

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Contents lists available at ScienceDirect

International Journal of Infectious Diseases



journal homepage: www.elsevier.com/locate/ijid

Case Report

Multisystem inflammatory syndrome in adults: A rare sequela of SARS-CoV-2 infection



Faran Ahmad^{a,*}, Arslan Ahmed^a, Sanu S. Rajendraprasad^a, Austin Loranger^a, Sonia Gupta^a, Manasa Velagapudi^a, Renuga Vivekanandan^{a,b,c}, Joseph A. Nahas^a, Robert Plambeck^a, Douglas Moore^a

- ^a Creighton University Medical Center Bergan Mercy, 7500 Mercy Road, Omaha, NE 68124, USA
- ^b Creighton University, School of Medicine, Omaha, NE 68178, USA
- ^c Dr C.C. and Mabel L. Criss Health Sciences Complex II, 2621 Burt Street, Omaha, NE 68178, USA

ARTICLE INFO

Article history: Received 15 April 2021 Received in revised form 14 May 2021 Accepted 21 May 2021

Keywords: Multisystem inflammatory syndrome in adults (MIS-A) SARS-CoV-2 infection COVID-19

ABSTRACT

Multisystem inflammatory syndrome in adults (MIS-A) came to attention back in June 2020, when the United States Center for Disease Control and Prevention (CDC) received initial reports regarding patients who had presented delayed and multisystem involvement of the disease, with clinical course resembling multisystem inflammatory syndrome in children (MIS-C). This study introduces a case of MIS-A, where the patient presented 3 weeks after initial COVID-19 exposure. His clinical course was consistent with the working definition of MIS-A as specified by the CDC. Aggressive supportive care in the intensive care unit, utilization of advanced heart failure devices, and immunomodulatory therapeutics (high-dose steroids, anakinra, intravenous immunoglobulin) led to clinical recovery. Management of MIS-A is a topic of ongoing research and needs more studies to elaborate on treatment modalities and clinical predictors. © 2021 The Author(s). Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Most of our understanding of MIS-A is based on various case reports and case series shared by the CDC and published in the medical literature (Bastug et al., 2021; Morris et al., 2020). Here we describe a case of MIS-A in a patient admitted to the Creighton University Medical Center —Bergan Mercy campus in Omaha, Nebraska with clinical presentation and diagnostics suggestive of MIS-A.

Abbreviations: AF, atrial fibrillation; CDC, Center for Disease Control and Prevention; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; CRRT, continuous renal replacement therapy; ICU, intensive care unit; IVIG, intravenous immunoglobulin; LDH, lactate dehydrogenase; LHC, left heart catheterization; LVEF, left ventricular ejection fraction; MIS, multisystem inflammatory syndrome; MIS-A, multisystem inflammatory syndrome in adults; MMWR, Morbidity and Mortality Weekly Report; RT-PCR, reverse transcriptase-polymerase chain reaction; SCAD, spontaneous coronary artery dissection; TTE, transthoracic echocardiogram; VA-ECMO, veno-arterial extracorporeal membrane oxygenation; VF, ventricular fibrillation.

E-mail address: faranahmad@creighton.edu (F. Ahmad).

Case

A 26-year-old Caucasian male nonsmoker presented to the emergency room with 5 days of diffuse abdominal pain, constant in nature, described as 5 out of 10 in intensity, and associated with fever, nausea, loose stool, and decreased urine output. He additionally noted a rash on his hands and feet that started 3 days prior to the presentation. His roommate had COVID-19 three weeks ago. The patient self-quarantined for 10 days and his reverse transcriptase-polymerase chain reaction (RT-PCR) test for SARS-CoV-2 was reported negative at the end of quarantine. He was afebrile, had a blood pressure of 98/48 mmHg, a respiratory rate of 35/minute, and 94% saturation on room air. On chest auscultation, the lungs were clear bilaterally. His abdomen was soft and non-distended, with generalized tenderness to deep palpation. Initial abnormal laboratory results included BUN 38 mg/dl, creatinine 4.66 mg/dl, CRP 246 mg/l, ferritin 1657 ng/ml, LDH 236 U/L, procalcitonin 105.12 ng/ml, D-dimer 2.03, venous lactate 9.7 mg/dl, and WBC count 21 700/U/L with 71% bands (Table 1). At this point he tested positive for SARS-CoV-2 by nasopharyngeal PCR test, with SARS-CoV-2 antibody testing also positive. A duplex venous scan of the lower extremities revealed an acute left peroneal deep vein thrombosis. His initial chest X-ray revealed mild peribronchial

^{*} Corresponding author at: Infectious Diseases and Critical Care Medicine, Creighton University Medical Center — Bergan Mercy, 7500 Mercy Rd, Omaha, NE 68124 USA

Table 1Clinical features and laboratory results of the patient with MIS-A.

