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Short Communication

A Case of 'Multi-Inflammatory Syndrome in Children' Complicated with Cardiogenic Shock

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ABSTRACT

SARS Cov-2 infection causes Multi-Inflammatory Syndrome in Children (MIS-C), a serious condition that affects children. We report an 18-year-old Turkish male who was diagnosed with MIS-C and successfully treated. He was diagnosed with MIS-C and required invasive mechanical ventilation due to cardiogenic shock, after what he recovered. With a high temperature, rash, and conjunctival hyperemia, the patient was taken to the emergency department. He had no symptomatic COVID-19 in his medical history, although he had had contact with a COVID-19 positive patient in the near past. Physical examination revealed an erythematous maculopapular rash on the back and neck, as well as hepatosplenomegaly. SARS-CoV-2 IgM and IgG positivity were detected in the rapid antibody test. Following the procedure, rectal bleeding and tachypnea developed. Inflammation indicators and pro-BNP levels both increased. With echocardiogenic examination, the ejection fraction decreased from 50-55 percent to 35%. He needed invasive mechanical ventilation. As a result, the case was classified as MIS-C with predominant cardiac and gastrointestinal involvement. The patient was discharged after a successful multidisciplinary approach. Although COVID-19 infection in children and adolescents is asymptomatic or minimally symptomatic, clinicians should be aware of post-infection autoimmune complications.

Keywords: COVID 19, MIS-C, SARS-CoV 2, Cardiogenic Shock

INTRODUCTION

The World Health Organization (WHO) confirmed a new pandemic caused by SARS-CoV-2 on March 11, 2020 (1). According to WHO statistics, COVID-19 has affected approximately 250 million people in 222 countries, resulting in the deaths of almost five million people (2). Despite the fact that the disease is characterized by respiratory tract infections, the virus has evolved to damage systems other than the lungs (3). The incidence of COVID-19 in children is relatively lower than in adults, and it is assumed that children overcome this disease mildly (4).

SARS-CoV-2 has the potential to cause Multi-Inflammatory Syndrome in Children (MIS-C), which is a rare but serious illness in children (5). The abnormal immunological response against the virus is assumed to be the origin of MIS-C, which has clinical similarities to Kawasaki Disease (KD), Macrophage Activation Syndrome (MAS), and Cytokine Release Syndrome. MIS-C is responsible for 1% of hospital admissions in the pediatric population during the pandemic period. Most of the patients are required intensive care support and the mortality rate is around 1.5-2% (6). The majority of the cases had a negative PCR test but a positive serology. This condition offers to the theory that it is linked to immunological dysfunction after the acute infection has cleared. Myocardial injury mechanisms have yet to be identified. Systemic inflammation-related injury, acute viral myocarditis, hypoxia, stress cardiomyopathy, and ischemia caused by coronary artery involvement are all potential causes of myocardial damage. Fever, hypotension, rash, myocarditis, and gastrointestinal problems are some of the clinical symptoms. Inflammation is on the increase, according to laboratory results. Symptoms of respiratory disorders may not be observed in this disease (7).

In our report, we present a MIS-C case that required invasive mechanical ventilation due to cardiogenic shock.

CASE REPORT

An 18-year-old Turkish male patient was taken to the emergency department with a four-day high fever and a red, extensive rash that began the day after the fever. Before his symptoms began, he was a student with no chronic diseases, drug or substance addiction history. His vital signs were high fever: 39.1 ^{0}C, pulse: 131 / min, respiratory rate: 20 / min, and blood pressure: 108/60 mm Hg. On physical examination, the patient appeared to be in good health, aware, and oriented, with bilateral conjunctival hyperemia and an extensive maculopapular rash on the erythematous floor of the back, trunk, and arms (Figure 1). The liver edge was palpable under the right costal margin on abdominal examina-

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tion. The results of the whole physical examination were normal. The examinations performed at the time of admission revealed lymphopenia and an increase in acute phase reactants. Liver and renal function tests showed no abnormalities (Table 1).

