



Multisystem Inflammatory Syndrome in Children (MIS-C) with COVID-19

Key Article

Gottlieb M, Bridwell R, Ravera J, Long B. Multisystem inflammatory syndrome in children with COVID-19. *The American Journal of Emergency Medicine*. 2021; 49:148-152.

Background

- Multisystem inflammatory syndrome in children (MIS-C) is a condition among pediatric patients with coronavirus disease of 2019 (COVID-19), resulting in inflammation of a variety of organ systems, including the heart, lungs, brain, kidneys, gastrointestinal system, skin, and eyes.
- Overall the condition is rare, estimated to be approximately 322 patients/100,000 COVID-19 infected children, but has been reported across the globe.
- Onset is usually delayed from the initial infection – usually 2-6 weeks from the initial infection
- Median age: 7-11 years old
- Complications can be severe including cardiogenic or distributive shock

History and physical exam

- Clinical Presentation can vary and mimic inflammatory cardiovascular diseases such as Kawasaki disease (often in kids < 5 years old)
 - GI symptoms are common (60-100% of patients)
 - Other common symptoms include: lethargy, confusion and respiratory symptoms such as shortness of breath, cough, and sore throat
 - Critically ill patients can present with myocardial dysfunction (up to 55%), cardiogenic shock (66%), and multiorgan failure.
 - MIS-C has been labeled as a Kawasaki mimic (Both often present with fever), but there are some key distinctions:
 - MIS-C kids are often older (>7 years old), often have GI symptoms, have elevated inflammatory markers such as (CRP, D-dimer, ferritin), and commonly have low lymphocyte and platelet counts
 - Kawasaki disease kids are younger (< 5 years old), GI symptoms are NOT common, pts more commonly have leukocytosis and normal platelet counts, with a lower incidence of myocardial dysfunction and shock.
- Physical exam findings
 - Conjunctivitis and mucus membrane inflammation (up to 80% of patients)
 - Variable forms of a skin rash
 - Abdominal tenderness
 - Occasionally seizure, AMS, encephalopathy can occur (5-15% of patients)

Diagnostic testing

- Most pediatric emergency departments will have individual testing algorithms, but if you don't have one readily available, toxic-appearing or sick kids should have a:
 - CBC, CMP, ESR/CRP, coags, d-dimer, troponin, BNP, ferritin, fibrinogen, Procalcitonin and COVID testing (to confirm)
- Well-appearing but where MIS-C is of concern – 2 step approach is recommended by the American College of Rheumatology
 - **Step 1:** Obtain CBC, CMP, CRP, and ESR

- **If CRP ≥ 5 or ESR ≥ 40 ; PLUS Absolute lymphocyte count < 1.5 , PLT count $< 150k$, sodium < 135 , neutrophilia or hypoalbuminemia then**
 - **Step 2:** send full panel of tests above to include other inflammatory and cardiac tests
 - **High Inflammatory markers are common:** Up to 92% of patients with MIS-C will have at least 4 abnormal diagnostic blood tests
- Cardiovascular testing
 - EKG: Conduction blocks including AV and bundle branch blocks are common
 - CXR: can reveal cardiomegaly (up to 60% of patients) and pulmonary edema, pleural effusions, and occasionally ARDS.
 - Echocardiogram ordered on most patients (MIS-C patients are at risk for coronary artery aneurysms and myocarditis)
 - Reduced LVEF (45-60% of patients)
 - Pericardial effusions
 - Mitral regurgitation
 - Coronary artery diameters (not usually measured in adults)

Resuscitation and Management

- Initial management of the toxic appearing child will start similarly to managing the child with septic shock
 - IV fluid resuscitation
 - Broad spectrum antibiotics
 - Vasoactives to manage vasoplegia or cardiogenic shock
- **Early ultrasound can help distinguish vasodilatory vs. cardiogenic pathophysiology**
- **Critical difference in MIS-C treatment compared to sepsis resuscitation**
 - Intravenous immunoglobulin (IVIG) is considered first-line therapy
 - Dose: 2mg/kg/day divided in 3 doses for 10 days
- Steroids: Unlike adults, glucocorticoid treatment is less often used
 - Methylprednisolone (2mg/kg/day divided into twice a day dosing)
 - Usually given for 2-4 weeks
- Anticoagulation:
 - Therapeutic anticoagulation should be initiated (lovenox) if there is evidence of acute thrombosis, LVEF $< 35\%$, or evidence of coronary aneurysm on echo
 - Low dose aspirin (3-5 mg/kg/day; max 81 mg/day) is recommended for patients with a platelet count $\geq 450K$ or Kawasaki disease like features on echo
 - Avoid aspirin in patients with thrombocytopenia (PLT $< 80k$)
- **Disposition:** Transfer (to a specialty center)! Once stabilized.
 - As many as 60-80% of patients will require PICU admission

Final Points

- We've talked a lot about COVID over the past few months... much about adult resuscitation and care.
- Thankfully, COVID-19 has largely spared our younger patients but it is important that emergency physicians are able to identify this rare but life-threatening complication of a pediatric COVID infection.