



EM CASES SUMMARY

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Episode 68 – Emergency Management of Sickle Cell Disease

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Sickle Cell Pain Crisis

The majority of Sickle Cell Disease patients suffer real pain, but may not look uncomfortable because they have learned to adapt to a lifetime of chronic pain. In the ED, they may appear calm, preoccupied with their handheld device or casually chatting. The typical appearance of a non-sickle cell patient in pain may be absent.

The rates of true opioid addiction in sickle cell patients are low (< 5% of patients), and the literature suggests that emergency physicians under-treat pain in sickle cell patients.

Our experts recommend that unless there is clear evidence the patient does *not* have Sickle Cell Disease, take the patient's complaint seriously and use analgesics aggressively.

Sickle Cell Pain Crisis is a Diagnosis of Exclusion

- Sickle Cell Disease has been described in *all* races. Do not assume that a patient does not have sickle cell disease just because they have a light skin colour
- Ask patients whether this is their usual pain or not; if the pain is different from baseline, broaden your differential diagnosis to include not only all the painful conditions that we consider in *all* emergency patients but also the sickle cell-specific conditions such as acute chest syndrome
- The diagnosis of a pain crisis is a *clinical* diagnosis - no laboratory test will reliably determine whether the patient is having a pain crisis or not
- Patients with a higher baseline serum hemoglobin level are *more* likely to have pain episodes due to vaso-occlusion - a normal serum hemoglobin level does not rule out a sickle cell pain crisis

History Taking in the Patient Suspected of a Sickle Cell Pain Crisis

- What Sickle Cell complications has the patient had in past?
- How often does the patient have pain, and how often does the patient come to the ED for pain?

- Has the patient ever required multiple transfusions?
- Is the patient currently taking analgesics, antibiotics or *hydroxyurea*?
- What is the patient's baseline hemoglobin level?

Physical Exam in the Patient Suspected of a Sickle Cell Pain Crisis

The goal of physical exam is to rule out sickle cell complications such as acute infection, acute chest crisis, aplastic crisis and splenic sequestration.

Remember that sickle cell patients presenting with an uncomplicated pain crisis will often have normal vital signs, despite experiencing significant pain.

- Examine joints and soft tissues looking for evidence of cellulitis, septic joints, osteomyelitis, joint avascular necrosis
- Perform a careful respiratory exam looking for evidence of an acute chest syndrome
- Look for hepatosplenomegaly if you have a concern for splenic sequestration

Take fever in Sickle Cell Disease patients seriously!

Sickle Cell patients are functionally asplenic, therefore, they are at an increased risk of infection (i.e. meningitis, septic arthritis, osteomyelitis, etc.). Patients are especially at risk for infection with encapsulated organisms. In Sickle Cell Disease patients with fever, have a very low threshold to do a septic work up and start empiric

antibiotics. Consider admission for febrile patients without an identified source.

Do Sickle Cell Patients Suffering a Pain Crisis Require Lab Tests?

If you are familiar with caring for patients with sickle cell disease and they are suffering from an uncomplicated pain crisis lab tests are generally *not* required. Lab tests, including CBC, reticulocyte count, LFTs, bilirubin, LDH, electrolytes, should be considered if:

- The patient is being admitted
- You suspect another diagnosis
- The patient is systemically unwell
- You suspect worsening anemia or jaundice

The **reticulocyte count** is of particular value in sickle cell patients who presents with a sudden drop in their serum hemoglobin level in order to distinguish a sequestration crisis from an aplastic crisis. The reticulocyte count helps assess whether diminished RBC production (low reticulocyte count, as can occur in parvovirus infection resulting in aplastic crisis), or sequestration in the lungs, spleen, or liver is responsible for the acute anemia.

Aggressive Analgesia for Pain Crisis

One of the reasons that managing Sickle Cell pain crises can be challenging is that emergency physicians often under-dose analgesics in these patients. Use IV opioids for rapid effect. The SQ route is more reliable than the IM route if no IV is available.

A general rule of thumb as outlined in [Evidence-Based Management of Sickle Cell Disease: Expert Panel Report, 2014](#) for initial dosing of opioids is to administer the patient's usual total daily dose in a single IV dose. Frequent reassessments with self-reported pain should guide repeat doses. Consider hydromorphone or morphine q15-30min until pain is under control, and escalate the dose by 25% for uncontrolled pain. Initiate continuous infusion if required.

