

Multisystem Inflammatory Syndrome Following COVID-19: A Rare Presentation in Adults

VIRENDRA KR GOYAL*, JITESH AGGARWAL†, BHARAT GUPTA‡

ABSTRACT

Background: A growing number of reports from around the world has described a severe inflammatory syndrome in children similar to Kawasaki's disease. This syndrome has been named multisystem inflammatory syndrome in children (MIS-C). There have been anecdotal reports of MIS-C-like illness in young adults in their early twenties as well. We present the case of a healthy 33-year-old woman who developed coronavirus disease 2019 (COVID-19) with clinical characteristics resembling MIS-C, a rare form of COVID-19 described primarily in children under 21 years of age. **Case presentation:** The patient presented with abdominal pain, loose motions, difficulty in breathing since 3 days and fever since 1 day. She was otherwise healthy, with no prior medical history. Her hospital course was notable for leukocytosis, bradycardia, acute heart failure (myocarditis) and pulmonary edema. MIS-C like illness secondary to COVID-19 was suspected due to presentation of myocarditis, bradyarrhythmia and pulmonary edema. She improved after giving IV steroids, diuretics, anticoagulation and supportive care and was discharged on hospital Day 5. **Conclusion:** MIS-C like illness should be considered in adults presenting with atypical clinical findings and concern for COVID-19. Further research is needed to support the role of IVIG and aspirin in this patient population.

Keywords: COVID-19, multisystem inflammatory syndrome in children, myocarditis

Coronavirus disease 2019 (COVID-19) is increasingly recognized to have a protean range of clinical manifestations in adults, from respiratory illness to hyperinflammatory and coagulative complications, as well as a broad-spectrum of disease severity. When the epidemic began in China in late December 2019, case reports of pediatric illnesses were absolutely rare, and almost all children had mild clinical courses. However, a growing number of reports from the United Kingdom, Italy, the United States and elsewhere has now described a severe inflammatory syndrome in children similar to Kawasaki's disease, a vasculitic illness of unclear etiology originally described in Japan in 1967. This syndrome has

been named multisystem inflammatory syndrome in children (MIS-C). Case series of MIS-C have described multisystem organ involvement including the mucocutaneous, cardiac, gastrointestinal (GI) and respiratory systems. The mortality rate of MIS-C appears to be low, though severe illness is common and a number of fatalities in children have been reported. Anecdotal reports of MIS-C-like illness have been reported in young adults in their early twenties, raising concern that this rare presentation of COVID-19 may also have some penetrance into younger adult age groups. Herein, we describe a unique case report of MIS-C-like illness in a young adult with COVID-19.

CASE PRESENTATION

A 33-year-old previously healthy woman presented to us in emergency department at GBH General Hospital, Udaipur on 28th May, 2021 with the chief complaints of abdominal pain, loose motions, difficulty in breathing since 3 days and fever since 1 day. She was diagnosed with COVID-19 infection on 17th May, 2021. After taking treatment at home, patient was asymptomatic on 25th May, 2021. She was a nonsmoker, nonalcoholic and didn't use recreational drugs. She was not on any chronic medications and had no known allergies.

*Professor and Head

†Assistant Professor

Dept. of Medicine

‡Assistant Professor

Dept. of Radiology

American International Institute of Medical Sciences (AIIMS), Udaipur, Rajasthan

Address for correspondence

Dr Virendra Kr Goyal

Professor and Head, Dept. of Medicine

American International Institute of Medical Sciences (AIIMS), Udaipur, Rajasthan

8 Faculty Quarter, AIIMS, Bedwas, Udaipur - 313 001, Rajasthan

E-mail: virendra601@yahoo.co.in

On presentation, she was running a fever of 100.4°F, pulse rate varied from 56 to 64 beats per minute, blood pressure of 100/60 mmHg, oxygen level of 91% without oxygen therapy. She appeared ill. On auscultation, patient had bilateral fine crepitations involving lower lobes of the lungs suggestive of heart failure. Cardiac auscultation appeared to be normal. Laboratory work up was notable for profound leukocytosis and acute kidney injury. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction (PCR) from nasopharyngeal swab was found to be positive. Chest X-ray and computed tomography (CT) scan were done for the patient. CT scan report of the patient, as shown in Figure 1 a and b, was suggestive of area of ground-glass haziness in bilateral lungs in

