UMMC GUIDANCE FOR MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C) VERSION 2

Note: Guidance is based on expert consensus. Subspecialty consultation for individualized recommendations for suspected cases is strongly recommended.

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

- A patient aged <21 years presenting with fever, laboratory evidence of inflammation, 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 recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within 4 weeks prior to the onset of symptoms

COMMENTS:
- Fever >38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours
- Evidence of inflammation: an elevated CRP, ESR, fibrinogen, procalcitonin, d-dimer, ferritin, lactate dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin
- Some individuals may fulfill full or partial criteria for Kawasaki disease but should be reported (MSDH at 601 576 7725) if they meet the case definition for MIS-C
- Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection

* (https://emergency.cdc.gov/han/2020/han00432.asp)

INITIAL LABS AND DIAGNOSTICS

*Figure 1 below used with Copyright License: https://www.rheumatology.org/Portals/0/Files/ACR-COVID-19-Clinical-Guidance-Summary-MIS-C-Hyperinflammation.pdf

Figure 1. Diagnostic Pathway for MIS-C

An epidemiologic link to SARS-CoV-2 infection is defined as a child with ANY of the following criteria: positive SARS-CoV-2 polymerase chain reaction (PCR), positive SARS-CoV-2 serologies, preceding illness resembling COVID-19, or close contact with confirmed or suspected COVID-19 cases in the past 4 weeks.

1. Rash, polymorphic, maculopapular, or petechial, but not vesicular; GI symptoms, (diarrhea, abdominal pain, or vomiting); oral mucosal changes, (red and/or cracked lips, strawberry tongue, or erythema of the oropharyngeal mucosa); conjunctivitis, (bilateral conjunctival injection without exudate); neurologic symptoms, (altered mental status, encephalopathy, focal neurologic deficits, meningismus, or papilledema).
2. Complete metabolic panel: Na, K, CO2, Cl, BUN, Cr, glucose, Ca, albumin, total protein, AST, ALT, ALP, Bilirubin.
3. Send procalcitonin and cytokine panel, if available.
4. If not sent in tier 1 evaluation, if possible, send SARS-CoV-2 IgG, IgM, IgA.

INITIAL INPATIENT CONSULTS

- All children admitted with concern for MIS-C: Peds ID, Peds Cardiology*, Peds Rheumatology, Peds Hematology
- If with concern for thrombosis/HLH/MAS: Peds Heme/Onc and Peds Rheumatology
- If with severe abdominal pain: Peds GI, Peds Surgery
- If with neurologic findings: Peds Neurology
- Additional consults based on presenting symptoms and clinical indications (Peds Nephrology, Peds Neurology, Dermatology)

*Please note Pediatric Cardiology UMMC Guidelines for MISC posted also at this website
PRELIMINARY MANAGEMENT PLANS FOR MIS-C

Therapeutic Categories:
- Steroid Initial Dosing – the use of steroid should be discussed with Peds Rheumatology
- Immunosuppressors – the use of anakinra or other biologics for refractory illness course should be discussed with Peds Rheumatology and Peds Heme Onc
- Anticoagulation – the use of LMWH or other anticoagulation regimen should be discussed with Peds Heme Onc
- GI prophylaxis with PPI – while on steroid c/o primary team
- Steroid taper – with subspecialty consultation Peds Rheumatology

IVIG
- All children meeting MIS-C criteria or with coronary ectasia should receive IVIG 2g/kg after subspecialty discussion
- If 2-19 years of age should dose per IBW if actual body weight is > IBW by 20%. (and adults with BMI >30kg/m2)
- Steroids should be considered also and discussed with Peds Rheum and Peds ID

OTHER MANAGEMENT CONSIDERATIONS
- Antibiotics: Ceftiraxone (alternative, cefazidime) should be used as first-line empiric antibiotic coverage.
  - Add vancomycin if concerned for MRSA infection, including skin or soft tissue source, pneumonia, Gram positive bacteremia
  - Add meropenem if concerned for intra-abdominal infection.
  - Use cefepime (alternative, meropenem) for patients who are immunocompromised, have a history of multi-drug resistant gram-negative bacterial infections, are critically ill, or if otherwise clinically indicated.
  - Consider further coverage for toxic shock syndrome or Rickettsia infection depending on patient presentation.
- Anticoagulation: Please consult Heme/Onc to discuss. Please consider contraindications to anticoagulation (i.e., patients w/ PLT <30,000-80,000/uL, active bleeding, or significant bleeding risk). In general low dose ASA 3-5 mg/kg/day should be given until normalization of platelet count and confirmed normal coronaries at >/= 4 weeks after diagnosis. Enoxaparin should be considered also as prophylaxis/treatment (treatment dosing considered with coronary artery aneurysms with z score >/=10 or patients with documented thrombosis or an ejection fraction <35%).
- Patients with GI Symptoms: These patients have higher risk of bowel perforation with pulse steroids. Consider risk/benefit of therapy in these patients.
- Patients with Renal Injury: Consult Peds Nephrology and pediatric pharmacy for assistance in dosing medications.

ORGAN-SPECIFIC WORK-UP BASED ON PATIENT SYMPTOMS

Dermatologic: Take photo of rash/upload to Epic, Consider the following tests (HSV, VZV, enterovirus PCR); GI: Consider GI pathogen PCR panel; C difficile toxin PCR; Stool culture; Neurologic: Head imaging – consider if with focal neurologic deficit, altered mental status, seizure, severe headache with meningeal signs. If no contraindications, perform lumbar puncture (cell count, protein, glucose, culture, meningoencephalitis panel) AND CONSULT NEUROLOGY

FOLLOW-UP INPATIENT LAB & IMAGING

PICU
- Cardiac enzymes & BNP – every 48 hours (trend daily if abnormal)
- 12L ECG every 1-2 days
- ECHO – timing– discuss with Peds Cardiology

General Pediatric Floor
- Cardiac enzymes & BNP – weekly (trend daily if abnormal)
- 12L ECG every 2 days
- ECHO –discuss with Peds Cardiology
- Discuss with Peds Rheumatology regarding daily labs (CBC diff, CMP, ferritin, fibrinogen, D-dimer, triglycerides) for patients concerning for cytokine storm
- Clinical change or abnormal trends/other labs warrant further evaluation to be determined by primary team

DISCHARGE FOLLOW UP
- Steroid taper plan should be determined and clarified with Pediatric Rheumatology.
- Ensure that plan for discharge ASA and enoxaparin are clear with Cardiology and Hematology and the parent. (e.g., if patient needs ASA if it is not given as an RX (tell the parents they have to get it separately).
- Consider GI protective agent as many patients will be going home on ASA and steroid weans.
- All patients should have follow-up within 2 weeks post discharge with Pediatric Cardiology, Pediatric Infectious Disease (Dr C. Hobbs), Pediatric Rheumatology, and Pediatric Hematology (e mail Dr C. Gordon) for clinical evaluation, repeat echocardiogram. ALL APPOINTMENTS SHOULD BE MADE PRIOR TO DISCHARGE.
- Exercise should be LIMITED until outpatient Cardiology appointment clears the child for resumption of activity
- Live vaccines are not to be administered within 11 months of IVIG due to decreased potential efficacy.
- Consider influenza shot (killed vaccine) if due, but ideally at least 1 month after cessation of steroids.
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LAST GUIDANCE UPDATE: MARCH 2021

Suggested readings and additional online resources for specialists caring for children with MIS-C:


