Multisystem Inflammatory Syndrome in a Child Associated with COVID-19

Mary Canders MD[1], Jesse Cheung MD[1], Maria Christina Tolentino DO[1]
[1]Pomona Valley Hospital Medical Center Family Medicine Residency Program, UCLA-Affiliated Program

Introduction

- Children who have COVID-19 generally have less severe symptoms, but detrimental effects are possible.
- Multisystem Inflammatory Syndrome in Children (MIS-C) is a rare and potentially life-threatening effect of COVID-19 infection.[1,2,3,4]
- Early recognition and treatment of MIS-C are crucial.

Case Presentation

HISTORY:

- 8-year-old healthy immunized female presented with:
  - 5 days of fever, lethargy, decreased appetite, dry cough, and full body rash.
  - 2 days of periumbilical abdominal pain, nausea, vomiting, diarrhea, and eye redness.
- Family member had COVID-19 3 weeks prior.

PHYSICAL EXAM:

- **Vitals:** T_{max} 39.6˚C (103˚F), RR 20-33, BP 77-91/35-55, HR 140-160, saturating 97-100% on room air.
- **General :** Appeared ill and fatigued.
- **HEENT:** Mucous membranes dry, erythematous cracked lips. Bilateral conjunctival injection, erythema and edema of upper and lower eyelids. No cervical lymphadenopathy.
- **Heart:** Sinus tachycardia. No murmurs, rubs, or gallops.
- **Lungs:** Clear, unlabored breathing.
- **Abdomen:** Normoactive bowel sounds, soft, no masses or organomegaly. Nondistended. Tenderness in RUQ, negative Murphy's sign. Negative Rovsing's and Obturator's signs. No rebound or guarding.
- **Extremities:** No edema, cyanosis, or clubbing.
- **Neuro:** AAOx3. Nonfocal.
- **Integumentary:** Erythematous, flat, non-blanching, warm, polymorphic rash, confluent on back, chest, extremities, and bilateral soles, and macular on neck and left cheek.

LABS AND IMAGING:

- **Serum:** WBC 10.6 / Plt 101 / BUN 16 / Cr 0.5 / ALP 340 / AST 52 / ALT 119 / T. bili 3.5 / Lipase 3 / ESR 28 / CRP 10.9 / Fibrinogen 544 / D-dimer 2138 / LDH 193 / Lactic acid 2.0 / Procal 7.84 / Troponin <0.03 / BNP 314
- **Urine:** Pregnancy and UA negative.
- **Imaging:** Abd US, CXR, CT abd/pelvis with PO + IV contrast all negative.
- **EKG:** Sinus tachycardia to 156.
- **Pending:** Respiratory swab, blood cultures.

Differential Diagnoses

- Acute appendicitis, Kawasaki Disease (KD), bacterial sepsis, toxic shock syndrome, Staph scalded skin syndrome, Hemophagocytic lymphohistiocytosis (HLH)/macrophage activation syndrome (MAS).

Treatment Course

- **ED:** Given 2 doses of Tylenol, 2 normal saline boluses, cefoxitin for empiric broad coverage and transferred for ICU-level care.
- **Hospital:** Admitted to the PICU in acute hypoxemic respiratory failure and decompensated shock and started on HFNC, dopamine and epinephrine drips, ceftriaxone and clindamycin, one dose of IVIG and aspirin. Echocardiogram showed LV dysfunction and RCA dilatation and milrinone was added. Antibiotics were stopped after blood and urine cultures were negative for 48 hours. COVID-19 serology and PCR were both positive. Methylprednisolone was added for 5 days given that patient continued to require vasopressor support and rheumatology was consulted. Anakinra was started.

	Kawasaki Disease (KD)	Toxic Shock Syndrome	MIS-C
Common Presenting Symptoms	Fever ≥5 days + ≥4 (complete) or 2-3 (incomplete): conjunctivitis, rash, adenopathy, strawberry tongue, hand/foot swelling	Fever, rash, hypotension, weakness, confusion, GI symptoms (esp diarrhea)	Fevers 1+ days, GI symptoms (abd pain, N/V, diarrhea), rash, conjunctivitis, mucus membrane involvement
Etiology	Vasculitis w/inflammatory dysregulation	Release of bacterial toxins	Inflammatory dysregulation, details TBD
Average Age	1-4yo	Any	9-13yo
Population Most Affected	Asian males	Menstruating females	Black and Hispanic, any gender
Cardiac Changes	Coronary artery (CA) abnormalities	Usually none	Decreased LV function, CA abnormalities

Table 1. Comparison of Kawasaki Disease, Toxic Shock Syndrome, and MIS-C.[1,2,5]

Outcome

- Patient fully recovered after 2-week hospital course. EKG and echocardiogram prior to discharge showed return of cardiac function.

Discussion

- MIS-C is rare, with reported incidence as low as 2/100,000.[1]
- Diagnosis requires age <21 years old with fever, lab evidence of inflammation, requiring hospitalization, with at least 2 organ system involvement; AND no alternative plausible diagnoses; AND positive for current or recent COVID-19 infection by RT-PCR, serology, or antigen test; or exposure to suspected or confirmed COVID-19 case within 4 weeks prior to the onset of symptoms.[2,3]
- The pathophysiology of MIS-C is currently not well understood.[1]
- Labs typically show lymphocytopenia, cardiac involvement with elevated troponin and/or BNP, and elevated inflammatory markers.
- Imaging often reveals lung consolidations, abdominal free fluid, adenopathy, and/or mesenteric inflammation, and depressed LV function and coronary artery abnormalities on echocardiogram.[2,4]
- Patients are managed similarly to Kawasaki disease with IVIG if they meet criteria for complete or incomplete KD.
- Epinephrine or norepinephrine are preferred for shock with steroids added if refractory. Milrinone can be added for LV dysfunction.
- Broad spectrum antibiotics should be started but stopped once bacterial infection is excluded. There is unclear benefit of antivirals (e.g. remdesivir), IL-1 inhibitors (Anakinra, canakinumab), IL-6 inhibitors (tocilizumab), and convalescent plasma.
- The minimum dose of aspirin should be given if features of Kawasaki Disease are present and systemic anticoagulation is recommended for the presence of LV dysfunction.[1,3]
- Prognosis is uncertain, with an estimated 1.7% death rate. Most patients regain cardiac function prior to discharge, however, long term effects are unknown.[1]

References

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