

A Review of Multisystem Inflammatory Syndrome Cases in Coronavirus Disease-19 Infection

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is responsible for more than 6 million cases worldwide, as of June 1, 2020; a condition characterized by mild-to-severe symptoms ranging from fever, cough, muscle aches to shortness of breath, pneumonia, and chest pain. COVID-19 has spread internationally causing a global pandemic involving 216 countries. At present, nucleic acid-based tests by real-time reverse transcription-polymerase chain reaction (RT-PCR) and serological based tests are available to test for COVID-19. There are no drugs, vaccines, or other therapeutics available to prevent and treat COVID-19. The purpose of this case review is to assess cases of children and adolescents who were positive for COVID-19 and presented with the multisystem inflammatory syndrome.

Key words: Coronavirus disease-19, Cytokine storm, Kawasaki disease, Multiple organ dysfunction syndromes, Multisystem inflammatory syndrome, Sepsis, Severe acute respiratory syndrome coronavirus 2, Toxic shock, Vasculitis

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus which causes coronavirus disease (COVID-19), a present-day illness that is responsible for more than 6 million cases worldwide, as of June 1, 2020.^[1] The virus is linked to the same family of coronaviruses that cause the common cold and SARS-CoV-1.^[2] Symptoms range from a mild-to-severe illness which includes but are not limited to flu-like symptoms, the development of pneumonia, persistent or new chest pain, confusion, and blue lips or face.^[3]

There are several emerging cases suggesting a multisystem inflammatory syndrome in children (MSI-C) <18 years of age that is related to COVID-19.^[4] The exact case definition is yet to be established; however, it displays features similar to that of Kawasaki disease (KD) and toxic shock syndrome.^[5] Diagnosis of MSI-C can be made in children and adolescents

aged 0–19 years who are confirmed COVID-19 cases with the use of real-time reverse transcription-polymerase chain reaction (RT-PCR), a positive antigen and/or serology test, who present initially with fever for ≥ 3 days and elevated inflammatory markers with no definitive microbial cause of inflammation or infection, in addition to any two of the following symptoms: Rash or non-purulent conjunctivitis; mucocutaneous inflammation of oral cavity, hands or feet; hypotension or shock; myocardial infarction; pericarditis; valvulitis or coronary abnormalities; coagulopathies; diarrhea; vomiting; or abdominal pain.^[5] The purpose of this case review article is to assess cases of COVID-19 presenting with MSI-C.

CASE REPORTS

Case one

A 12-year-old female with no prior medical history presented with a 5-day history of fever and non-productive cough,

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a 2-day history of non-bloody emesis, hematuria, and worsening shortness of breath. The child's temperature was 39.6°C, pulse 129 beats/minute, respiratory rate 26 breaths/minute, and oxygen saturation 89% in room air on presentation. Her weight was 60 kg and her body mass index was 25 kg/m². Physical examination (PE) showed that she was dyspneic, had diminished breath sounds, and petechiae. Bilateral diffuse airspace opacities and small pleural effusion were demonstrated on chest X-ray (CXR). Laboratory investigations revealed severe macrothrombocytopenia, lymphopenia, and elevated inflammatory markers. The following were obtained from her hospitalization record.^[6]

- Hospital day (HD) 1: Intubation and mechanical ventilation on 100% oxygen, inhaled nitric oxide (iNO) and empiric antibiotics, intravenous immunoglobulin (IVIG) (1 g/kg per dose)
- HD 2: IVIG administered along with methylprednisolone (1.5 mg/kg) + azithromycin (AZT)
- HD 3: AZT
- HD 4: AZT; positive SARS-CoV-2 RT-PCR even though the patient had no known exposure to COVID-19 cases or recent travel history; hydroxychloroquine (400 mg) twice a day (BID)
- HD 5-6: Hydroxychloroquine (200 mg BID)
- HD 7: Hydroxychloroquine (200 mg BID); two doses of tocilizumab (8 mg/kg every 12 h); humanized monoclonal interleukin-6 antibody; changed to airway pressure release ventilation; remdesivir (200 mg)
- HD 8: Weaned off iNO
- HD 8–12: Remdesivir (100 mg)
- HD 14: Extubated
- HD 24: Discharged; inpatient rehabilitation stay.

Case two

An obese 10-year-old previously healthy African-American male, presented with hypotensive shock after 7-days of fever, vomiting, and severe abdominal pain. PE revealed a toxic male, tachypneic with a respiratory rate of 39, tachycardic with a heart rate of 117 beats/minute, and systolic hypotension 85 mmHg, despite a crystalloid volume bolus (20 mL/kg) that was administered during pre-hospital care. The patient's lactate concentration was mildly elevated (2.8 mmol/L). The adolescent was given volume resuscitation (a total of 50 mL/kg of crystalloids), septic workup was done, broad-spectrum antibiotic therapy and a vasopressor were administered. Laboratory findings revealed elevated inflammatory markers with lymphopenia and multiple organ dysfunction syndrome, with acute renal failure and cholestasis. Computerized tomography scan identified diffuse bilateral consolidations and mesenteric lymphadenitis. SARS-CoV-2 infection was confirmed serologically. His respiratory status further deteriorated, requiring intubation. Treatment was started with hydroxychloroquine and AZT; due to suspicion of a cytokine

storm, anakinra was also given. Subsequently, the patient's renal function also deteriorated, requiring hemodialysis. On day 8 of hospitalization, echocardiography showed the left anterior descending artery and right coronary aneurysms. The patient remained in hospital admission but was transferred out of the intensive care unit.^[7]