Consider **multimodal analgesia** as an adjunct to opioids:

- Acetaminophen
- NSAIDs (note that while NSAIDs have been shown to be effective in managing sickle cell pain crises, they should be avoided for long term treatment of pain because of the potential renal side effects, as sickle cell patients are at increased risk for chronic renal failure - a short course of NSAIDs (<72h) may be appropriate)
- Ketamine - case reports support the effectiveness of ketamine as an opioid-sparing drug

Note that while corticosteroids have been shown to reduce pain scores and length of stay, there are associated with high rates of pain recurrence, and so they are not recommended by our experts.

For more on the opioid-sparing effects of Ketamine go to [Journal Jam 4 - Low Dose Ketamine Analgesia](#)

Supportive Measures

Oxygen

Reserve supplemental oxygen for patients who are hypoxic.

Oxygen has never been shown to improve outcomes in Sickle Cell patients suffering from a pain crisis.

Supplemental oxygen is thought to:

1. Suppress bone marrow (myelosuppression) and
2. Increase transfusion requirements

If the oxygen saturation is >92%, NO supplemental O₂ is needed.

Fluids

Reserve fluid boluses for patients who are hypovolemic.

While it is thought that *dehydration may precipitate pain crisis*, overhydration — especially with isotonic crystalloid — does not help resolve a pain crisis and may have *detrimental* effects:

1. *Atelectasis*, which may precipitate *acute chest syndrome*.
2. *Hyperchloremic metabolic acidosis*, which may *promote sickling*.
3. The concurrent use of opiates for pain control can increase vascular leak and predisposes sickle cell disease patients to *pulmonary edema*.

Boluses of IV fluid should not be given unless patients are overtly hypovolemic (sepsis, diarrheal illness, vomiting). In these situations, resuscitate only to euvoolemia and for maintenance fluids use a *hypotonic solution* such as ½ NS or D5-½ NS.

Is There a Role for RBC Transfusion in Sickle Cell Pain Crisis?

There is *no* role for red cell transfusions in an uncomplicated acute pain crisis. Transfusions can lead to an increased risk of alloimmunization and may *increase* pain by increasing viscosity of blood leading to vaso-occlusion as well as precipitate acute chest syndrome, and stroke.

While red cell transfusions can be life-saving in the Sickle Cell Disease patients with an Acute Chest Syndrome, for example, they should be avoided in the patient with an uncomplicated pain crisis. Any decision to transfuse a Sickle Cell patient should ideally be done in consultation with a transfusion specialist or hematologist as there are many nuances involved in decision making around transfusions in this population.

Why Emergency Physicians Should Know About Hydroxyurea

Oral hydroxyurea increases production of fetal hemoglobin, thereby decreasing sickled hemoglobin. It has been shown to decrease the incidence of pain episodes, acute chest crises, and the number of transfusions required. Because frequent monitoring and a lot of patient education is required, patients should be followed by a hematologist to start this medication. Our experts suggest that the role of the emergency physician is to identify patients with frequent pain episodes who may benefit from hydroxyurea treatment and refer accordingly.

Aplastic Crisis

Illustrative Case: A 24 year old man comes back to your ED for the 24th time, but this time he's rushed into your resuscitation room as his BP is in the boots. EMS tells you that he had been feeling generally unwell for the past 24hrs with fatigue, SOB and a low grade fever. His girlfriend called 911 when he had a syncopal episode trying to get out of bed. On Physical exam his GCS is 13, his heart rate is 130, blood pressure 70/40, oxygen saturation 90% on a non-rebreather and he has crackles bilaterally to the midscapula. You do your usual resuscitation magic to stabilize him, send off sepsis blood work and Trops and a while later his hemoglobin comes back at 30 - A huge drop from his previous 110. A quick rectal exam reveals normal stool with no melena or hematochezia. You think to yourself, why in the world is this Sickle Cell patient suddenly in shock with severe acute anemia?

