

PEDIATRIC ACUTE CHEST SYNDROME (ACS)

Patients with sickle cell disease presenting with 1) a new pulmonary infiltrate on chest radiography AND 2) evidence of lower airway disease (e.g. cough, shortness of breath, retractions, rales, etc.)

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TARGET POPULATION

Inclusion Criteria

- Patients with sickle cell disease (SS, SC, S β 0 thalassemia, S β + thalassemia)
- Patients of all ages
- Patients treated year round

Exclusion Criteria

- Patients without infiltrate on chest radiograph (e.g. asthma exacerbation)
- Patients with severe pulmonary hypertension
- Patients post bone marrow transplant
- Well children with pneumonia

BACKGROUND | DEFINITIONS

Acute chest syndrome (ACS) is the second most common reason for hospitalization in children with sickle cell disease and a leading cause of mortality. ACS is defined as a new pulmonary infiltrate on chest radiograph in the presence of evidence of lower respiratory tract disease (e.g. some combination of cough, shortness of breath, retractions, rales, etc.). In the majority of cases of ACS, an etiology is unable to be identified. The most common identified etiology of ACS is infection but it may also result from pulmonary vaso-occlusion, pulmonary infarction or fat embolism. The primary infectious agents implicated in ACS include: *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, *Streptococcus pneumoniae*, and viruses. Risk factors for ACS include vaso-occlusive pain crisis, anesthesia, and surgery. Patients are at increased risk for stroke in the two weeks immediately following an episode of ACS.

CLINICAL MANAGEMENT

- Hospitalize on hematology service
- Vital signs q 2-4 hours depending upon degree of respiratory compromise
- Record pain score every 4 hours
- Continuous cardiorespiratory monitor and pulse oximetry
- Encourage ambulation: out of bed to chair or ambulating at least 2-3 times per day
- Droplet precautions
- Continue medication for reactive airway disease if applicable

DIAGNOSTIC TESTS

- CBC with differential, platelet count, and reticulocyte count initially and daily until improving (compare with patient's baseline values)
- CXR initially, repeat for clinical deterioration (be aware that the x-ray often underestimates the degree of involvement and may appear worse when the child is clinically improving)
- Consider:
 - Type and crossmatch for severe illness or if Hb is greater than 1 g/dL below baseline. Request minor-antigen-matched, sickle-negative, leukocyte-depleted RBC
 - Blood cultures if febrile (greater than or equal to 38.3°C) or history of recent fever (do not need to repeat daily)
 - Arterial blood gas per clinical discretion
 - Renal (BUN, creatinine) and liver (fractionated bilirubin, ALT) function tests for severe illness or if diffuse encephalopathy present (rule out acute multi-organ failure syndrome)
 - If severe abdominal pain consider an ultrasound for gallstones
 - Influenza A& B screening during the appropriate season
 - We do not recommend routinely sending a respiratory pathogen PCR
- Echocardiography is not recommended routinely in patients with acute chest syndrome. Consult cardiology if concern for pulmonary hypertension arises (prolonged hypoxemia, fixed split S2 or pronounced pulmonary component of S2, hepatomegaly, persistent peripheral edema, or persistent pulmonary edema despite adequate fluid status)

FLUIDS | NUTRITION

- Daily weight
- Record intake and output strictly

- Maintain "euvoemia". IV + P.O. = 1 x maintenance. More fluid is appropriate only if patient is dehydrated or if insensible losses are increased (e.g. persistent fever). IV fluid should be D5 1/4 NS to avoid exacerbating the sickling process.

RESPIRATORY THERAPY

- Consult pulmonology
- Clinical features suggestive of asthma or acute bronchospasms make an initial assessment using the Pediatric Asthma Score (PAS); trial Albuterol 4 puffs with a spacer or 2.5 mg nebulized once. Reassess using the PAS, a positive response is a decrease of 2 or more in the PAS. If a positive response is noted, order Albuterol 2-4 puffs or Albuterol 2.5mg nebulized Q4 and PRN. If at any time PAS worsens by 2 or more increase frequency of the Albuterol and notify the provider
- Lung expansion strategies: EzPAP (along with IS) Q4 hours for 72 hours. After 72 hours of the initiation of the therapy, the patient will be evaluated by the respiratory therapist for pulmonary stability. If the chest x-ray (if done) remains stable, there are no signs of pulmonary infection, there is good aeration throughout all lung fields upon auscultation, and the patient can consistently achieve 14ml/kg with the IS, the EzPAP will then be discontinued. The patient will then receive IS Q2 hours while awake and Q4 hours at night by their RN
- Transfer to the ICU if patient is requiring Heated High Flow Nasal Cannula (HHFNC), invasive or non-invasive (CPAP, BiPAP) mechanical ventilation is being considered