Age 26 Sex Male Ethnicity Not Hispanic or Latino Race White BMI 31.39 Comorbidities Obesity, generalized anxiety disorder Maximum body temperature 39.8 °C (103.6 °F) Evidence of clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement Towns (10.6 °F) Cardia (e.g., settek defice) miny or renal failure) Yes Respiratory (e.g., pneumonia, ARDS, pulmoanry embolism) Yes Respiratory (e.g., elveated Dilirobin, elveted liver enzyme, or diarrhea) Yes Gastronitestinial (e.g., elveated bilirobin, elveted liver enzyme, or diarrhea) Yes Neurological (e.g., CVA, aseptic meningitis, encephalopathy) Yes No. alternative plausible diagnosis Yes COVID-19 exposure within the 4 weeks prior to the onset of MIS-A symptoms Yes RF-CRY Seasongly, Rea, and other abnormal laboratory results for current admission (with normal reference range) RF-CRY Seasongly, Rea, and other abnormal laboratory results for current admission (with normal reference range) RF-CRY Seasongly, Rea, and other abnormal laboratory results for current admission (with normal reference range)		
Enhicity Not Hispanic or latino Race White BMI 31.39 Comorbidities Obesity, generalized anxiety disorder Maximum body temperature 39.8 ° € (103.6 °F) Evidence of Clinically severe illness requiring hospitalization, with multisystem (≥2) organi involvement 198.8 ° € (103.6 °F) Cardiac (e.g., shock, clevated troponin, BNR) ahonral echocardiogram, arrhythmia) Yes Respiratory (e.g., pneumonia, ARDS, pulmonary embolism) Yes Henatological (e.g., elevated bilirubin, elevated liver enzymes, or diarrhea) Yes Castroinestinal (e.g., elevated bilirubin, elevated liver enzymes, or diarrhea) Yes Neurological (e.g., achymato-plassible diagnostic, elevated bilirubin, elevated liver enzymes, or diarrhea) Yes OVID-19 exposure within the 4 weeks prior to the onset of MIS-A symptoms Yes COVU-2 serology, PCR, and other abnormal laboratory results for current admission (with the plassible diagnostic (e.g., achymato-plassible diagnostic (e.g., achymato-plassible diagnostic) Positive (Ct value: 34.1) ARS-COV-2 total antibody 17 and 78.5 (4-12) 11 mitial and peak WEC (k/m) 17 and 78.5 (4-12) 11 mitial and peak CRP (mgf) 18 cas 4 cono (84-246) 18 cas 4 cono (84-246) 18 cas 4 cono (84-246) 18 cas 4 cono (Age	26
Bace White BMI 31.99 Comorbidities Obesity, generalized anxiety disorder Maximum body temperature 39.8° (103.6° F) Evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement Evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement Evaluate Cardiac (e.g., sokock, elevated troponin, BNP, abnormal echocardiogram, arrhythmia) Yes Renal (e.g., acute kidney injury or renal failure) Yes Hematological (e.g., elevated D-dimers, thrombophilia, or thrombocytopenia) Yes Gastrointestinal (e.g., elevated billiurbin, elevated live renzymes, or diarrhea) Yes Dermatological (e.g., rash, mucocutaneous lesions) Yes Neurological (e.g., rash, mucocutaneous lesions) Yes Neurological (e.g., rash, mucocutaneous lesions) Yes No 1 acute anxiety plausible diagnosis Yes SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with mornal reference range) Positive (C value: 34.1) RT-PCR Positive (C value: 34.1) RT-CCR Positive (C value: 34.1) Initial and peak WBC (k/ul) 16.6 and 6.79 (0.6-1.3) <td< td=""><td>Sex</td><td>Male</td></td<>	Sex	Male
BMI 31.39 Comorbidities Obesity, generalized anxiety disorder Maximum body temperature 39.8°C (103.6°F) Evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organi involvents Yes Cardiac (e.g., shock, clevated troponin, BNP, abnormal echocardiogram, arrhythmia) Yes Respiratory (e.g., pneumonia, ARDS, pulmonary embolism) Yes Castrointestinal (e.g., elevated brilienthin, elevated liver enzymes, or diarrhea) Yes Castrointestinal (e.g., elevated brilienthin, elevated liver enzymes, or diarrhea) Yes Formatological (e.g., arch, mucoutaneous lesions) Yes Neurological (e.g., arch, mucoutaneous lesions) Yes Neurological (e.g., arch, mucoutaneous lesions) Yes No alternative plausible diagnosis Yes COVID-19 exposure within the 4 weeks prior to the onset of MIS-A symptoms Yes COVID-19 exposure within the 4 weeks prior to the onset of MIS-A symptoms Yes SARS-COV-2 strolagy, PCR, and other abnormal laboratory results for current admission (with number Creating C.g., vol. 3, and 7, 10.00 Arch 76.5 (4-12) Initial and peak CRP (mgl) 4.66 and 6.79 (90.9) Alba 76.5 (4-12) Initial and peak LDH (units)L) Yes <td>Ethnicity</td> <td>Not Hispanic or Latino</td>	Ethnicity	Not Hispanic or Latino
BMI 31.39 Comorbidities Obesity, generalized anxiety disorder Maximum body temperature 39.8°C (103.6°F) Evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organi involvents Yes Cardiac (e.g., shock, clevated troponin, BNP, abnormal echocardiogram, arrhythmia) Yes Respiratory (e.g., pneumonia, ARDS, pulmonary embolism) Yes Castrointestinal (e.g., elevated brilienthin, elevated liver enzymes, or diarrhea) Yes Castrointestinal (e.g., elevated brilienthin, elevated liver enzymes, or diarrhea) Yes Formatological (e.g., arch, mucoutaneous lesions) Yes Neurological (e.g., arch, mucoutaneous lesions) Yes Neurological (e.g., arch, mucoutaneous lesions) Yes No alternative plausible diagnosis Yes COVID-19 exposure within the 4 weeks prior to the onset of MIS-A symptoms Yes COVID-19 exposure within the 4 weeks prior to the onset of MIS-A symptoms Yes SARS-COV-2 strolagy, PCR, and other abnormal laboratory results for current admission (with number Creating C.g., vol. 3, and 7, 10.00 Arch 76.5 (4-12) Initial and peak CRP (mgl) 4.66 and 6.79 (90.9) Alba 76.5 (4-12) Initial and peak LDH (units)L) Yes <td>Race</td> <td>White</td>	Race	White