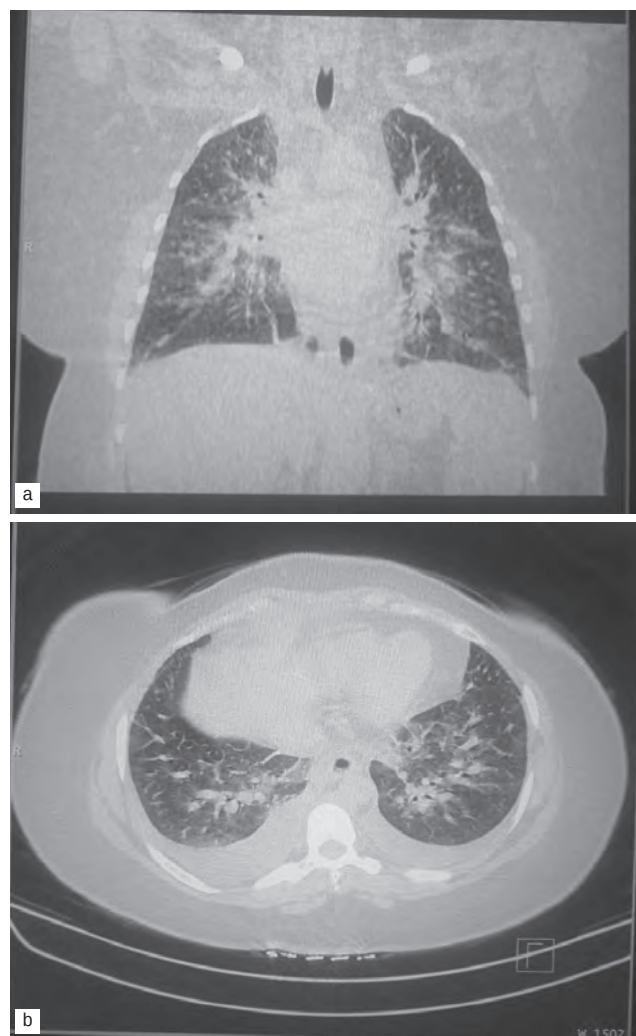


Figure 1 a and b. Area of ground-glass haziness in bilateral lungs in perihilar location, smooth interlobular septal thickening with associated smooth thickening of bilateral oblique fissure, subpleural smooth reticular opacities in basal segments of bilateral lungs, mild bilateral pleural effusion suggestive of pulmonary edema.

perihilar location, smooth interlobular septal thickening with associated smooth thickening of bilateral oblique fissure, subpleural smooth reticular opacities seen in basal segments of bilateral lungs, and mild bilateral pleural effusion suggestive of pulmonary edema. 2D Echocardiography of the patient was also done which was suggestive of no chamber dilatation with normal left ventricular ejection fraction. Patient was admitted in hospital for hypotension with diagnosis of COVID-19 and concern for possible MIS-C-like illness due to renal, cardiac and GI involvement.

The patient's blood pressure initially normalized and her creatinine improved to 1.1 mg/dL with the help of vasopressors. During the hospital course, she developed recurrent episodes of bradycardia. Cardiac opinion was taken and creatine phosphokinase-MB (CPK-MB),

Table 1. Laboratory Findings on Admission and at Discharge

Parameters	On Admission	At Discharge	Reference
WBC ($\times 10^3/\mu\text{L}$)	13.6	10.2	4-10
Hemoglobin (g/dL)	11.2	10.6	13.5-17.5
Platelets (k/uL)	149	152	150-400
Sodium (mmol/L)	135	136	135-145
Potassium (mmol/L)	3.2	3.5	3.4-5.4
Carbon dioxide (mmol/L)	14	24	22-32
Blood urea (mg/dL)	63	45	15-45
S. creatinine (mg/dL)	1.5	0.7	0.5-1.2
Alanine amino-transferase (ALT) (U/L)	25	20	0-40
Aspartate amino-transferase (AST) (U/L)	29	39	0-40
Troponin I (ng/mL)	0.15	0.05	0-0.04
B-natriuretic peptide (BNP) (pg/mL)	293	80	0-99
C-reactive protein (mg/L)	296	28	0-10
Urinalysis	6-7 WBC/hpf	3-4 WBC/hpf	0-5 WBC/hpf
D-dimer (ng/mL)	680	320	0-574
Ferritin (ng/mL)	798	320	11-307