The spleen was 15.5 cm in diameter and had a homogenous density when abdominal imaging was done to determine the origin of the fever. The liver measured 19 cm in diameter and had a homogeneous density. The thoracic tomography revealed no infiltration. In the nasopharyngeal smear, a real-time reverse transcription-polymerase chain reaction (RT-PCR) results came back negative. He was transferred to the Clinic of Infectious Diseases. The rapid antibody test performed in the clinic provided a positive result.

Treatment with Favipravir and low molecular weight heparin were started. Ejection fraction (EF) was 50-55 percent on transthoracic echocardiography performed at the bedside, with mild global hypokinesia, 1st-degree mitral insufficiency, 1st-degree tricuspid insufficiency, and enlargement of the right spaces. Cardiac troponin was 0.283 ng/mL, and pro-BNP was higher than 35000 pg/mL. Two days later, the patient complained of diarrhea and rectal bleeding. The patient's fever persisted, so empiric piperacillin-tazobactam treatment was initiated after blood, stool, and urine cultures were taken. Two g / kg intravenous immunoglobulin (IVIG) was started with the pre-diagnosis of MIS-C, with cardiac and gastrointestinal involvement predominant. Pulse-methyl-prednisolone was also started, at a dose of one gram per day for three days. The patient was transferred to the intensive care unit due to hypotension and tachycardia. On echocardiography done in the intensive care unit, the ejection fraction was 35 percent, and diffuse global hypokinesia and perimyocarditis were detected. With the pre-diagnosis of shock, noradrenaline and dobutamine treatment proceeded. The patient's antibiotherapy was changed to meropenem plus vancomycin after a rise in acute phase reactants (CRP: 222 mg/l, procalcitonin: 13 ng/ml). The patient needed invasive mechanical ventilation on the same day. Because of his anuric course and chronic acidosis, he was administered with continuous renal replacement. Cardiopulmonary resuscitation was performed for 17 minutes after cardiac arrest occurred. The patient was monitored in Synchronized Intermittent Mandatory Ventilation (SIMV) mode with high PEEP and oxygen support. The patient was extubated with reduced support after four days of intubation. After the negative culture results, the meropenem and vancomycin therapies were terminated. Control transthoracic echocardiography, EF was 45% with mild global hypokinesia, 1st-degree mitral insufficiency, 1st-degree tricuspid failure. He was discharged with a beta-blocker and furosemide medications on the 16th day of his hospitalization.

Written consent was obtained from the patient to be presented in the case presentation.

Figure 1. Maculopapular eruptions on erythematous on the arm (A), back (B) and trunk (C) at the time of admission and intensive care follow-up