TABLE 1. PEDIATRIC ASTHMA SCORE

Score	1	2	3
Respiratory Rate 2 to 3 years 4 to 5 years 6 to 12 years Older than 12 years	34 or less 30 or less 26 or less 23 or less	35 to 39 31 to 35 27 to 30 24 to 27	40 or greater 36 or greater 31 or greater 28 or greater
Oxygen Requirements	Greater than 90% on room air	85% to 90% on room air	Less than 85% on room air
Auscultation	Normal breath sounds to end-expiratory wheeze only	Expiratory wheezing	Inspiratory and expiratory wheezing to diminished breath sounds or poor aeration
Retractions	Zero to one site	Two sites	Three or more sites
Dyspnea	Speaks in sentences, coos and babbles	Speaks in partial sentences, short cry	Speaks in single words/ short phrases/grunting

Note: Use PAS Score to guide intervention & response to treatment. *Older pediatric*

TREATMENT

- Antipyretics
 - Acetaminophen dose according to manufacturer's recommendations PRN temperature greater than or equal to 38.3°C after blood cultures have been obtained on at least one occasion
- Antibiotics (see [Table 2](#) for choices and doses)
 - Ceftriaxone and azithromycin is the regimen of choice for initial inpatient management
 - If a respiratory pathogen PCR is sent for another reason and is negative for *Mycoplasma* and *Chlamydothila*, azithromycin may be discontinued
 - If there is a known or suspected cephalosporin allergy, levofloxacin is the regimen of choice and azithromycin can be omitted because levofloxacin has adequate coverage of atypical organisms
 - Strongly consider adding vancomycin for severe illness, or if large infiltrate with pleural effusion present and *S. aureus* is suspected
 - Prophylactic penicillin should be discontinued while patient is receiving antibiotics
 - If antibiotics are continued upon discharge, an appropriate oral antibiotic should be continued to complete a course of 7-10 days (including inpatient IV therapy received): Amoxicillin-clavulanate is recommended as first line, cefpodoxime is the drug of choice in the presence of a penicillin allergy, and levofloxacin is the drug of choice in the presence of a cephalosporin allergy.
- Analgesia (if indicated)
 - If pain is present patients should be started on scheduled anti-inflammatories and opiates if there are no contraindications
 - Start ketorolac, but limit to 48 hour maximum duration then start ibuprofen PO q6h (not PRN) if no contraindication present (i.e. gastritis, ulcer, coagulopathy, renal impairment).
 - If pain does not respond to anti-inflammatory alone, consult the sickle cell vaso-occlusion guidelines. Be aware narcotic administration may further suppress respiration
- Transfusions
 - Give simple blood transfusion (10 mL/kg red blood cells) to improve oxygen carrying capacity to people with symptomatic ACS whose hemoglobin concentration is greater than 1 g/dL below baseline and hemoglobin would not rise to more than 10 g/dL. If baseline hemoglobin is 9 g/dL or higher, may require red cell exchange transfusion. Do not transfuse acutely to Hb greater than 10 g/dL, Hct greater than 30 percent if percent sickle hemoglobin is or is presumed to be greater than 30 percent since it is associated with inducing pain and stroke
 - Urgent exchange transfusion may be indicated after consultation from hematology, critical care, and apheresis specialists – when there is rapid progression of ACS as manifested by oxygen saturation below 90 percent despite supplemental oxygen, increasing respiratory distress, progressive pulmonary infiltrates, and/or decline in hemoglobin concentration despite simple transfusion and/or inability to transfuse due to high baseline hemoglobin. May require transfer to ICU and transfusion medicine consult for erythrocytapheresis. Remove femoral or central venous catheters as soon as possible after exchange transfusion to reduce risk of thrombosis