CASE REPORT

troponin I, and B-type natriuretic peptide (BNP) levels were sent for analysis. Work-up for these new symptoms revealed evidence of worsening cardiac dysfunction. Level of troponin I was detectable at 0.15 ng/mL and BNP increased to 293 pg/mL (Table 1). She was immediately shifted to contemporary cardiac intensive care unit (CICU) for further management. As the CT scan findings were suggestive of pulmonary edema, with bradyarrhythmia on electrocardiogram, with increase in cardiac markers, the possibility of myocarditis was suspected. Patient was given IV methylprednisolone, IV antibiotics, diuretics and injectable anticoagulants in the form of enoxaparin. Patient was given oxygen support to help in recovering from pulmonary edema early.

With this treatment, patient recovered successfully with mild weakness remaining. Repeat CT scan was done which suggested reduced pulmonary edema. Patient was successfully discharged on oral antibiotics, oral anticoagulation in the form of aspirin, dabigatran, short course of diuretics and mefenamic acid for fever. Patient was followed-up with stable vitals.

DISCUSSION

The Centers for Disease Control and Prevention (CDC)'s case definition for MIS-C is - 1) An individual less than 21 years of age presenting with fever; 2) laboratory evidence of inflammation by one or more markers (such as C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], fibrinogen, etc.); 3) evidence of clinically severe illness requiring hospitalization, with greater than 2 organ systems involved (cardiac, renal, respiratory, hematologic, GI, mucocutaneous or neurological); 4) no other plausible alternative diagnosis; and 5) SARS-CoV-2 infection confirmed by reverse transcription polymerase chain reaction (RT-PCR), serology or antigen testing (or exposure to a suspected or confirmed COVID-19 case within 4 weeks before the symptom onset).

Our patient, a previously healthy young adult woman in her mid-30's, met these criteria with exception of age.

Several features of our patient's presentation raised concern for MIS-C-like illness. First, she was noted to have GI tract symptoms in the form of acute abdominal pain and loose motions upon evaluation in emergency department. Additionally, our patient had hypovolemia, bradycardia, acute kidney injury, which responded to vasopressors. While GI symptoms do occur in adults with COVID-19, they are typically less severe; by contrast, prominent GI symptoms are seen in many patients with MIS-C. Finally, our

patient's stable respiratory status was itself a feature shared by patients with MIS-C, who often lack intrinsic respiratory disease.

Other features were potentially compatible with MIS-C-like illness, including low blood pressure, cardiac dysfunction, bradyarrhythmia. Like many patients with MIS-C, our patient required treatment with vasopressors in the ICU. Her low blood pressure was thought to be multifactorial including hypovolemic and cardiogenic. She had elevated troponin and BNP unlike many patients with MIS-C. She didn't have left ventricular dysfunction, coronary aneurysms or valvular dysfunction, as have been described in pediatric patients with MIS-C.

Several other features of our patient's clinical presentation were less consistent with MIS-C as it has been described in the pediatric population. Her profound kidney injury and leukocytosis were not features described in majority of MIS-C cases.

CONCLUSION

We describe an unusual case of MIS-C-like illness in a young adult with COVID-19. MIS-C is an emerging and poorly understood clinical entity associated with COVID-19 that has been described in children with the illness and has features similar to Kawasaki's disease. Children with MIS-C are increasingly treated with IVIG, aspirin and steroids; it is not clear if any clinical feature in adults may warrant similar treatment approaches. Our patient was treated with IV antibiotics, anticoagulation and steroids. Further research into COVID-19 in the young adult population is needed to better characterize the full range of clinical manifestations, and to identify potential opportunities for targeted treatment of inflammatory processes.

SUGGESTED READING

1. Kawasaki T. Acute febrile mucocutaneous syndrome with lymphoid involvement with specific desquamation of the fingers and toes in children. *Arerugi*. 1967;16(3):178-222.
2. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. *Lancet*. 2020;395(10237):1607-8.
3. Verdoni L, Mazza A, Gervasoni A, Martelli L, Ruggeri M, Ciuffreda M, et al. An outbreak of severe Kawasaki-like disease at the Italian epicenter of the SARS-CoV-2 epidemic: an observational cohort study. *Lancet*. 2020;395(10239):1771-8.
4. Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, et al. Multisystem inflammatory