Aplastic Crisis is a life threatening Sickle Cell Disease condition that can often be elusive. The diagnostic clues that will help emergency physicians make an early diagnosis are:

- There is usually a viral prodrome
- Acute severe drop in serum hemoglobin
- Often present hemodynamically compromised, in shock
- The reticulocyte count is dramatically decreased or even zero

The usual clinical picture is gradual onset of fatigue, SOB and sometimes syncope as in the illustrative case.

Fever may be present as well. Do not assume an infectious cause in Sickle Cell Patients who present with fever.

Physical exam may reveal lethargy, rapid heart rate and occasionally frank heart failure.

The most important aspect of treatment in Aplastic Crisis is *immediate red cell transfusion*

The other diagnosis to think about in a sickle cell patient who presents in shock with a severe drop in haemoglobin is

Sequestration Syndrome which is mostly seen in children because they still have splenic remnant. Sequestration Syndrome is also in adults with SC or SB-Thal. Look for tender palpable organomegaly, high indirect bilirubin, ALT and LDH (from hemolysis) and a high reticulocyte count high (to compensate for the sequestered blood).

Practical Tip: When ordering red cell transfusions, tell the blood bank that the patient has sickle cell disease which will allow the blood bank to provide blood that has minimal risk of causing allo-immunization.

Acute Chest Syndrome

Illustrative Case: A 35 year old otherwise healthy woman with a known history of sickle cell disease comes in a week after her last uneventful pain crisis with a 2 day history of non-productive cough and gradual onset non-pleuritic severe central chest pain radiating to both shoulders. She admits to being short of breath on exertion. Her vitals show that she is bit

tachycardic and dyspneic with a normal blood pressure, an oxygen saturation of 92% on room air and a borderline Temp of 37.8. Her cardiovascular exam is essentially normal and her chest is clear. The CXR, however, shows multilobar infiltrates.

Acute Chest Syndrome is the most common cause of death in sickle cell disease with a case fatality rate of 10%. Like all classic triads in medicine the classic triad of Acute Chest Syndrome (fever, hypoxia and pulmonary infiltrate) is often not present. However, the presence of any of this triad should raise the suspicion for the diagnosis. Acute Chest Syndrome can present fairly benignly with bronchitis-like or pneumonia-like clinical picture with cough, SOB, but often do not develop a fever. The pain of Acute Chest Syndrome is characterized by a *T-shirt distribution*.

Any sickle cell patient with hypoxia should be presumed to have Acute Chest Syndrome until proven otherwise.

What makes acute chest syndrome special isn't so much *what* is happening, it's *where* it's happening – sickling blocks blood flow causing local hypoxemia and ischemia and in Acute Chest Syndrome the sickling is in the pulmonary vasculature. As a result the patient becomes more hypoxic, which drives more sickling, which drives more vaso-occlusion, which drives more hypoxia, so that a vicious cycle is created leading to a spiral ending in death.

Differentiating Pain Crisis and Acute Chest Syndrome

A sickle cell patient with ***isolated*** chest pain without any other symptoms can be safely presumed to be suffering from a sickle pain

crisis, whereas any associated respiratory symptoms should raise the possibility of an Acute chest Syndrome.

Any degree of hypoxia, even if the chest x-ray is initially normal, should be considered an Acute Chest Syndrome until proven otherwise.

Have a low threshold for admission for any sickle cell patient with a new infiltrate on chest x-ray or any degree of hypoxia.

Why is it Important to Diagnose Acute Chest Syndrome Early?

The sooner the patient with an Acute Chest Syndrome is diagnosed the sooner they can receive life-saving treatment with a simple red cell transfusion or exchange transfusion in consultation with a hematologist. In addition to usual resuscitative measures, patients should be initiated on broad spectrum empiric antibiotics.

Indications for Exchange Transfusion in Acute Chest Syndrome:

- Severe Acute Chest Crisis
- Rapid or significant clinical deterioration
- Worsening chest radiography
- PO₂ < 70mmHg
- Baseline hemoglobin >90 (which precludes use of simple transfusion due to risk of hyperviscosity)

Listen to Dr. Ward's [Best Case Ever of a Sickle Cell Acute Chest Syndrome](#)

Rapid and severe sequestration of RBCs in spleen, causing circulatory collapse. More common in children, but can occur at any age.

