Evaluation and Management of Acute Chest Syndrome

Clinical Practice Guideline

Approved by SSM Health Cardinal Glennon Clinical Practice Guideline Committee June 22, 2023

SSMHealth CardinalGlennon Children's Hospital

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Evaluation and Management of Acute Chest Syndrome in Children with Sickle Cell Disease in the Emergency Department Clinical Practice Guideline

Inclusion Criteria
- Any patient with Sickle Cell Disease (all subtypes)
- Presence of concerning presenting symptoms, including:
  - Fever
  - Cough (productive or unproductive)
  - Tachypnea
  - Chest pain
  - Shortness of Breath
  - Increased work of breathing (nasal flaring, retractions)
  - Wheezing
  - Cyanosis

↓

Perform physical exam

↓

Presence of hypoxemia, increased work of breathing, tachypnea, or abnormal breath sounds

NO →
- Consider alternative diagnosis (other Sickle Cell Disease CPGs)
- Discuss with Hematology

YES ↓

EVALUATION
- Obtain Chest X-ray (CXR)
- Obtain Labs
  - CBC with differential
  - Reticulocyte Count
  - Blood cultures
  - CMP
  - Respiratory PCR panel
  - Consider VBG/ABG for severe distress or significant hypoxemia

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ED MANAGEMENT
- Medications
  - IV fluids (Maintenance fluids, consider 10mL/kg normal saline bolus if moderate to severe dehydration present)
  - Antibiotics, including antivirals if influenza positive (*see Box 1*)
  - Pain control (*see Sickle Cell Pain Management CPG*)
  - Bronchodilators (patient with wheezing or history of asthma)
  - Corticosteroids (patients with history of asthma)
- Admit to Hospital
  - Notify Hematology
  - Notify PICU as needed

SSMHealth Cardinal Glennon Access Center Transfer Line

888-229-2424

1. SSMHealth Cardinal Glennon CPG Home

2. Resources

- National Heart,Lung, and Blood Institute's Evidence-Based Management of Sickle Cell Disease: Expert Panel Report, 2014
- Vichinsky et al (1997). Acute Chest Syndrome in Sickle Cell Disease: Clinical presentation and course. Blood 89, 1787-1792.
- Vichinsky et al (2000). Causes and Outcome of the Acute Chest Syndrome in Sickle Cell Disease. NEJM 342, 1855-1865.
- Ogu UO, Badamosi NU, Camacho PE, Freire AX, Adams-Graves P. Management of Sickle Cell Disease Complications Beyond Acute Chest Syndrome. J Blood Med. 2021 Feb 25;12:101-114.

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Committee Chair: Andrew Ellis, MD (Andrew.Ellis@ssmhealth.com)

Box 1: Medications

(Note: Dosing Based on Normal Renal Function)

- Antibiotics
  - Ceftriaxone 50mg/kg IV every 24 hours (max 2000mg)
    PLUS
  - Azithromycin 10mg/kg (max 500mg) IV/PO day 1, then 5mg/kg (max 250mg) IV/PO day 2-5

  - Cephalosporin Allergy OR Severe Allergy to Penicillin
    - Levofloxacin IV/PO monotherapy
      - < 5 years old: 10 mg/kg (max 750mg) BID
      - ≥ 5 years old: 10mg/kg (max 750mg) daily
    OR
    - Clindamycin 40mg/kg/day divided every 8 hours (max dose 600mg) PO
      PLUS
    - Azithromycin 10mg/kg (max dose 500mg) IV/PO on day 1, followed by 5mg/kg (max 250mg) IV/PO day 2-5

  - Consider adding vancomycin "Per Pharmacy" OR 15mg/kg (max 1500mg) IV every 6 to 8 hours for severe illness, pleural effusion

- Antivirals
  - Influenza A Positive
    - Oseltamivir, dosed by mouth for 5 days
      ≤ 15kg: 30mg two times daily
      16-23kg: 45mg two times daily
      24-40kg: 60mg two times daily
      ≥ 41kg: 75mg two times daily

