Multisystem inflammatory syndrome in children (MIS-C) with COVID-19 infection

EBM Guidelines
13.9.2021 • New article
Heikki Tuikkala

Essentials

- In children, the COVID-19 infection caused by the SARS-CoV-2 virus causes mostly mild symptoms or even none. Most patients only have mild upper respiratory tract symptoms.
- Nevertheless, paediatric patients have been described with a rare and serious inflammatory syndrome associated with COVID-19 infection. In the international literature, the syndrome usually goes by the abbreviation MIS-C (Multisystem Inflammatory Syndrome in Children).
- Its symptoms resemble those of Kawasaki disease . It involves serious cardiovascular symptoms, and patients often need intensive care.
- The pathophysiology is unclear but the syndrome is believed to be due to an abnormally delayed immune response to COVID-19 infection.

Epidemiology

- MIS-C is a rare syndrome developing in less than 1% of children about 3–5 weeks after COVID-19 infection.
  - In a US study, its incidence in patients below 21 years of age was estimated at about 2/100 000.
- MIS-C is more common in older children (median age 9 years) compared to Kawasaki disease where 80% of patients are below 5 years of age.
- The children developing the syndrome are usually basically healthy.

Symptoms and findings

- A multisystem disease where 90% of patients develop symptoms in four or more organ systems.
- In addition to prolonged high fever, the most common findings include
  - abdominal pain
  - vomiting
  - rash
  - diarrhoea
  - conjunctival injection.
- Respiratory symptoms are clearly rarer than in COVID-19 infections requiring hospital treatment.
- 80% of patients with the syndrome have cardiovascular findings, such as cardiac failure, shock, pericarditis, myocarditis or changes in coronary arteries.
  - It should be noted that half of the patients have hypotension and one in three have symptoms of shock.
- Laboratory findings are consistent with a severe inflammatory reaction.
  - Of inflammatory markers, CRP and IL-6, and cardiac enzymes, such as troponin (TnI, TnT) and BNP/proBNP, are considerably elevated.
  - In addition, thrombocytopenia and lymphocytopenia are common.

Diagnostic criteria

- WHO criteria for MIS-C (all six must be fulfilled)
  1. Age 0–19 yrs
  2. Fever for at least 3 days
  3. Evidence of a multisystem disease (with at least 2 of the following 5 findings)
     a. Rash, non-purulent conjunctival injection or muco-cutaneous inflammation signs in hands, feet or oral mucosa

b. Hypotension or shock
c. Cardiac involvement, such as pericarditis, valvulitis or coronary abnormalities (ultrasound finding or elevated cardiac enzyme levels)
d. Coagulopathy (APTT, prothrombin time, d-dimer).
e. Gastrointestinal symptoms (diarrhoea, vomiting, abdominal pain)

4. Elevated inflammatory markers (CRP, ESR, or procalcitonin)
5. No other explanatory infection (such as sepsis, toxic shock syndrome)
6. Evidence of SARS-CoV-2 infection (PCR, serology or positive antigen test or contact with a patient with COVID-19)

Workup and treatment

- The children are very sick and always require hospital treatment and investigations. Half of the patients need intensive care.
- All of them need echocardiography and close follow-up of haemodynamics.
- The treatment follows the lines of treatment of Kawasaki disease.
  - Patients are given high-dose intravenous immunoglobulin, often with a glucocorticoid.
  - In addition, pharmacotherapy is often needed for circulatory support.

Prognosis

- The prognosis is mostly good, and most children recover well.
- Mortality has been 1–2%.
- The long-term consequences of severe disease are unknown, and follow-up studies are needed.

References

1. Belay ED, Abrams J, Oster ME et al. Trends in Geographic and Temporal Distribution of US Children With Multisystem Inflammatory Syndrome During the COVID-19 Pandemic. JAMA Pediatr 2021;175(8):837-845. PubMed
2. Multisystem inflammatory syndrome in children and adolescents with COVID-19. Scientific Brief. WHO 15.5.2020 1

Last reviewed as up-to-date 13.9.2021 • Latest change 13.9.2021
Article ID: ebm01187 (029.088)