Comorbidities Obesity, generalized anxiety disorder Maximum body temperature 39.8° C (103.6°F) Evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement Cardiac (e.g., shock, elevated troppoin, BNP, ahonemal echocardiogram, arrhythmia) Yes Respiratory (e.g., preumonia, ARDS, pulmonary embolism) Yes Hematological (e.g., elevated D-dimes, thrombophila, or thrombocytopenia) Yes Castrointestinal (e.g., elevated D-dimes, thrombophila, or thrombocytopenia) Yes Pomitostigical (e.g., acts), uncourcutaeous lesions) No No alternative plausible diagnosis Yes COVID-19 exposure within the 4 weeks prior to the onset of MIS-A symptoms Yes SARS-COV-2 sotal antibody Positive (Ct value: 34.1) Initial and peak WBC (klul) 246° (<0.0)		
Maximum body temperature vidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement Cardiac (e.g., shock, elevated troponin, BNR, abnormal echocardiogram, arrhythmia) Respiratory (e.g., pneumonia, ARDS, pulmonary embolism) Hematological (e.g., elevated D-dimers, thrombophilia, or thrombocytopenia) Castroinestrian (e.g., elevated bilimbin, elevated liver enzymes, or diarrhea) Ves Castroinestrian (e.g., elevated bilimbin, elevated liver enzymes, or diarrhea) Ves Castroinestrian (e.g., elevated bilimbin, elevated liver enzymes, or diarrhea) Ves CovID-19 exposure within the 4 weeks prior to the onset of MIS-A symptoms SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with normal reference range) RT-PCR SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with normal reference range) RT-PCR SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with normal reference range) RT-PCR SARS-COV-2 total annihody 1 positive (Ct value: 34.1) SARS-COV-2 total annihody 1 positive (C		
Evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (2g, acute kidney injury or renal failure)		
Cardiac (e.g., shock, elevated rroponin, BNP, abnormal echocardiogram, arrhythmia) Yes Respiratory (e.g., pneumonia, ABDS, pulmonary embolism) Yes Respiratory (e.g., pneumonia, ABDS, pulmonary embolism) Yes Gastrointestinal (e.g., elevated bilirubin, elevated liver enzymes, or diarrhea) Yes Dermatological (e.g., extah, mucocutaneous lesions) Yes No alternative plausible diagnosis Yes COVID-19e syosure within the 4 weeks prior to the onset of MIS-A symptoms Yes SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with rarrange) Positive (Ct value: 34.1) SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with normal reference range) RT-PCR Positive (Ct value: 34.1) SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with normal reference range) RT-PCR Positive (Ct value: 34.1) SARS-COV-2 total antibody Positive (Ct value: 34.1) Initial and peak WBC (Klul) 11 11 11 11 12 12 13 13	· ·	· · · · ·
Renal (e.g., acute kidney injury or renal failure) Respiratory (e.g., pneumonia, ABDS, pulmonary embolism) (Pessipatory (e.g., pneumonia, ABDS, pulmonary embolism) (Penatological (e.g., elevated D-dimers, thrombophilia, or thrombocytopenia) (Penatological (e.g., clevated D-dimers, thrombophilia, or thrombocytopenia) (Penatological (e.g., cash, mucocutaneous lesions) (Pessourous plausible diagnosis (COVID-19 exposure within the 4 weeks prior to the onset of MIS-A symptoms (COVID-19 exposure within the 4 weeks prior to the onset of MIS-A symptoms (Part-PCR SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with normal reference range) (Positive (Ct value: 34.1) (Positive (Value: 34.1) (Positive (Value: 34.1) (Positive (Value: 34.1) (
Respiratory (e.g., pneumonia, ARDS, pulmonary embloism) (es hematological (e.g., elevated D-dimens, thrombophilia, or thrombocytopenia) (es hematological (e.g., elevated Dilirubin, elevated liver enzymes, or diarrhea) (es hematological (e.g., rash, mucocutaneous lesions) (es hematological (e.g., rash, es hematological (e.g., rash) (es hematological (e.g., rash) (e.		
Hematological (e.g., elevated D-dimers, thrombophilia, or thrombocytopenia) Castroinestral (e.g., erated bilirubin, elevated liver enzymes, or diarrhea) Permatological (e.g., rash, mucocutaneous lesions) Neurological (e.g., rash, mucocutaneous lesions) Neurological (e.g., rash, mucocutaneous lesions) No alternative plausible diagnosis COVID-19 exposure within the 4 weeks prior to the onset of MIS-A symptoms COVID-19 exposure within the 4 weeks prior to the onset of MIS-A symptoms SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with normal reference range) RT-PCR SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with normal reference range) RT-PCR SARS-COV-2 to tal antibody Initial and peak WBC (k/ul) Positive		
Gastroinestinal (e.g., elevated bilirubin, elevated liver enzymes, or diarrhea) Yes Dermatological (e.g., rash, mucocutaneous lesions) Yes Neurological (e.g., rash, succottaneous lesions) Yes No alternative plausible diagnosis Yes COVID-19 exposure within the 4 weeks prior to the onset of MIS-A symptoms Yes SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with normal reference range) Positive (Ct value: 34.1) SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with normal reference range) Positive (Ct value: 34.1) SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with normal reference range) Positive (Ct value: 34.1) SARS-COV-2 storal antibody Positive (Ct value: 34.1) Initial and peak RPC (k/u) 21.7 and 76.5 (4-12) Initial and peak RPC (k/m) 105.12** (<0.05)		
Permatological (e.g., rash, mucocutaneous lesions)		
Neurological (e.g., CVA, aseptic meningitis, encephalopathy) No alternative plausible diagnosis COVID-19 exposure within the 4 weeks prior to the onset of MIS-A symptoms SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with normal reference range) RT-PCR Positive (Ct value: 34.1) SARS-COV-2 total antibody Positive (Ct value: 34.1) Initial and peak CRP (mg/l) Initial and peak treatinine (mg/dl) Initial and peak procalcitonin (ng/ml) Initial mg/mg and cardiac catheterization Initial Initial mg/mg (ng/mg/mg/mg/mg/mg/mg/mg/mg/mg/mg/mg/mg/mg		
No alternative plausible diagnosis COVID-19 exposure within the 4 weeks prior to the onset of MIS-A symptoms SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with normal reference range) RT-PCR SARS-COV-2 total antibody Initial and peak WRC (kJul) Initial and peak WRC (kJul) Initial and peak WRC (kJul) Initial and peak CRP (mg/l) Initial and peak procalictionin (ng/ml) Initial and peak ferritin (ng/ml) Initial and peak (ng/ml) Initial and p		Yes