Diagnosis based on:

- Severe anemia
- Increased reticulocyte count
- Hemolysis: increased indirect bilirubin, ALT & LDH
- Splenomegaly

Treatment: immediate RBC transfusion, IV fluids. Patients will need splenectomy because of high recurrence rate.

Sickle Cell Disease and Stroke

Sickle cell patients are at higher risk for both ischemic and hemorrhagic stroke.

The prevalence of stroke in children with Sickle Cell disease is as high as 10%. The mechanism of stroke in children with sickle cell disease is usually due to abnormal cell adhesion. So, if a 3 year old patient with sickle cell disease presents refusing to move their arm, don't presume that the diagnosis is a pulled elbow - do a neurologic exam, and if it is consistent with a stroke, an urgent CT head is required to rule out a bleed and arrangements for an exchange

transfusion should be made in consultation with a neurologist and hematologist.

Exchange transfusion, rather than thrombolysis, is the treatment of choice for stroke in children with Sickle Cell Disease.

Eye Trauma in Sickle Cell Disease

Illustrative Case: A 35 year old sickle cell patient comes in after getting elbowed in the right eye during a basketball game 2 hours ago. He complains of pain, but no blurry vision. His visual acuity is 20/20 bilaterally and a quick look at his right eye under the slit lamp reveals a corneal abrasion, but not much else.

Both Sickle Cell Disease and sickle cell trait increase the risk for catastrophic ophthalmologic complications after blunt eye trauma. For Sickle Cell Disease patients who have sustained even *minor* trauma, always consider a subtle hyphema and traumatic glaucoma. Hyphema may not be visible to the naked eye. A careful slit lamp exam to explore the anterior chamber for an occult hyphema is mandatory. All patients need intraocular pressure measured. Have a low threshold for ophthalmology consultation and admission for serial intraocular pressures.

Management of Elevated Intra-ocular Pressures with Traumatic Hyphema or Suspected Hyphema in Sickle Cell Disease or Sick Cell Trait Patients:

- Elevate head of bed to 30 degrees
- Topical timolol
- Topical brimonidine or apraclonidine (second agent)

- Topical dorzolamide (third agent)

Avoid:

- Mannitol
- Glycerin
- Acetazolamide
- Topical epinephrine

Take Home Points in The Emergency Management of Sickle Cell Disease

- Unless there is clear evidence that the patient does not actually have sickle cell disease, take the patient's pain complaints seriously and use opiates aggressively
- Most patients with a sickle cell pain crisis will not exhibit vital sign abnormalities! Normal vital signs to *do not* rule out sickle cell pain crisis and *do not* rule in malingering
- Patients may show behaviour that emergency physicians consider inconsistent with pain, including walking, engaging in conversations, or having a calm appearance although they still report high levels of pain. Don't assume low pain in patients who appear calm!

- Sickle cell pain crisis is a *diagnosis of exclusion*. Pain in a patient with sickle cell disease does not rule out appendicitis! Keep your differential wide.
- Always consider meningitis, septic arthritis, and osteomyelitis (specifically within the spine) in addition to standard infections in patients with fever.
- Do not assume that a patient can't have sickle cell disease just because they skin colour is light. Sick cell disease has been described in all races and should no longer be considered exclusive to people with dark skin.
- Patients with normal serum hemoglobin levels are *more* likely to be suffering from a pain crisis, have higher rates of vaso-occlusive symptoms such as pain, stroke and acute chest syndrome as apposed to patients with low serum hemoglobin levels who tend to suffer from less pain, but more pulmonary hypertension and skin ulcers.
- In patients presenting with simple pain without other symptoms who are not being admitted, lab tests are generally *not* necessary. The reticulocyte count is the most useful blood test in those patients who present with complicated pain crises.
- Use NSAIDS sparingly in Sickle Cell Disease! While NSAIDs for acute pain crises have been shown to be effective in reducing pain and decreasing hospital

length of stay, many patients with sickle cell disease have progressive chronic renal failure as a result of renal infarcts and their serum creatinine level may appear normal despite this.

- Reserve supplemental oxygen for patients who are hypoxic and fluid boluses for patients who are hypovolemic. Use hypotonic fluids at maintenance for uncomplicated pain crisis.

Key References

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