TABLE 2. ANTIMICROBIAL MEDICATIONS

Medication	Dosing	Indication/Notes
Amoxicillin-clavulanate (PO)	90 mg/kg/day (maximum 3,000 mg/day if using suspension and 2,625 mg/day if using tablet) PO divided TID	Antimicrobial – Outpatient 1 st Choice Use either amoxicillin-clavulanate ES suspension 600-42.9mg/5mL or 875-125 mg tablet formulations
Azithromycin (IV/PO) *Highly Bioavailable*	10 mg/kg/day (maximum 500 mg/day) PO x 1 dose, followed by 5 mg/kg/day (maximum 250 mg/day) PO once daily x 4 doses	Antimicrobial – Inpatient/Atypical Coverage Discontinue if RPP results negative for <i>Chlamydophila</i> and <i>Mycoplasma</i> Not necessary to use azithromycin with levofloxacin as levofloxacin covers atypical bacteria
Cefpodoxime (PO)	10 mg/kg/day (maximum 400 mg/day) PO divided BID	Antimicrobial – Outpatient for penicillin allergy *Ensure prescription sent in advance (variable stock at some outpatient pharmacies)
Ceftriaxone (IV)	50 mg/kg/day (maximum 2,000 mg/day) IV q24h	Antimicrobial – Inpatient 1 st Choice Discontinue prophylactic penicillin while patient is receiving broad-spectrum antimicrobials
Levofloxacin (IV/PO) *Highly Bioavailable*	Less than 5 years: Levofloxacin 20 mg/kg/day (maximum 750 mg/day) IV or PO divided q12h Greater than or equal to 5 years: 10 mg/kg/day (maximum 750 mg/day) IV or PO q24h	Antimicrobial – Inpatient and/or Outpatient for cephalosporin allergy Discontinue prophylactic penicillin while patient is receiving broad-spectrum antimicrobials Not necessary to use azithromycin with levofloxacin as levofloxacin covers atypical bacteria
Vancomycin (IV)	Contact pharmacy for recommended dosing Dosing interval based on age/renal function)	Antimicrobial – Inpatient for patients with severe illness or with large infiltrate with pleural effusion present and <i>S. aureus</i> suspected *Must monitor renal function (SCr, BUN, urine output) at baseline and minimum twice weekly thereafter

TABLE 3. RESPIRATORY MEDICATION TABLE

Medication	Dosing	Indication
Albuterol	4 puffs OR 2.5 mg nebulized x 1 dose. If effective (improved working of breathing, respiratory rate, wheezing, aeration) order scheduled albuterol 2-4 puffs with spacer or 2.5 mg nebulized q4h	Increased work of breathing
Prednisone or Methylprednisolone	1 mg/kg (maximum 40 mg/dose) PO/IV q12h x 5 days Followed by steroid wean to prevent rebound: 0.5 mg/kg (maximum 20 mg/dose) PO/IV q12h x 3 <u>days</u> 0.5 mg/kg (maximum 20 mg/dose) PO/IV q24h x 3 <u>days</u> 0.25 mg/kg (maximum 10 mg/dose) PO/IV q24h x 3 <u>days</u>	<u>Consider</u> in patients if wheezing/crackles/rales present or history of asthma
Ranitidine	1 mg/kg (maximum 150 mg/dose) PO q12h OR 1 mg/kg (maximum 50 mg/dose) IVq8h	GI prophylaxis for steroid use
Furosemide	0.5 – 1 mg/kg (maximum 40 mg/dose)	Consider if signs of fluid overload present

TABLE 4. PAIN MEDICATION

Medication	Dosing	Indication
Acetaminophen	Dose according to manufacturer’s recommendations Maximum daily dose 75 mg/kg/day or 4,000 mg/day	Temperature greater than or equal to 38.3°C
Ketorolac	0.5 mg/kg (maximum 30 mg/dose) IV q6h x 48 hours	Pain/Inflammation
Ibuprofen	10 mg/kg (maximum 600 mg/dose) PO q6 <u>after 48-hours of ketorolac completed</u> Maximum daily dose 2.4 g/day	Pain/Inflammation
Morphine	<u>Intermittent Dosing:</u> 0.1 – 0.15 mg/kg (maximum 8 mg/dose) IV x 1 dose followed by 0.05 – 0.15 mg/kg (maximum 4 mg/dose) IV q2-4hr <u>PCA Dosing:</u> PCA Dose: 0.01 – 0.02 mg/kg (maximum 10 mg/hr) with lockout of 8 minutes Continuous Rate: 0.03 – 0.05 mg/kg/hr	Pain
Hydromorphone	<u>Intermittent Dosing:</u> 0.015 – 0.02 mg/kg (maximum 2 mg/dose) followed by 0.015 – 0.02 mg/kg (maximum 1 mg/dose) q3-4hr <u>PCA Dosing:</u> PCA Dose: 2 – 3 mCg/kg (maximum dose 1.2 mg/hr) with a lockout of 1.2 mg/hr Continuous Rate: 3 – 5 mCg/kg/hr	Pain

DISCHARGE CRITERIA

- Improved pulmonary symptoms and documentation of adequate oxygenation on room air
- Negative cultures for greater than or equal to 24-48 hours if applicable
- Stable hemoglobin/hematocrit
- Taking adequate oral fluids and able to take oral medications if applicable
- Adequate pain relief, if needed, with oral analgesics
- Follow-up plans coordinated with sickle cell team
- Pulmonology follow up arranged

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