MedStar Health

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COVID-19

Multisystem Inflammatory Syndrome in Children (MIS-C)
ED Evaluation & Treatment

Situation: In the past 2 months during the COVID-19 pandemic there have been a small number of children who have developed a significant systemic inflammatory response possibly associated with SARS-CoV-2. The exact etiology is still being investigated.

Background: Recent reports from Europe and the US (NYC Detroit, Washington DC, and many others) describe a novel pediatric vasculitis notable for persistent fever and clinical features of Kawaski disease (KD) or toxic-shock syndrome (TSS) associated with rash and abdominal symptoms such as abdominal pain, vomiting, and/or diarrhea. Some patients have presented with a toxic shock-like picture, with or without cardiogenic shock, and required intensive care with respiratory and cardiac support. As a reminder, the major concerns with KD are the complications that include coronary aneurysms (causing thrombosis, MI, and cardiac tamponade), myocarditis, and bleeding due to aspirin.

This hyperinflammatory shock syndrome as described above was initially named Pediatric Multi-System Inflammatory Syndrome, (PMIS or PIMS) but the CDC has named it Multisystem Inflammatory Syndrome in Children (MIS-C). A possible association with COVID-19 is based on positive PCRs or antibody to SARS-CoV-2; however, it can occur in SARS CoV-2-PCR negative patients as well.

An Italian study in *The Lancet* (May 13, 2020) noted that pediatric patients with MIS-C were older in age (2-16 years w/an average age of 7.5 years), had more cardiac involvement prior to COVID-19 outbreak, and more often presented in shock compared to those diagnosed with KD. The CDC issued a health alert on May 14, 2020 with the case definition for MIS-C and a recommendation that providers who have cared for or are caring for patients younger than 21 years with MIS-C should report cases to their local, state, or territorial health department. Case definitions may vary between health organizations and health departments. Below is the CDC's latest case definition.

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Case Definition for Multisystem Inflammatory Syndrome in Children (MIS-C)

- An individual aged <21 years presenting with fever[i], laboratory evidence of inflammation[ii], and evidence of clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); **AND**
- No alternative plausible diagnoses; **AND**
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms

[i]Fever ≥38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours
[ii]Including, but not limited to, one or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin

Additional comments

- Some individuals may fulfill full or partial criteria for Kawasaki disease but should be reported if they meet the case definition for MIS-C
- Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection

Assessment Patients with MIS-C may not meet all criteria for KD and diagnosis is not limited to patients with complete or incomplete KD-like presentations. Some patients may present in fulminant shock with hypotension, but children may also present with milder disease. Consider a broad range of diagnoses, evaluate, and treat appropriately.

Signs and symptoms: persistent and often high fever, abdominal pain, vomiting, and/or diarrhea. Variable but may include rash, mucous membrane changes (lips, tongue, o/p, non-purulent conjunctivitis). Signs of possible cardiogenic shock respiratory compromise, tachycardia, hypotension, JVD, gallop, poor perfusion.

Laboratory values: Evidence of dehydration and/or shock, end-organ dysfunction w/abnormal liver enzymes, elevated BUN/creatinine, elevated troponin and BNP, elevated CRP, ESR, WBC, increased ferritin; evidence of lymphopenia and coagulopathy.

Recommendation: Patients may initially look well but rapidly deteriorate. It is best to admit/transfer these patients to a pediatric tertiary care hospital even if they are well appearing.

Please note MGUH is not admitting these patients currently. MGUH PICU and Peds ID on call (contact hospital operator at 202-444-7243) are available for discussion as well as the

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Emergency Department team at Children's National Medical Center (CNMC Lifeline 202-476-5433).

For pediatric patients evaluated at MHH, MGSH, MUMH, MFSMC, refer to the following institutions: Greater Baltimore Medical Center (GBMC), Sinai, University of Maryland Medical Center (UMMC), Johns Hopkins Children's Center (JHCC) or John's Hopkins Bayview.

Plan of Care:

- Place on COVID-19 isolation precautions
- Obtain COVID-19 PCR NP (rapid testing) and RVP (if unable to be performed then send rapid RSV and rapid influenza)
- Blood cultures x 2 (may need more if multi-lumen catheter)
- UA/Ucx
- CSF culture and studies if primary neurological presentation
    - Cover empirically with IV clindamycin, vancomycin, and ceftriaxone
- CBC/diff, CMP, Triglycerides, LDH, Ferritin, CRP, ESR, Procalcitonin, Troponin, BNP, PT/INT, aPTT, Fibrinogen, D-Dimer
- Chest x-ray
- EKG
- Echocardiogram, if available
- Consider sending cytokine panel; SARS CoV-2 antibody panel; urine random protein to creatinine ratio; stool sample
- If TSS and evidence of cardiogenic shock, consider limiting fluid resuscitation
    - If undifferentiated shock, start with 10 cc/kg vs. 20 cc/kg NS bolus. Re-evaluate after each bolus for worsening clinical status, respiratory compromise, worsening tachycardia, new crackles or rales on lung exam, descending liver edge, worsening hypotension, poor perfusion, or new gallop
    - If vasopressors are needed, consider norepinephrine.

Evaluation & treatment after admission/transfer will include specialty evaluation by pediatric cardiology and pediatric infectious disease. Treatment may include IVIG, aspirin, and/or steroids and other therapeutic agents such as immunomodulatory therapies and/or anti-viral agents and/or other experimental therapies. Coordinate with the accepting hospital and available specialists to determine whether therapy should be initiated prior to transfer.

Sources:

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1. CDC Health Advisory: Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease 2019. May 14, 2020.
2. WHO Scientific Brief: Multisystem inflammatory syndrome in children and adolescents with COVID-19. May 15, 2020.
3. "An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study." Verdoni L, et al. *The Lancet.* May 13, 2020.
4. Mass General for Children's Pediatric Screening and Referral Guideline for COVID-19 Multisystem Inflammatory Syndrome. May 14, 2020.
5. Children's National Medical Center MIS-C Taskforce Guidelines for Initial Evaluation and Management of Multisystem Inflammatory Syndrome in Children (MIS-C). May 15, 2020
6. "Ask the Expert: What are the presenting signs and symptoms in children with COVID-19 Disease". Meissner, Cody. AAP News. May 11, 2020