- syndrome in U.S. children and adolescents. *N Engl J Med*. 2020;383:334-46.
5. Cha AE, Janes C. Young adults are also affected by Kawasaki-like disease linked to coronavirus, doctors say. *Washington Post*. 2020. Available from: <https://www.washingtonpost.com/health/2020/05/21/misc-c-kawasaki-coronavirus-young-adults/>
 6. Ovanesov MV, Menis MD, Scott DE, Forshee R, Anderson S, Bryan W, et al. Association of immune globulin intravenous and thromboembolic adverse events. *Am J Hematol*. 2017;92(4):E44-E45.
 7. Hennon TR, Penque MD, Abdul-Aziz R, Alibrahim OS, McGreevy MB, Prout AJ, et al. COVID-19 associated multisystem inflammatory syndrome in children (MIS-C) guidelines; a Western New York approach. *Prog Pediatr Cardiol*. 2020;57:101232.
 8. Dallaire F, Fortier-Morissette Z, Blais S, Dhanrajani A, Basodan D, Renaud C, et al. Aspirin dose and prevention of coronary abnormalities in Kawasaki disease. *Pediatrics*. 2017;139(6):e20170098.
 9. Platt B, Belarski E, Manaloor J, Ofner S, Carroll AE, John CC, et al. Comparison of risk of recrudescence fever in children with Kawasaki disease treated with intravenous immunoglobulin and low-dose vs. high-dose aspirin. *JAMA Netw Open*. 2020;3(1):e1918565.
 10. Xia J, Tong J, Liu M, Shen Y, Guo D. Evaluation of corona virus in tears and conjunctival secretions of patients with SARS-CoV-2 infection. *J Med Virol*. 2020;92(6):589-94.
 11. Dufort EM, Koumans EH, Chow EJ, Rosenthal EM, Muse A, Rowlands J, et al; New York State and Centers for Disease Control and Prevention Multisystem Inflammatory Syndrome in Children Investigation Team. Multisystem inflammatory syndrome in children in New York State. *N Engl J Med*. 2020;383(4):347-58.
 12. Miller J, Cantor A, Zachariah P, Ahn D, Martinez M, Margolis KG. Gastrointestinal symptoms as a major presentation component of a novel multisystem inflammatory syndrome in children that is related to coronavirus disease 2019: A single center experience of 44 cases. *Gastroenterology*. 2020;159(4):1571-1574.e2
 13. Belhadjer Z, Méot M, Bajolle F, Khraiche D, Legendre A, Abakka S, et al. Acute heart failure in multisystem inflammatory syndrome in children in the context of global SARS-CoV-2 pandemic. *Circulation*. 2020;142(5):429-36.
 14. Information for healthcare providers about multisystem inflammatory syndrome in children (MIS-C). CDC. Available from: <https://www.cdc.gov/mis/hcp/index.html>
 15. Sethi SK, Rana A, Adnani H, McCulloch M, Alhasan K, Sultana A, et al. Kidney involvement in multisystem inflammatory syndrome in children: a pediatric nephrologist's perspective. *Clin Kid J*. 2021;14(9):2000-11.

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NIH Starts Long-term Study of Children with COVID

The National Institutes of Health (NIH) has initiated a new long-term study to evaluate the impact of COVID-19 on children and young adults.

A total of 1,000 children and young adults, 3 to 21 years of age, who have tested positive for COVID-19, will be followed. The study will evaluate the effects of COVID-19 on their physical and mental health, including their development and immune responses to the virus. The NIH stated that while evaluating the long-term health effects of COVID-19, the researchers will also assess the risk factors that cause complications. They will also screen for genetic factors that could affect the response to the virus, and also determine if immunological factors have an impact on long-term outcomes... (Source: *Medscape*)

Antibiotic Misuse During Pandemic Giving Rise to Resistant Bacteria

The Pan American Health Organization (PAHO) has cautioned that overuse of antibiotics and other antimicrobial agents during the COVID-19 pandemic is leading to the development of resistance among bacteria, which will eventually make these medicines ineffective.

Countries in the Americas, such as Argentina, Uruguay, Ecuador, Guatemala and Paraguay, are reporting increased rates of drug-resistant infections which have possibly led to the rise in mortality among hospitalized COVID-19 patients, stated the agency.

Data available from hospitals in the region indicates that 90-100% of hospitalized COVID-19 patients received an antimicrobial agent during treatment, when just 7% of them had a secondary infection, requiring the use of these medications, said PAHO director Carissa Etienne... (Source: *Reuters*)