Case three

A 6-month-old, full-term, previously healthy, and immunized female presented to the pediatric urgent care facility with a 1-day history of fever, fussiness, and refusal to eat. PE revealed a fussy infant with a temperature of 38.8°C and no focal signs of infection. The following report was noted based on the infant's days of fever (FD).^[8]

- FD 1: Diagnosed with a viral infection and was sent home
- FD 2: Erythematous, non-pruritic, blotchy rash
- FD 4: Return to the clinic with fever, persistent rash, and possible mild congestion; the temperature was 38.3°C, there was sinus tachycardia (200 beats/minute), and tachypnea with an oxygen saturation of 100%; PE showed an irritable child, with limbic sparing conjunctivitis, dry cracked lips, and mild subcostal retractions. Laboratory investigations revealed a left shift in the white blood cell count with bandemia, normocytic anemia, elevated inflammatory markers, hyponatremia, and hypoalbuminemia; CXR showed a faint opacity in the left midlung zone; patient admitted to the pediatric unit
- FD 5: Limbic sparing conjunctivitis, prominent tongue papillae, maculopapular rash, and swelling of the hands and lower extremities, thus diagnosed with KD; treated with a single dose of 2 g/kg IVIG and 20 mg/kg 4 times daily of high-dose acetylsalicylic acid (ASA); RT-PCR testing for COVID-19 was positive, was discharged and instructed to self-quarantine for 14-days while on a low-dose ASA (3 mg/kg daily) with plans to follow-up with a pediatric cardiologist for a repeat echocardiographic evaluation 2-weeks after discharge.

DISCUSSION

COVID-19, which was first diagnosed in November 2019 in China, has spread internationally causing a global pandemic affecting 216 countries.^[9] According to the World Health Organization (WHO), as of June 1, 2020, there are 6,057,853 COVID-19 positive cases, and 371,166 confirmed deaths worldwide due to this virus.^[9]

COVID-19 presents with a wide range of mild-to-severe symptoms such as fever, cough, muscle aches, gastrointestinal distress such as diarrhea, headaches, and shortness of breath to pneumonia.^[10] All patients in a prospective observational study presented with gastrointestinal symptoms; diarrhea was seen in 100% (17/17) of the cases in the early stage

of illness, along with high levels of inflammatory markers and fever.^[10] Whereas, in another observational cohort study, only 40% of the children had diarrhea, but fever and muscle aches were noticed in all patients from their group.^[11] Furthermore, 100% of the patients (3/3) in case study 2 presented with fever, difficulty in breathing, and gastrointestinal distress.^[11] Even though COVID-19 can start as an asymptomatic disease, the patient can progress to a hypoxic state.^[11] Due to COVID-19 being a relatively new and understudied disease, available information is limited and more research is needed in this regard.

Presently, nucleic acid-based tests RT-PCR and serological based tests are available to test for COVID-19.^[11] Approximately 82% of patients with KD in the prospective observational study had evidence of a recent SARS-CoV-2 infection, testing positive using RT-PCR (7/17) and positive for IgG and IgM with antibody detection test (14/16).^[10] Nasopharyngeal and oropharyngeal swab sampling for SARS-CoV-2 was positive in 2 of 10 (20%) patients in the observational cohort study from Group 2 and serology for SARS-CoV-2 antibodies showed IgG-positive results for 8 of the 10 (80%) patients.^[11]

Currently, there are no drugs or other therapeutics approved by the U.S. Food and Drug Administration (FDA) for the prevention or treatment of COVID-19. Furthermore, there is no vaccine to prevent COVID-19, but researchers are racing to create one as soon as possible. However, symptoms may be relieved with some medications, such as using pain relievers (ibuprofen or acetaminophen), corticosteroids, cough syrup, rest, and by increasing fluid intake.^[12] Three patients in the prospective observational study received corticosteroids (2–10 mg/kg/day), and broad-spectrum antibiotics were administered to 14-patients (82%).^[10] In the other observational cohort study, 100% of the patients were treated with aspirin plus methylprednisolone (2 mg/kg per day) for 5-days, followed by tapering of methylprednisolone for over 2-weeks.^[11] The FDA has also granted permission to use two malaria drugs (hydroxychloroquine and chloroquine), to treat severe COVID-19 cases when no other options are available, and an antiviral drug; remdesivir, has also been approved for this use.^[12] A 14-day quarantine, use of face masks, and handwashing are advised for everyone to prevent the spread of this virus.^[12]

CONCLUSION

Since November 2019, COVID-19 has been wreaking havoc across the globe. Classically, most patients present with very mild symptoms and others may be asymptomatic. The severe cases often result in high fever, cough, and ultimately pneumonia. The symptoms for COVID-19 are still evolving with new symptoms such as anosmia, ageusia, and gastrointestinal distress being reported. The newest set of symptoms seems to be affecting children and the adolescent

group (0–19 years of age). The cases above give insight into the presentation of COVID-19 infection in various children and adolescent groups. These groups presents with a positive COVID-19 test along with a rash or non-purulent conjunctivitis; mucocutaneous inflammation of oral cavities, hands, or feet; hypotension or shock; they may also present with myocardial infarction, pericarditis, valvulitis, or coronary abnormalities; and coagulopathies, in addition to the classic COVID-19 symptoms. The etiology of this syndrome is yet to be defined, but these symptoms should be added to the list of symptoms associated with COVID-19. The health workers and the general public need to be aware of this information to enable individuals to identify those who may have this disease as early as possible, to avoid further spread of the disease in the community.

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