  - COVID-19 Positive
    - Outpatient Use (Must be positive within 5 days of symptom onset and ≥ 12 years old)
      - Nirmatrelvir/ritonavir (Paxlovid) 300/150 mg PO twice daily for 5 days
    - Inpatient Use (Must be positive and within 7 days of symptom onset)
      - Remdesivir
        - 3kg to < 40 kg: 5mg/kg IV on Day 1, followed by 2.5mg/kg IV on days 2-5
        - ≥ 40kg: 200mg IV on Day 1, followed by 100mg on days 2-5

- Corticosteroids
  - Concern for Asthma
    - Methylprednisolone (IV) or Prednisone (PO) 1-2mg/kg/day (max 60mg), max 5 days
    OR
    - Dexamethasone 0.6mg/kg (max 16mg) IV or PO as a single dose

  - COVID-19 Positive Patients (Requiring Admission AND supplemental oxygen)
    - Dexamethasone 0.15mg/kg (max 6mg) IV or PO daily for 5-10 days

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Management of Acute Chest Syndrome in Hospitalized Children with Sickle Cell Disease Clinical Practice Guideline

INPATIENT MANAGEMENT

MONITORING/LABS
- Vitals every 4 hours
- Continuous pulse oximetry
- Daily Hemoglobin/Hematocrit and reticulocyte count until patient is improving (full CBC only if needed)
- Follow blood cultures
- Strict I/O's
- Daily weight

RESPIRATORY INTERVENTIONS
- Supplemental oxygen to keep SpO2 99-100%
- Incentive spirometry 10 breaths every 2 hours while awake
- Encourage ambulation
- Bronchodilators for patients with asthma and wheezing
- Repeat CXR if worsening

IV FLUIDS
- Normal saline (or D5 Normal saline) at maintenance rate for all patients
- Increase fluid rate for signs of volume depletion, fever, or excessive losses, targeting euvolemia
- If fluid rate is increased or additional fluid provided, reassess need every 12 hours and reduce fluid rate to maintenance once euvolemia established to avoid hyperhydration and fluid overload

MEDICATIONS
- Antibiotics (*see Box 1*)
- Antivirals (*see Box 1*)
- Corticosteroids (*see Box 1*)
- Bronchodilators (for patients with asthma and wheezing)
- Pain control (*see Sickle Cell Pain Management CPG*)

TRANSFUSION
- Transfuse at the discretion of Hematology attending

DISCHARGE CRITERIA
- Transition to oral antibiotics, if indicated
- Temperature < 100.4F for over 24 hours off IV antibiotics
- Normal and stable or at baseline oxygen levels off supplemental oxygen
- Normal respiratory rate
- If continuing oral antibiotics, instruct patient to resume prophylactic oral Penicillin V after treatment course is complete
- Re-enforce initiation or continuation of hydroxyurea
- Evaluate vaccination status for annual influenza vaccine, Meningococcal vaccine, pneumococcal vaccine
- Outpatient appointment arranged with sickle cell clinic

CLINICALLY DETERIORATING
- Patients with acute chest syndrome are at risk for rapid deterioration
- Clinical deterioration may be suggested by:
  - Decreasing level of consciousness
  - Decreasing oxygen saturations
  - Increasing oxygen requirement or failure to respond to oxygen therapy
  - Increased pain
  - Increased tachypnea
  - Increased shadowing on CXR
  - Falling Hgb with or without rising WBC count
- Transfer to PICU

ASSESS FOR IATROGENIC CONTRIBUTION
- Assess for volume overload
- Assess for opioid toxicity

INTERVENTIONS
- Imaging
  - Repeat CXR (if not already obtained)
  - Consider CTA of the Chest to assess for pulmonary embolism
    - Particularly in adolescents or patients with other prothrombotic risk factors
    - Progressive respiratory difficulty without obvious cause
    - Rapid clinical deterioration with worsening/refractory hypoxemia and/or cardiac dysfunction
- Respiratory support
  - Escalate support to target improved oxygenation, respiratory effort, mental status (NIPPV or mechanical ventilation)
  - Up to 10% may require mechanical ventilation
- Transfusion
  - At the discretion of Hematology attending
- Medications
  - Consider addition or escalation of antibiotic/antiviral as clinically indicated

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    OR
    - Clindamycin 40mg/kg/day PO divided every 8 hours (max dose 600mg) PO
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  - Concern for Asthma
    - Methylprednisolone (IV) or Prednisone (PO) 1-2mg/kg/day (max 60mg), max 5 days
    OR
    - Dexamethasone 0.6mg/kg (max 16mg) IV or PO as a single dose