COVID-19 exposure within the 4 weeks prior to the onset of MIS-A symptoms SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with normal reference range) RT-PCR Positive (Ct value: 34.1) SARS-COV-2 total antibody Positive Initial and peak WBC (k/lul) Initial and peak WBC (k/lul) Initial and peak WBC (k/lul) Initial and peak CRP (mg/l) Initial and peak CRP (mg/l) Initial and peak proactictionin (ng/ml) Initial and peak past Drift (missly) Initial and peak post LDH (unitsly) Initial and peak bus (missly) Initial and peak bus (missly) Initial and peak bus (missly) Initial and peak ferritin (ng/ml) Initial and	Neurological (e.g., CVA, aseptic meningitis, encephalopathy)	No
SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with normal reference range) RT-PCR SARS-CoV-2 total antibody Positive [Ct value: 34.1] SARS-CoV-2 total antibody Positive [Initial and peak WBC (kylul) 21.7 and 76.5 (4-12) Initial and peak (Proghl) 105.12° (<0.05) Initial and peak creatinine (mg/dl) 105.12° (<0.05) Initial and peak kreatinine (mg/ml) 105.12° (<0.05) Initial and peak procalcitonin (ng/ml) 105.12° (<0.05) Initial and peak kreitin (ng/ml) 105.12° (<0.05) Initial and peak	No alternative plausible diagnosis	Yes
RT-PCR SARS-COV-2 total antibody Initial and peak WBC (k/ul) Initial and peak KPC (m/ll) Initial and peak CRP (mg/ll) Initial and peak procalcitonin (ng/ml) Initial and peak procalcitonin (ng/ml) Initial and peak procalcitonin (ng/ml) Initial and peak beat procalcitonin (ng/ml) Initial and peak beat procalcitonin (ng/ml) Initial and peak ferritin (ng/ml) Initial and peak territin (ng/ml) Init	COVID-19 exposure within the 4 weeks prior to the onset of MIS-A symptoms	Yes
RT-PCR SARS-COV-2 total antibody Initial and peak WBC (k/ul) Initial and peak KPC (mg/l) Initial and peak CRP (mg/l) Initial and peak procalcitonin (ng/ml) Initial and peak procalcitonin (ng/ml) Initial and peak procalcitonin (ng/ml) Initial and peak beat procalcitonin (ng/ml) Initial and peak beat procalcitonin (ng/ml) Initial and peak ferritin (ng/ml) Initial and neak trate, 6000 (8-246) Initial and peak territin (ng/ml) Initi		
SARS-CoV-2 total antibody Initial and peak WBC (k/lu) Initial and peak CRP (mg/l) Initial and peak CRP (mg/l) Initial and peak CRP (mg/l) Initial and peak procalcitonin (mg/ml) Initial and peak IDH (units/L) Initial and peak EPH (units/L) Initial and peak iDH (units/L) Initial and peak iDH (units/L) Initial and peak fore interest i	SARS-COV-2 serology, PCR, and other abnormal laboratory results for current admission (with	th normal reference range)
SARS-CoV-2 total antibody Initial and peak WBC (k/lu) Initial and peak CRP (mg/l) Initial and peak CRP (mg/l) Initial and peak CRP (mg/l) Initial and peak procalcitonin (mg/ml) Initial and peak IDH (units/L) Initial and peak EPH (units/L) Initial and peak iDH (units/L) Initial and peak iDH (units/L) Initial and peak fore interest i	RT-PCR	Positive (Ct value: 34.1)
Initial and peak WBC (k/ul) Initial and peak CRP (mg/l) Initial and peak CRP (mg/l) Initial and peak CRP (mg/l) Initial and peak procalcitonin (ng/ml) Initial and peak ferritin (ng/ml) Initial and peak ferritin (ng/ml) Initial and peak ferritin (ng/ml) Initial mediator active cardiac catheterization Initial Mild mitral regurgitation; severe global hypokinesis of the left ventricle; LVEF 10–15% Prior to discharge IVEF 06–65% Coronary artery evaluation TO ask and Severe global hypokinesis of the left ventricle; LVEF 10–15% Prior to discharge Coronary artery evaluation TO ask and the Cn evidence of coronary artery aneurysm, severe cardiomyopathy with cardiogenic shock Imaging studies Abdominal imaging CT abdomen/pelvis with contrast: mesenteric lymphadenopathy, bilateral perinephric edema extending to the adrenal glands Chest imaging Management Supplemental O ₂ requirements Wes ECMO No Hemodialysis Yes ECMO No Hemodialysis Yes ECMO Norepinephrine, vasopressin, epinephrine, dobutamine Steroids Yes IVIG Two doses Immune modulators Anakinra Anticoagulation Anticoagulation Fleaprin drip, rivaroxaban Attention fospital stay (days)		,
Initial and peak CRP (mg/ll) Initial and peak CRP (mg/ll) Initial and peak creatinine (mg/dl) Initial and peak procalcitonin (ng/ml) Initial and peak LDH (units/L) Initial and peak Erritin (ng/ml) Initial and peak LDH (units/L) Initial and peak Erritin (ng/ml) Initial and each 6000 (2-388) Initial and each 6000 (2-38) Initial and each 6000 (2-38) Initial erritin (ng/ml) Initial and each 6000 (2-38) Initial and ea	•	
Initial and peak creatinine (mg/dl) Initial and peak procalcitonin (ng/ml) Initial and peak IDH (units/L) Initial and peak ferritin (ng/ml) Initial and peak ferritin (ng/ml) Initial and peak ferritin (ng/ml) Initial and peak IDH (units/L) Initial and peak ferritin (ng/ml) Initial and peak territin (ng/ml) Initial and peak ferritin (ng/ml) Initial and peak territin (ng/ma) Initial end peak territins, seere global hypotines of		
Initial and peak procalcitonin (ng/ml) Initial and peak LDH (units/L) Initial and peak (pricin (ng/ml) Initial and peak (pricin (ng/ml) Initial and peak ferritin (ng/ml) Initial and peak erritin (ng/ml) Initial new georgies (net perritin) Initial new georgies (net perritin) Initial new georgies (net perritin) Initial new georgies (net perrite) Initial new georgies (net perritin) Initial new georgie	1 (0,)	• ,
Initial and peak LDH (units/L) Initial and peak ferritin (ng/ml) Initial regurgitation; severe global hypokinesis of the left ventricle; LVEF 10–15% Prior to discharge LVEF 06–65% Coronary artery evaluation RHC and LHC — no evidence of coronary artery aneurysm, severe cardiomyopathy with cardiogenic shock Imaging studies Abdominal imaging CT abdomen/pelvis with contrast: mesenteric lymphadenopathy, bilateral perinephric edema extending to the adrenal glands Chest imaging Management Supplemental O ₂ requirements Yes Mechanical ventilation Yes ECMO No Hemodialysis Yes Vasoactive medications Yes Vasoactive medications Norepinephrine, vasopressin, epinephrine, dobutamine Steroids Yes Immune modulators Anticoagulation Heparin drip, rivaroxaban Total length of hospital stay (days)	1 0, ,	, ,
