Sickle Avascular Necrosis

Ify Osunkwo, MD, MPH
Assistant Professor
Pediatric Hematology/Oncology/BMT
Emory University

Objectives
Definition, epidemiology
Pathophysiology
Clinical Presentation
diagnostic tools
classification
Public Health burden
Treatment options
Research opportunities

Avascular Necrosis of Femoral Heads
Bilateral Femoral Arthroplasty

What do they have in common?
Avascular Necrosis

Definition

- Osteonecrosis, Aseptic necrosis, ischemic bone necrosis.
- Complete disruption of vascular supply to the articular surfaces and ends of long bones.
- Cellular death (necrosis) of bone due to interruption of the blood supply.
- Osteonecrosis is bone death caused by poor blood supply to the area.

Epidemiology

- Femoral head > shoulder > knees
- Can occur in any bone with blood supply
- Extremely common, starts early
  - 26% by age 10y
  - 48% by 27y
  - >50% prevalence by age 35y
- 4y progression rate of 67%
  - Bilateral in 41-90%
  - Progression to collapse in 3-5y

Pathophysiology

- Obstructed perfusion
- Ischemia -> Necrosis
- Hemolysis -> NO deficit -> Oxidant stress
- Inflammation – Edema -> Increased intra-osseous pressure
- Failure of weight bearing
- Collapse of joint/bone

Mechanisms

Vaso-occlusion

- Genetics
- Geography
- Opiates
- Endocrine
- Diet/nutrition
- Iron overload
- Hydrea therapy
- Weight bearing
- Muscle strength

Risk Factors for AVN

- Male
- High Hgb
- Low Hgb F
- Vitamin D deficiency
- Frequent VOC
- Alpha thal trait

Case I

- 16y Hgb SC,
- Frequent VOC, psychiatric symptoms
- Chronic knee pain
- Severe Headaches
- Unable to stand up straight
- Neurology referral
- Hip AVN
Case I
- 14y Hemoglobin SS, Abnormal TCD, delayed puberty
- Chronic transfusion x 4 years
- Weaned to Hydrea
- Limping, no admits for pain x 4 years
- Home Pain diary showed daily pain after school
- PE = unequal limb length

Case II
- 17y Hemoglobin SS, recurrent ACS
- Early Retinopathy since 7y
- Frequent VOC, gall stones
- Short Stature and delayed growth
- Vitamin D deficiency
- On Hydrea with good response
- Playing on inflatable gym → hip dislocation

Case III
- Clinical presentation
  - Variable
  - X-ray and symptoms don’t always match up
  - Pain in back, hip, knee, ankle or shoulder
  - Reduced Range of Motion at joint
  - Limp, “popping sound”
  - Limb length discrepancy
**FICAT STAGING**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Pain</th>
<th>X-ray image</th>
<th>Magnetic resonance image</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>+</td>
<td>Normal</td>
<td>+</td>
</tr>
<tr>
<td>II</td>
<td>+</td>
<td>Changes on bone trabecula with sclerosis or osteolysis areas</td>
<td>+</td>
</tr>
<tr>
<td>III</td>
<td>+</td>
<td>Osteochondral fracture with sequestrum and flattening of the head</td>
<td>+</td>
</tr>
<tr>
<td>IV</td>
<td>+</td>
<td>Advanced lesions</td>
<td>+</td>
</tr>
</tbody>
</table>

*Table 1 – Classification by Ficat et al. and Swingberg.*

**Avascular Necrosis**

**Consequences**

- Pain
- Depression
- Death
- Poor QOL
- Unequal Limbs
- Loss of Ambulation
- High Cost
- Job Loss
- Polypharmacy

**Compression fractures - fish mouthing**

**Treatment**

- **Physical Therapy**
  - Strengthen limb girdle, joint
  - Flexibility
  - Re-perfusion and healing
- **Non weight bearing**
  - If advanced/collapse
- Core decompression +/- osteotomy
- Inject stem cells
- **Hip replacement**
  - Longevity limited 10-15y, failure
  - Location (poor in shoulder)
  - Muscle imbalance, joint instability, length discrepancy.
Differences
- Older (>50y)
- Caucasian
- Female
- No hemoglobinopathy
- Insurance
- Drinks milk
- Prevention possible

What do they have in common?
- Young (<20y)
- African descent
- Male
- Sickle Cell Disease
- Self pay
- Lactose Intolerance
- No data on effective prevention - YET!

Similarities
- Osteoporosis
- Hip replacement
- Chronic back/limb pain
- Wheelchair confined
- Poly pharmacy pain meds
- High risk of fall, death

Take Home
- AVN is VERY common in SCD
- Occurs as early as age 7y
- May be asymptomatic in early stages
- X-ray may miss early stage
- All SCD genotype are at risk
- No proven prevention

Research directions
- Epidemiology in era of Hydroxyurea
- GWAS to identify gene polymorphisms e.g. BMP
- Mouse models of bone disease
- Perfusion imaging of target bone
- Platelet pore plasma injected into core
- Others

Resources
- www.scinfo.org
- www.cdc.gov/ncbddd/sicklecell
- www.choa.org/sicklecell