  - COVID-19 Positive Patients (Requiring Admission AND supplemental oxygen)
    - Dexamethasone 0.15mg/kg (max 6mg) IV or PO daily for 5-10 days

Evaluation and Management of Acute Chest Syndrome in Children with Sickle Cell Disease
Clinical Practice Guideline

Authors: Lily Dolatshahi, MD (Pediatric Hematology/Oncology), Susan Oo, MD (PGY-3, Pediatrics), Gunjanpreet Kaur, MD (PGY-3, Pediatrics)
Date: June 2023

Population
This guideline is aimed at children of any age with sickle cell disease presenting with respiratory symptoms where the Acute Chest Syndrome may be the cause.

Definition
Acute chest syndrome (ACS) is defined as the presence of a new pulmonary infiltrate, irrespective of the etiology of the infiltrate, in a child with sickle cell disease (SCD).

Background
ACS is the second most common cause of hospital admission in children with SCD, and is the most common cause of death. ACS is multifactorial in origin, with contributions from infection, vaso-occlusion, fat embolism, and disturbed nitric oxide metabolism. The prevalence of both viruses and atypical bacteria as common infectious causes suggest that the clinician must carefully consider appropriate antimicrobial agents, and provide coverage against atypical bacteria.

History and Physical Examination
Some of the following symptoms and signs are typically present in patients with ACS:
Symptoms:

- Chest pain, which may be absent, particularly in younger children
- Cough, which may be productive
- Breathlessness
- Wheezing
- Fever/rigors

Signs:

- Fever
- Tachypnea
- Wheeze, crackles
- Bronchial breathing
- Cyanosis
- Tachycardia
- Hypoxia

- Retractions
- Nasal flaring
- Abnormal breath sounds- rhonchi, decreased breath sounds, pleural rub, crackles

Diagnostic Evaluation

25% of patients with ACS have a normal physical exam, and up to 60% are do not trigger suspicion based on clinical findings alone. As such, diagnostic evaluation is recommended as follows:

- CBC with differential, Reticulocyte count
- CXR
- Consider Type and Screen
- Basic biochemistry (creatinine and liver function tests)
- Blood cultures
- VBG /ABG measurement (at physician discretion)
- Respiratory PCR panel
- Pulse oximetry in room air
- CTA Chest for deteriorating patient and concern for pulmonary embolism
    - Pulmonary embolism should be considered in individuals with ACS and progressive respiratory difficulty where the cause remains unclear, especially when there is rapid clinical deterioration with worsening hypoxemia and/or cardiac dysfunction).

Monitoring and Treatment

Disposition and Monitoring:

- All patients with ACS should be admitted to the hospital
- The hematology team should be informed
- The critical care team should also be made aware of the patient, even in mild cases of ACS, because clinical deterioration often occurs rapidly and unexpectedly
- Monitor vital signs every 4 hours until patient improves
- CBC and reticulocyte count should be obtained daily until the patient improves

Treatment:

- Oxygen
    - All patients should be given oxygen to maintain their oxygen saturations at 99-100%.
- Incentive spirometry
    - 10 breaths q 2 hours while awake, may help prevent children with acute pain developing acute chest syndrome.
- Intravenous Fluids
    - All patients with ACS should receive intravenous fluids at maintenance rates, which may need to be modified according to fluid loss and fever. If patients are considered to be dehydrated and require higher rates of IV fluid replacement, this must be reviewed at minimum every 12 hours and reduced once patients

are adequately hydrated, to reduce the risk of fluid overload which can complicate ACS and lead to clinical deterioration.