Initial and peak ferritin (ng/ml) Echocardiogram and cardiac catheterization Initial Mild mitral regurgitation; severe global hypokinesis of the left ventricle; LVEF 10–15% Prior to discharge LVEF 60–65% Coronary artery evaluation RHC and LHC — no evidence of coronary artery aneurysm, severe cardiomyopathy with cardiogenic shock Imaging studies Abdominal imaging CT abdomen/pelvis with contrast: mesenteric lymphadenopathy, bilateral perinephric edema extending to the adrenal glands Chest imaging Chest imaging Chest X-ray: peribronchial thickening without focal consolidation Management Supplemental O ₂ requirements Wechanical ventilation ECMO No Hemodialysis Yes Vasoactive medications Steroids Ves IVIG Two doses Immune modulators Anticoagulation Heparin drip, rivaroxaban Total length of hospital stay (days)	1 1 , 0, ,	· · · ·
Echocardiogram and cardiac catheterization Initial Mild mitral regurgitation; severe global hypokinesis of the left ventricle; LVEF 10–15% Prior to discharge LVEF 60–65% Coronary artery evaluation RHC — no evidence of coronary artery aneurysm, severe cardiomyopathy with cardiogenic shock Imaging studies Abdominal imaging CT abdomen/pelvis with contrast: mesenteric lymphadenopathy, bilateral perinephric edema extending to the adrenal glands Chest imaging Chest X-ray: peribronchial thickening without focal consolidation Management Supplemental O ₂ requirements Yes Mechanical ventilation Yes Mechanical ventilation ECMO No Hemodialysis Yes Vasoactive medications Steroids Norepinephrine, vasopressin, epinephrine, dobutamine Steroids Yes IVIG Two doses Immune modulators Anticoagulation Heparin drip, rivaroxaban Total length of hospital stay (days)		, , ,
Initial Mild mitral regurgitation; severe global hypokinesis of the left ventricle; IVEF 10–15% Prior to discharge Coronary artery evaluation RHC and LHC — no evidence of coronary artery aneurysm, severe cardiomyopathy with cardiogenic shock Imaging studies Abdominal imaging Chest X-ray: peribronchial thickening without focal consolidation Management Supplemental O2 requirements Wechanical ventilation Yes ECMO No Hemodialysis Yes Vasoactive medications Steroids Vasoactive medications Steroids Norepinephrine, vasopressin, epinephrine, dobutamine Steroids Immune modulators Antiplatelets Antiplatelets Anticoagulation Total length of hospital stay (days) Total length of hospital stay (days)	1 , 0, ,	1657 and >20 000 (22-388)
Prior to discharge Coronary artery evaluation RHC and LHC — no evidence of coronary artery aneurysm, severe cardiomyopathy with cardiogenic shock Imaging studies Abdominal imaging CT abdomen/pelvis with contrast: mesenteric lymphadenopathy, bilateral perinephric edema extending to the adrenal glands Chest imaging Chest X-ray: peribronchial thickening without focal consolidation Management Supplemental O ₂ requirements Wechanical ventilation Yes ECMO No Hemodialysis Yes Vasoactive medications Steroids Norepinephrine, vasopressin, epinephrine, dobutamine Steroids IVE IVIG Two doses Immune modulators Antiplatelets Antiplatelets Antiplatelets Aspirin Anticoagulation Total length of hospital stay (days)	· ·	
Prior to discharge Coronary artery evaluation RHC and LHC — no evidence of coronary artery aneurysm, severe cardiomyopathy with cardiogenic shock Imaging studies Abdominal imaging CT abdomen/pelvis with contrast: mesenteric lymphadenopathy, bilateral perinephric edema extending to the adrenal glands Chest imaging Chest imaging Chest imaging Chest X-ray: peribronchial thickening without focal consolidation Management Supplemental O2 requirements Yes Mechanical ventilation Yes ECMO Hemodialysis Yes Vasoactive medications Steroids Norepinephrine, vasopressin, epinephrine, dobutamine Steroids Yes IVIG Two doses Immune modulators Antiplatelets Anticoagulation Heparin drip, rivaroxaban Total length of hospital stay (days)	Initial	
Coronary artery evaluation RHC and LHC — no evidence of coronary artery aneurysm, severe cardiomyopathy with cardiogenic shock Imaging studies Abdominal imaging CT abdomen/pelvis with contrast: mesenteric lymphadenopathy, bilateral perinephric edema extending to the adrenal glands Chest imaging Chest imaging Chest X-ray: peribronchial thickening without focal consolidation Management Supplemental O ₂ requirements Mechanical ventilation Yes ECMO No Hemodialysis Vasoactive medications Norepinephrine, vasopressin, epinephrine, dobutamine Steroids IVIG IVIG Two doses Immune modulators Antiplatelets Antiplatelets Antiplatelets Antiplatelets Antipoagulation Total length of hospital stay (days)		·
Imaging studies Abdominal imaging CT abdomen/pelvis with contrast: mesenteric lymphadenopathy, bilateral perinephric edema extending to the adrenal glands Chest imaging Chest imaging Chest imaging Chest x-ray: peribronchial thickening without focal consolidation Management Supplemental O ₂ requirements Mechanical ventilation ECMO Mo Hemodialysis Ves ECMO No Hemodialysis Ves Vasoactive medications Steroids Ves VIG IMIG Two doses Immune modulators Antiplatelets Antiplatelets Anticoagulation Heparin drip, rivaroxaban Total length of hospital stay (days) arabication such adaptation cardiomyopathy with cardiogenic shock CT abdomen/pelvis with contrast: mesenteric lymphadenopathy, bilateral perinephrity, etherotes: mesenteric lymphadenopathy, bilateral perinephrite edema extending to the adrenal glands Chest X-ray: peribronchial thickening without focal consolidation No Hemodialysis Anakinra Antiplateral perinephrite edema extending to the adrenal glands Chest X-ray: peribronchial thickening without focal consolidation No Hemodialysis Anakinra Antiplateral perinephrite edema extending to the adrenal glands Chest X-ray: peribronchial thickening without focal consolidation No Hemodialysis Anakinra Antiplateral perinephrite edema extending to the adrenal glands Chest X-ray: peribronchial thickening without focal consolidati	Prior to discharge	LVEF 60-65%
