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

Key Article

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)
  o GI symptoms are common (60-100% of patients)
  o Other common symptoms include: lethargy, confusion and respiratory symptoms such as shortness of breath, cough, and sore throat
  o Critically ill patients can present with myocardial dysfunction (up to 55%), cardiogenic shock (66%), and multiorgan failure.
  o 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
  o Conjunctivitis and mucus membrane inflammation (up to 80% of patients)
  o Variable forms of a skin rash
  o Abdominal tenderness
  o 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:
  o 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
  o 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 ≥ 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.