- Antibiotics - The most common bacterial organism in children is Mycoplasma pneumoniae and the commonest virus identified is the respiratory syncytial virus (RSV). Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenza and respiratory viruses other than RSV are also seen.
    - Ceftriaxone 50mg/kg IV every 24 hours (max 2000mg) PLUS Azithromycin 10mg/kg (500mg) PO or IV day 1, followed by 5mg/kg (max 250mg) PO or IV days 2-5
    - Cephalosporin Allergy OR Severe Allergy to Penicillin
        - Levofloxacin IV/PO Monotherapy
            - < 5 years old: 10mg/kg (max 750mg) BID
            - ≥ 5 years old: 10mg/kg (max 750mg) daily

        OR
        - Clindamycin 40mg/kg/day divided every 8 hours (max 600mg/dose) PO
    - Severe illness, clinical deterioration, pleural effusion
        - Add vancomycin "Per Pharmacy" OR 15mg/kg (max 1500mg) IV every 6 to 8 hours
- Antivirals
    - Influenza A positive
        - Oseltamivir PO for 5 days
            - ≤15kg = 30mg PO BID
            - 16-23kg= 45mg PO BID
            - 24-40kg= 60mg PO BID
            - ≥41kg=75mg PO BID
    - COVID-19 Positive
        - Outpatient Use (Must be positive within 5 days of symptom onset and ≥ 12 years of age)
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        - Inpatient Use (Must be positive and within 7 days of symptom onset)
            - Remdesivir
                - 3kg to < 40kg: 5mg/kg IV on day 1, followed by 2.5mg/kg IV on days 2-5
                - ≥ 40kg: 200mg IV on Day 1, followed by 100mg on days 2-5
- Bronchodilators
    - Nebulized albuterol should be used if there is wheezing, a history of reactive airway

- Corticosteroids
    - Concern for or history of asthma
        - Methylprednisolone (IV) or Prednisone (PO) 1-2mg/kg/day (max 60mg) for 5 days

        OR
        - Dexamethasone 0.6mg/kg IV or PO (max 16mg) as a single dose
    - COVID-19 Positive (Requiring admission AND supplemental oxygen)
        - Dexamethasone 0.15mg/kg (max 6mg) IV or PO daily for 5-10 days
- Analgesia
    - Pain should be treated according to the Management of Sickle Cell Pain Crisis Clinical Practice Guideline
- Transfusion
    - Simple blood transfusion may be particularly useful if used early and when the Hgb is <7.0 OR more than 1.0 less than baseline, and nearly always if the Hb <5.0. The dose is 10mL/kg PRBC.

Deteriorating Patients

Patients with ACS can deteriorate rapidly and require close monitoring. Up to 10% of patients may require ventilatory support. The PICU should be alerted that a deteriorating ACS patient is on the floor. Deterioration is suggested by:

- Decreasing level of consciousness (note that the PEWS score does not record this)
- Decreasing oxygen saturations measured by pulse oximetry
- Increasing oxygen requirements to maintain 100% oxygen saturations, or failure of response to oxygen therapy
- Increasing tachypnea
- Increasing pain
- Decreasing hemoglobin level with or without rising white blood cell count

Assessment of the Deteriorating Patient

- Assess fluid balance for the possibility of fluid overload
- Assess for possibility of opioid toxicity for patients receiving opioids
- Repeat CXR – may see increased shadowing or evolution of prior infiltrate
- Consider CTA of the Chest to assess for pulmonary embolism
- Consider VBG/ABG

Additional Therapies

- Broadening of antibiotic therapy (see above)
- Escalate respiratory support to target adequate oxygenation, ventilation, respiratory effort
- Management of volume overload, if present
- Simple blood transfusion
    - If not previously given, if Hgb < 7.0 or > 1.0 below baseline
- Exchange transfusion
    - Indicated for rapidly deteriorating patients, especially with extensive CXR shadowing/infiltrates and low oxygen saturations (<90%) not responsive with

increased oxygen support, increasing respiratory distress, and or decline in hemoglobin concentration despite simple transfusion

Discharge from Hospital

- Temperature < 100.4F for 24 hours off IV antibiotics
- Able to tolerate oral antibiotics, if needed
- Normal and stable oxygen saturation measurements
- Normal respiratory rate
- Instructions to resume prophylactic Penicillin V when course of antibiotics complete
- Outpatient appointment arranged with sickle cell clinic
- Advice regarding vaccination status for Pneumovax, Meningococcal, and annual influenza vaccines
- Reinforce starting or continuing hydroxyurea

References

1. National Heart,Lung, and Blood Institute's Evidence-Based Management of Sickle Cell Disease: Expert Panel Report, 2014.
2. Vichinsky et al (1997). Acute Chest Syndrome in Sickle Cell Disease: Clinical presentation and course. Blood 89, 1787-1792.
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