Imaging studies Abdominal imaging CT abdomen/pelvis with contrast: mesenteric lymphadenopathy, bilateral perinephric edema extending to the adrenal glands Chest imaging Chest X-ray: peribronchial thickening without focal consolidation Management Supplemental O ₂ requirements Mechanical ventilation Yes Mechanical ventilation Yes ECMO No Hemodialysis Yes Vasoactive medications Norepinephrine, vasopressin, epinephrine, dobutamine Steroids Yes IVIG Two doses Immune modulators Antiplatelets Anticoagulation Heparin drip, rivaroxaban Total length of hospital stay (days)	Coronary artery evaluation	RHC and LHC — no evidence of coronary artery aneurysm, severe
Abdominal imaging CT abdomen/pelvis with contrast: mesenteric lymphadenopathy, bilateral perinephric edema extending to the adrenal glands Chest imaging Chest X-ray: peribronchial thickening without focal consolidation Management Supplemental O ₂ requirements Wechanical ventilation Yes ECMO No Hemodialysis Yes Vasoactive medications Norepinephrine, vasopressin, epinephrine, dobutamine Steroids Vyes IVIG Two doses Immune modulators Antiplatelets Anticoagulation Heparin drip, rivaroxaban Total length of hospital stay (days)		cardiomyopathy with cardiogenic shock
Chest imaging Chest X-ray: peribronchial thickening without focal consolidation Management Supplemental O ₂ requirements Mechanical ventilation FCMO No Hemodialysis Ves Vasoactive medications Steroids IVIG Immune modulators Antiplatelets Anticoagulation Total length of hospital stay (days) bilateral perinephric edema extending to the adrenal glands Chest X-ray: peribronchial thickening without focal consolidation Chest X-ray: peribronchial thickening without focal consolidation Yes Yes Yes Yes Vasoactive medications Norepinephrine, vasopressin, epinephrine, dobutamine Steroids Yes IVIG Heparin drip, rivaroxaban 24	Imaging studies	
Chest imaging Management Supplemental O ₂ requirements Mechanical ventilation Yes Mechanical ventilation Yes ECMO No Hemodialysis Vasoactive medications Steroids IVIG Immune modulators Antiplatelets Anticoagulation Antipoagulation Total length of hospital stay (days) Chest X-ray: peribronchial thickening without focal consolidation Yes Yes Yes Yes Vyes IVIG Anticoagulation Heparin drip, rivaroxaban Jean Antipra Antiplatelets Antipoagulation Total length of hospital stay (days)	Abdominal imaging	CT abdomen/pelvis with contrast: mesenteric lymphadenopathy,
Chest imaging Management Supplemental O ₂ requirements Mechanical ventilation Yes Mechanical ventilation Yes ECMO No Hemodialysis Vasoactive medications Steroids IVIG Immune modulators Antiplatelets Anticoagulation Antipoagulation Total length of hospital stay (days) Chest X-ray: peribronchial thickening without focal consolidation Yes Yes Yes Yes Vyes IVIG Anticoagulation Heparin drip, rivaroxaban Jean Antipra Antiplatelets Antipoagulation Total length of hospital stay (days)	· ·	bilateral perinephric edema extending to the adrenal glands
ManagementSupplemental O_2 requirementsYesMechanical ventilationYesECMONoHemodialysisYesVasoactive medicationsNorepinephrine, vasopressin, epinephrine, dobutamineSteroidsYesIVIGTwo dosesImmune modulatorsAnakinraAntiplateletsAspirinAnticoagulationHeparin drip, rivaroxabanTotal length of hospital stay (days)24	Chest imaging	Chest X-ray: peribronchial thickening without focal consolidation
Supplemental O_2 requirementsYesMechanical ventilationYesECMONoHemodialysisYesVasoactive medicationsNorepinephrine, vasopressin, epinephrine, dobutamineSteroidsYesIVIGTwo dosesImmune modulatorsAnakinraAntiplateletsAspirinAnticoagulationHeparin drip, rivaroxabanTotal length of hospital stay (days)24		J. P. S.
Mechanical ventilation ECMO No Hemodialysis Vasoactive medications Steroids IVIG Immune modulators Antiplatelets Anticoagulation Total length of hospital stay (days) Yes Yes Yes Yes Yor Yes Yes Two doses Anakinra Antaparin drip, rivaroxaban 24	· ·	Yes
ECMO Hemodialysis Yes Vasoactive medications Steroids IVIG Immune modulators Antiplatelets Anticoagulation Total length of hospital stay (days) No repinephrine, vasopressin, epinephrine, dobutamine Yes Two doses Immune modulators Anakinra Ansinra Ansiprin Heparin drip, rivaroxaban 24		
Hemodialysis Vasoactive medications Steroids IVIG Immune modulators Antiplatelets Anticoagulation Total length of hospital stay (days) Yes Yes Two doses Anakinra Anakinra Aspirin Heparin drip, rivaroxaban 24		
Vasoactive medications Steroids IVIG Immune modulators Antiplatelets Anticoagulation Total length of hospital stay (days) Norepinephrine, vasopressin, epinephrine, dobutamine Yes Ivis Two doses Anakinra Anakinra Anspirin Heparin drip, rivaroxaban 24		
Steroids Yes IVIG Two doses Immune modulators Anakinra Antiplatelets Aspirin Anticoagulation Heparin drip, rivaroxaban Total length of hospital stay (days) Yes Two doses Anakinra Aspirin Heparin drip, rivaroxaban 24	ž	
IVIG Two doses Immune modulators Anakinra Antiplatelets Aspirin Anticoagulation Heparin drip, rivaroxaban Total length of hospital stay (days) 24		
Immune modulatorsAnakinraAntiplateletsAspirinAnticoagulationHeparin drip, rivaroxabanTotal length of hospital stay (days)24		
Antiplatelets Aspirin Anticoagulation Heparin drip, rivaroxaban Total length of hospital stay (days) 24		
Anticoagulation Heparin drip, rivaroxaban Total length of hospital stay (days) 24		
Total length of hospital stay (days) 24	•	•
	· ·	
Number of days admitted in ICI	Total length of hospital stay (days)	
Number of days admitted in feo	Number of days admitted in ICU	21
Outcome Discharged to the skilled nursing facility	Outcome	Discharged to the skilled nursing facility