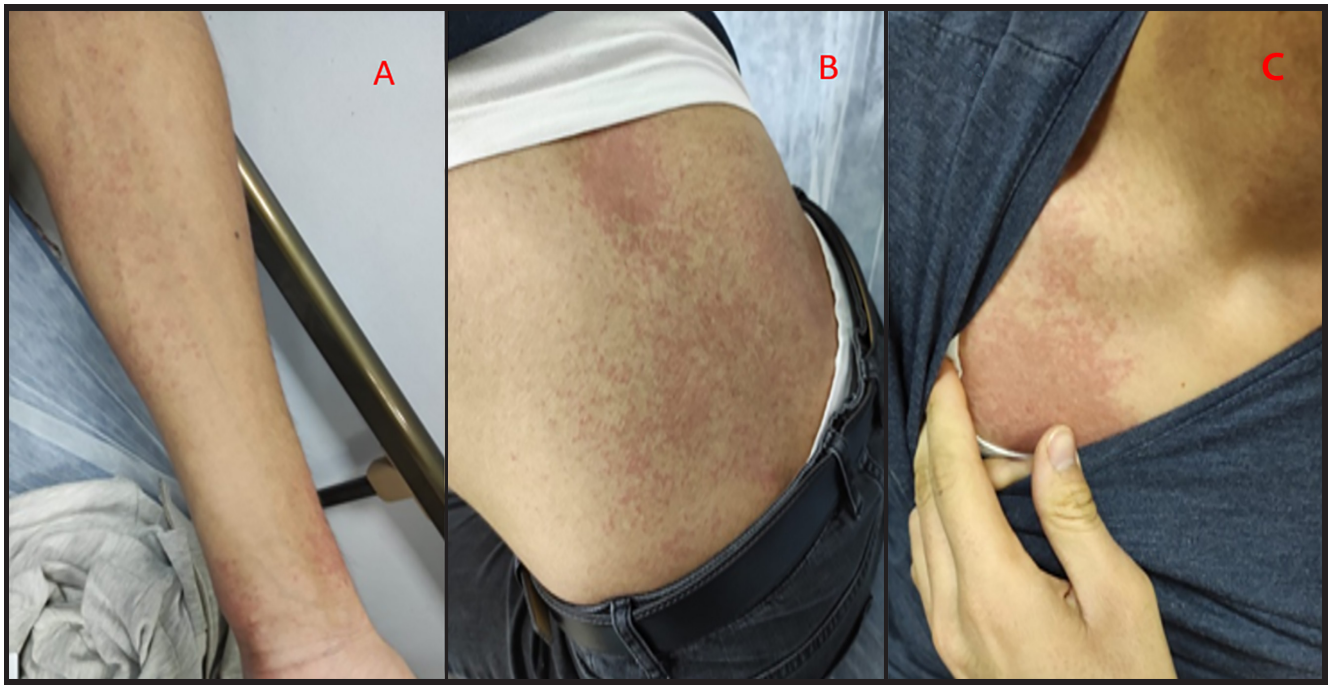

Table 1. Laboratory parameters of the patient on the admission, follow-up and discharged period

	Day 1	Day 2	Day 7	Day 16 (discharged)
White Blood Cell Count (4,8-10,7x10³/µL)	4.72	8.03	12,02	8,54
Lymphocyte (1,3-2,9 x10³/µL)	0.38	0.29	0,74	1,55
Hemoglobin (g/dL)	14,2	13,6	12,4	11,8
Hematocrit	42,1	40,8	38,2	36,3
Platelet (130-400x10³/µL)	155	127	133	207
Ferritin (20-500ng/ml)	341	443	546	469
Pro-BNP (0-125 pg/ml)	> 35.000	> 35.000	-	225
Troponin T (0-0,014 ng/ml)	0,159	0,283	0,168	0,185
Fibrinogen (180-350 mg/dl)	701	-	358	230
D-dimer (0-550µg/l)	1170	1770	2970	2700
INR	1,53	1,23	1,16	1,13
CRP (0-5 mg/dL)	115	223	60	6.6
Procalcitonin (0,5-2ng/ml)	0,68	5.57	4.44	0.11
ALT (0-40u/L)	15.8	18	1337	99
AST (0-40u/L)	35.2	22	687	34
Bilirubin (mg/dL)	0,72/0,41	0,98/0,56		0,55/0,18
Albumin (g/dL)	2,84	2,56	3,15	3,45
GGT (u/L)	23	17	18	25
Creatinine (0.5-1.2 mg/dl)	0.94	1.2	0.89	0.7

BNP, brain natriuretic peptide; INR, international normalized ratio; CRP, C-Reactive protein; ALT, alanine aminotransferase; AST: aspartate aminotransferase; GGT; gamma glutamine transferase

Table 2. Some of MIS-C cases reported in the literature, clinical symptoms, treatment and prognosis

