – Intimal proliferation
  – Weakening of medial layer of the artery
  – Can eventually lead to rupture of the artery and hemorrhage

• Progressive cerebral artery stenosis despite medical therapy

http://www.chop.edu/conditions-diseases/moyamoya-disease

Aflac Cancer and Blood Disorders Center
Cerebral revascularization

- **EncephaloDuroArterio-Synangiosis (EDAS)**
  - Superficial temporal artery
  - Distal branch of external carotid artery
- **STA sprouts branches into underlying brain.**

Images from Dr. Roger Hudgins MD

Aflac Cancer and Blood Disorders Center
Primary Stroke Prevention

• Cerebral artery blood flow velocities can be measured non-invasively by transcranial doppler (TCD) ultrasound
• Individuals with high TCD velocities are at higher risk for development of stroke
• 90% of strokes in this high risk group can be prevented by a chronic RBC transfusion program (STOP study)
  – However, not everyone with abnormal TCD velocities will go on to have stroke (11/67 = 16%)
• Low TCD velocities in ACA, MCA may reflect stenosis
Changing from Transfusions to HU?

- **SWITCH trial**: children with prior stroke who took hydroxyurea had a higher rate of neurologic events.
- **TWITCH trial**: children with abnormal TCD velocities (but no symptomatic stroke or severe cerebral artery stenosis) who took hydroxyurea had an equivalent rate of returning to high TCD velocities or neurologic events.
- Hydroxyurea is being considered as alternative stroke prevention therapy for children with abnormal TCD velocities who have been on RBC transfusions for > 18 months and are likely to be adherent with therapy.
Act FAST!

Treat stroke as early as possible!
• Educate patients and families about stroke symptoms and to seek medical attention ASAP
Contact information

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