- ^a Peribronchial thickening on chest X-ray in the absence of focal consolidation or diffuse multifocal infiltrates on presentation.
- b Initial values were the peak values.

 $^{\rm c}\,$ Peak values on the initial test.

thickening and a non-contrast CT scan of the abdomen illustrated lymphadenopathy in the ileocolic mesentery and bilateral peri-nephric edema. Over the course of the next 12 h, his mean arterial pressure dropped to less than 60 mmHg, requiring initiation of vasopressor support. A transthoracic echocardiogram (TTE) revealed a new, markedly reduced left ventricular ejection fraction (LVEF) of 15-20% and severe right ventricular dysfunction. He eventually required endotracheal intubation for rapidly progressive cardiogenic shock, along with commencement of mechanical ventilation prior to requiring Impella placement and continuous renal replacement therapy (CRRT). He received intravenous immunoglobulin (IVIG) at a dose of 1 mg/kg once followed by IV methyl-prednisolone 250 mg every 6 h, subcutaneous anakinra 100 mg every 6 h, and aspirin 325 mg daily. The anakinra dose was tapered over the course of 2 weeks. After 10 days in the intensive care unit, his

LVEF recovered to 60%. His presentation and clinical course were consistent with the working definition of MIS-A.

Discussion

According to the CDC, the working case definition for a typical MIS-A presentation includes the presence of a severe illness requiring hospitalization in persons aged 21 or older, positive test results for recent SARS-CoV-2 infection (PCR, antigen, or antibody), severe dysfunction of one or more extrapulmonary organ systems, as well as markedly elevated acute inflammatory markers, all in the absence of severe respiratory illness to exclude the subset of the patients in which organ dysfunction might be the result of tissue hypoxia (Morris et al., 2020).

In October 2020, the CDC published an initial review of 27 cases with a clinical course consistent with MIS-A (Chau et al., 2020;

Magro et al., 2020; Oxley et al., 2020). Those cases had heterogeneous involvement of cardiac, gastrointestinal, dermatological, and neurological symptoms without severe respiratory system involvement at presentation. The first reported case series of CDC Morbidity and Mortality Weekly Reports (MMWR) included 11 MIS-A patients based on data collected from March to August, 2020, seven of whom underwent cardiogenic shock on presentation (Morris et al., 2020). Similarly, a recent review of 51 cases with MIS-A highlighted that cardiovascular involvement has been the most frequently reported finding (82.4%), followed by gastrointestinal manifestations (72.5%) (Bastug et al., 2021). Importantly, in MIS-A, initial COVID-19 infection can be asymptomatic too (Morris et al., 2020). This has been further illustrated in a case-based review of 51 MIS-A cases, in which only 14 patients had previous symptomatic COVID-19 illness, while in the remaining cases the initial COVID-19 infection was either asymptomatic or there were no data available (Bastug et al., 2021). Elevated CRP, neutrophil count, ESR, and fibrinogen have been reported in more than 75% of MIS cases in adolescents (Feldstein et al., 2020).

The proposed COVID-19 infectious process includes three progressive clinical phases (Siddiqi and Mehra, 2020):

Stage I: Early infection phase, with clinical manifestations driven by actively replicating virus.

Stage II: Pulmonary phase, with an overlap of viral replication effects and host inflammatory response.

Stage III: Hyperinflammation phase, with the pathophysiological process driven by the host inflammatory response.

MIS-A is proposed to be a post-infectious phase driven by dysregulated immune complex activation, causing direct endothelial damage and associated thrombo-inflammation (Morris et al., 2020). Notably, as compared with severe COVID-19, patients with MIS are more likely to demonstrate cardiorespiratory involvement (56.0% vs 8.8%) and cardiovascular without respiratory involvement (10.6% vs 2.9%) on presentation (Feldstein et al., 2021).

It should be noted that while serology consistent with prior COVID-19 infection is required to fulfill the case definition of MIS-A, it has a minimal prognostic or diagnostic role due to various limiting factors, including persistent PCR detection of non-replicable SARS-CoV-2 RNA and persistent antibody positivity due to remote previous exposure (Bastug et al., 2021; Hékimian et al., 2021). The American College of Rheumatology has recently published its initial recommendations for the management of hyperimmune response in the post-infectious phase of COVID-19, with particular focus on MIS-C and the role of immunomodulatory therapies, i.e., intravenous immunoglobulin (IVIG) and anakinra (Henderson et al., 2020).