Number of the case	Age/ Gender	Clinical Symptoms	ICU need	Cardiac Involvement	Treatment	Outcome
1 [11]	36/F	Fever, abdominal pain, vomiting, diarrhea diffuse rash and arthralgia	No	Yes	IVIG, methylprednisolone	Alieved
2[12]	5month old/F	Fever and intermittent tachycardia	Yes	Yes	Methylprednisone	Alieved
3 [13]	12/F	Fever, breathlessness, skin rashes, mucosal excoriations, conjunctivitis and diarrhea	Yes	No	Methylprednisone	Alieved
4 [14]	8/F	Fever, rash, respiratory distress, hemodynamic instability, hyperglycemia, ketosis and metabolic acidosis	Yes	Yes	IVIG, infliximab, methylprednisolone	Alieved
5 [15]	16/F	Abdominal pain, vomiting, fever, headache, myalgia and cough	Yes	Yes	IVIG, aspirin, methylprednisolone and norepinephrine	Alieved
6 [16]	22/M	Asthenia, chills, diffuse myalgia, abdominal pain and diarrhea	Yes	Yes	IVIG and tocilisumab	Alieved
7 [17]	15/M	headaches, sore throat, and fever as well as one day of neck pain and stiffness	Yes	Yes	IVIG, dexamethasone and aspirin	Alieved

ICU, intensive care unit F, female; M, male; IVIG, intravenous immunoglobulin

DISCUSSION

Among the problems seen during and after SARS-CoV-2 infection are the amount of viral replication and an uncontrolled autoimmune response to viral replication (8). In addition to the viral cytopathic effect, Type 2 and Type 4 hypersensitivity responses play a role in the formation of the autoimmune response (8). Fever, rash, conjunctivitis, mucocutaneous ingestion, hypotension, and cardiac failure were the most commonly reported symptoms in a study of 9 MIS-C patients. Troponin and pro-BNP levels were shown to be higher in the same study (9). The high temperature, rash, hypotension, conjunctivitis, and cardiac failure seen in this case are similar to those seen in other cases in the literature.

The mortality rate was 2% in a review of 8 MIS-C trials with 440 individuals. The median age of the patients in this study ranged from 7.3 to 10. At the same time, most of the symptoms were gastrointestinal symptoms (87%), other symptoms reported as dermatological/mucocutaneous (73%), cardiovascular symptoms (71%), respiratory (47%), neurological (22%), and musculoskeletal (21%). In 26% of the patients, mechanical ventilation was required, and 6% of the cases required extracorporeal membrane oxygenation (10). According to the literature, the frequency of MIS-C cases requiring invasive mechanical ventilation and being discharged in the follow-up is extremely rare. Table 2 lists some of the MIS-C cases that have been reported (11-17). In this case report, a multidisciplinary approach was used to successfully discharge a patient with cardiological, gastrointestinal, dermatological/mucocutaneous symptoms, and invasive mechanical ventilation.

The diagnosis of MIS-C can be made using a variety of diagnostic criteria. According to WHO criteria, the presence of inflammatory markers between 0-19 years of age for more than three days, the presence of 2 clinical findings, and COVID-19 serological or PCR test are considered cases. According to the Centers for Disease Control and Prevention, patients under the age of 21 are actually covered (18). Both clinical and laboratory criteria are met in this case.

The cause for admittance to the hospital in this case was a high fever and rash. In an Italian research, 88 individuals diagnosed with Covid-19 were studied, excluding drug-related rashes, and skin findings were reported in 20.4 percent of the cases (18 patients). 14 patients had an erythematous rash, three had extensive urticaria, and one had varicella-like vesicles (19). Rashes on the skin are one of the most commonly reported symptoms in the literature, and these rashes are thought to be autoimmune in origin (11,13,14). Maculopapular rashes that appear during or after the disease process should be considered a rare COVID-19 clinical finding.

LESSONS LEARNED

Although COVID-19 infection in children and adolescents is asymptomatic or minimally symptomatic, clinicians should be aware of the possibility of autoimmune consequences. Patients admitted to the emergency department during the pandemic should be monitored for SARS CoV-2-related symptoms and complications, even if they do not have typical respiratory symptoms.

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