Guideline: Management of MIS-A secondary to COVID-19, Inpatient

Clinical algorithm:

Hospitalized patient with confirmed prior COVID-19 infection

- Fever > 38.5 for ≥ 3 days with no alternative explanation (i.e., infection – may need to consult ID for broad workup if ongoing fever)
- AND evidence of multi-system inflammation with the presence of ≥ of the following:
  - Cardiac abnormality (arrhythmia, elevated troponin, L or R ventricular dysfunction)
  - Gastrointestinal abnormality (abdominal pain, vomiting, diarrhea)
  - Dermatologic abnormality (rash, mucositis, etc.)
  - Neurologic abnormality (altered mental status, encephalopathy)

Consider MIS-A and order recommended initial lab workup

MIS-A Recommended Initial Labs:
- CBC with manual differential
- CMP
- ESR
- CRP
- D-dimer
- Fibrinogen
- HS-Troponin
- EKG
- Ferritin
- COVID-19 IgG antibody

(See Table 1 for interpretation in the setting of vaccination.)

Labs within concerning threshold?

- No
  - Consider alternative diagnosis
- Yes
  - Consider MIS-A – See suggested interventions below

MIS-A Daily Monitoring Labs:
- CBC with manual differential
- CMP
- ESR
- CRP
- D-dimer
- Fibrinogen
- Ferritin

Lab Threshold for Concern:
- Absolute Lymphocyte Count < 0.5 k/uL
- Albumin < 2 g/dL
- CRP > 100 mg/L
- D-dimer > 3000 ng/mL
- HS-Troponin > 30 ng/mL
- Ferritin > 350 ng/mL

NOTE: Data on the diagnosis and management are largely based on case reports, case series, and data extrapolated from MIS-C.

These recommendations are based on expert opinion and are subject to interpretation.
Clinical guideline summary

CLINICAL GUIDELINE NAME: Multisystem Inflammatory Syndrome in Adults, Inpatient

PATIENT POPULATION AND DIAGNOSIS: Adult inpatients

APPLICABLE TO: Adult inpatients, SHGR and regional sites

BRIEF DESCRIPTION: The purpose of this document is to provide guidance for the management of patients with suspected multi-system inflammatory syndrome in adults (MIS-A) secondary to infection with SARS-COV-2 until further information becomes available from the Centers for Disease Control and Prevention (CDC) and/or World Health Organization (WHO).

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OWNING EXPERT IMPROVEMENT TEAM (EIT): COVID-19 EIT

MANAGING CLINICAL PRACTICE COUNCIL (CPC): Clinical Excellence Council

CPC APPROVAL DATE: 6/24/2021

OTHER TEAM(S) IMPACTED: Nursing, adult hospital medicine, adult emergency department.

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Clinical pathways clinical approach

TREATMENT AND MANAGEMENT:

1. All patients with MIS-A should be evaluated for DVT prophylaxis. Therapeutic anticoagulation should be given for patients with proven or highly suspected of thrombosis.
2. Hemodynamic support and supportive care should be used for all MIS-A patients.
3. Patients with presumed MIS-A should have an ECHO performed for cardiac evaluation.
4. For patients with presumed MIS-A, please notify SH Infection Prevention via one of the following methods:
   a. Email: infeccont@spectrumhealth.org
   b. Phone: 616-391-1407
   c. Perfect Serve: Infection Prevention GR
5. Consider treatment with corticosteroids & IVIG if treating provider feels the benefits outweigh risks for patients with severe disease that are not improving with supportive care; some specific agents with recommended dosing are listed below.
   a. Very limited data support the use of these therapies for MIS-A. Most are extrapolated from case series, MIS-C, and similar disease states like Kawasaki’s disease in children.
b. Some patients that are not responding to the below interventions may benefit from additional immunomodulatory therapies like the IL-1 antagonist, Anakinra. Consider consultation to Rheumatology to discuss.

**Corticosteroids:**

1. Methylprednisolone has been described as the more commonly utilized corticosteroid in the treatment of MIS-A in case reports. Alternative corticosteroids for COVID-19 patients may be used at the discretion of the treating provider.
   a. MIS-A Dosing: 1 mg/kg twice daily
      i. Note: dose may need to be adjusted for patients already on corticosteroid therapy
   b. Duration: Clinical improvement, consider tapering over 2-4 weeks.

**IV Immunoglobulin:**

1. IVIG may be considered for use if patients requiring ionotropic and/or hemodynamic support that do not respond to steroid therapy after 24 hours
2. MIS-A Dosing: 2mg/kg (use ideal body weight unless actual body weight is less than ideal, then use actual. Round IVIG dose to nearest 5 gm to accommodate vial size) IV (max = 100 grams) x once

| Table 1 – SARS-CoV-2 Antibodies Natural vs Vaccinated Antibody Response |
|------------------------|------------------------|--------------------------------------------------|
| Anti-spike IgG neg     | Anti-nucelocaspid IgG neg | No immunity from prior COVID-19 infection or vaccine |
| Anti-spike IgG pos     | Anti-nucelocaspid IgG neg | Vaccine-associated immunity or immunity from prior COVID-19 infection |
| Anti-spike IgG neg     | Anti-nucelocaspid IgG pos | Immunity from prior COVID-19 infection |
| Anti-spike IgG pos     | Anti-nucelocaspid IgG pos | Immunity from prior COVID-19 infection plus possible vaccine-associated immunity |

**References:**