IVIG influences the number and function of regulatory T cells ($T_{\rm regs}$), which help control inflammation (Lo and Newburger, 2018). Based on its mechanism of action, IVIG is considered a first-tier therapy, and steroids can be used as adjunctive therapy in cases of distributive shock. The proposed starting dose of IVIG is 2 g/kg (liang et al., 2020).

Anakinra, a recombinant IL-1 receptor antagonist, is a well-known drug due to its role in the management of various autoimmune conditions. It has been shown to have a quick onset of action, short half-life (4 h), and a large therapeutic window. Moreover, anakinra is rather preferred over tocilizumab, given its safety profile and lesser myelosuppressive and hepatotoxic effects (Mehta et al., 2020). Interestingly, so far there has been no randomized controlled trial to elaborate on the role of anakinra in adults with MIS-A. Our case shows that, following a similar protocol to that carried out in children with MIS-C, anakinra is likely to be effective. In its recommendations regarding MIS-A, the American College of Rheumatology has mentioned that anakinra can be considered as an additional therapy in patients refractory to IVIG and glucocorticoids (Siddiqi and Mehra, 2020). The proposed starting dose is over 4 mg/kg/day IV, with an eventual plan to taper

the dose based on clinical recovery and resolution of the markers of inflammation.

Overall, we are still in the early stages of understanding MIS-A. More research is needed to further delineate diagnostic and prognostic markers of MIS-A, as well as to elaborate on disease management in critically ill patients.

Conflicts of interest

All authors declare:

- no financial relationships with any organizations that might have an interest in the submitted work.
- no other relationships or activities that could appear to have influenced the submitted work,

Funding source

There was no financial or funding support involved in the preparation of this manuscript.

Ethical approval

Not required. The individual case report submission was exempt from Institutional Review Board approval.

References

- Bastug A, Aslaner H, Aybar Bilir Y, Kemirtlek N, Gursoy FM, Bastug S, et al. Multiple system inflammatory syndrome associated with SARS-CoV-2 infection in an adult and an adolescent. Rheumatol Int 2021;41:993–1008, doi:http://dx.doi.org/10.1007/s00296-021-04843-1.
- Chau VQ, Giustino G, Mahmood K, Oliveros E, Neibart E, Oloomi M, et al. Cardiogenic shock and hyperinflammatory syndrome in young males with COVID-19. Circ Hear Fail 2020;13:, doi:http://dx.doi.org/10.1161/CIRCHEARTFAILURE.120.007485.
- 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, doi:http://dx.doi.org/10.1056/NEJMoa2021680.
- Feldstein LR, Tenforde MW, Friedman KG, Newhams M, Rose EB, Dapul H, et al. Characteristics and outcomes of US children and adolescents with multisystem inflammatory syndrome in children (MIS-C) compared with severe acute COVID-19. JAMA 2021;325:1074, doi:http://dx.doi.org/10.1001/jama.2021.2091.
- Hékimian G, Kerneis M, Zeitouni M, Cohen-Aubart F, Chommeloux J, Bréchot N, et al. Coronavirus disease 2019 acute myocarditis and multisystem inflammatory syndrome in adult intensive and cardiac care units. Chest 2021;159:657–62, doi:http://dx.doi.org/10.1016/j.chest.2020.08.2099.
- Henderson LA, Canna SW, Friedman KG, Gorelik M, Lapidus SK, Bassiri H, et al. American College of Rheumatology clinical guidance for multisystem inflammatory syndrome in children associated with SARS-CoV-2 and hyperinflammation in pediatric COVID-19: version 1. Arthritis Rheumatol 2020;72:1791-805, doi:http://dx.doi.org/10.1002/art.41454.
- Jiang L, Tang K, Levin M, Irfan O, Morris SK, Wilson K, et al. COVID-19 and multisystem inflammatory syndrome in children and adolescents. Lancet Infect Dis 2020;20:e276–88, doi:http://dx.doi.org/10.1016/S1473-3099(20)30651-4.
- Lo MS, Newburger JW. Role of intravenous immunoglobulin in the treatment of Kawasaki disease. Int J Rheum Dis 2018;21:64–9, doi:http://dx.doi.org/10.1111/ 1756-185X.13220.
- Magro C, Mulvey JJ, Berlin D, Nuovo G, Salvatore S, Harp J, et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: a report of five cases. Transl Res 2020;220:1–13, doi:http://dx.doi.org/10.1016/j.trsl.2020.04.007.
- Mehta P, Cron RQ, Hartwell J, Manson JJ, Tattersall RS. Silencing the cytokine storm: the use of intravenous anakinra in haemophagocytic lymphohistiocytosis or macrophage activation syndrome. Lancet Rheumatol 2020;2:e358–67, doi: http://dx.doi.org/10.1016/S2665-9913(20)30096-5.
- Morris SB, Schwartz NG, Patel P, Abbo L, Beauchamps L, Balan S, et al. Case series of multisystem inflammatory syndrome in adults associated with SARS-CoV-2 infection United Kingdom and United States, March-August 2020. Morb Mortal Wkly Rep 2020;69:1450-6, doi:http://dx.doi.org/10.15585/mmwr.mm6940e1.
- Oxley TJ, Mocco J, Majidi S, Kellner CP, Shoirah H, Singh IP, et al. Large-vessel stroke as a presenting feature of COVID-19 in the young. N Engl J Med 2020;382:e60, doi:http://dx.doi.org/10.1056/NEJMc2009787.
- Siddiqi HK, Mehra MR. COVID-19 illness in native and immunosuppressed states: a clinical-therapeutic staging proposal. J Hear Lung Transplant 2020;39:405–7, doi:http://dx.doi.org/10.1016/j.healun.2020.03.012.