

Mucocutaneous manifestations among adults hospitalized with multisystem inflammatory syndrome following SARS-CoV-2 infection



To the Editor: Multisystem inflammatory syndrome in adults (MIS-A) is temporally associated with SARS-CoV-2 infection. MIS-A manifests with fever, elevated inflammatory markers, and extrapulmonary disease with multiorgan dysfunction, including cardiac, abdominal, and neurologic symptoms, hypotension or shock, hypercoagulability, and mucocutaneous findings.^{1,2} The description of rash morphology in MIS-A is limited.³

We previously conducted a prospective study wherein hospitalized adults with COVID-19 at Northwell Health underwent integumentary examination. We estimated the prevalence of rash, characterized its morphology, and described related clinical courses for children and adolescents with COVID-19 and multisystem inflammatory syndrome and adults with COVID-19.^{4,5} In collaboration with the Centers for Disease Control and Prevention, we postulated that applying working MIS-A criteria to our cohort of hospitalized COVID-19 cases may identify cases and specify the morphology of mucocutaneous disease in MIS-A.

The retrospective application of the MIS-A criteria to 35 adults with COVID-19 and rash hospitalized between March 23, 2020, and December 18, 2020, identified 6 patients who developed hyperinflammation with mucocutaneous involvement 16 to 49 days (median, 30 days; interquartile range, 21-32 days) after acute illness. All 6 patients had respiratory illness and positive SARS-CoV-2 reverse transcription polymerase chain reaction testing before the onset of illness and multiorgan dysfunction. Serologic testing, although not confirmatory for MIS, was performed for patient 1 and indicated the presence of antibodies against SARS-CoV-2. The clinical characteristics of probable MIS-A included abdominal symptoms, neurologic signs and symptoms, severe cardiac symptoms, hypotension or shock, and thrombocytopenia or elevated D-dimer levels (Table 1).

Purpura, including petechiae, ecchymosis, retiform purpura, and necrosis on the cheeks, was observed in 5 patients. Morbilliform eruption on

the trunk and extremities were observed in 2 patients. More than 1 morphology was observed in 3 patients. One had bilateral, nonexudative conjunctivitis. Mucocutaneous findings identified in these 6 patients were captured once during hospitalization and could not be correlated with other systemic inflammatory manifestations.

Purpura, also described in a cohort of children and adolescents diagnosed with multisystem inflammatory syndrome, was observed in nearly all suspected cases.³ The presence of purpura implicates endothelial cell injury as a feature of post-COVID-19 hyperinflammation that also contributes to hematologic, cardiac, gastrointestinal, and neurologic features of MIS-A.

The influence of mucocutaneous disease on higher mortality observed in our MIS-A cohort is unclear. A higher mortality reported herein than that reported in other MIS-A cohorts may also be related to older age and severity of acute COVID-19 symptoms, which required hospitalization for this cohort.¹ Notably, 4 patients developed encephalopathy, which has also been reported in MIS-A.¹

The interpretation of our findings is limited by the retrospective approach and small sample size. Although it is possible that our observations were direct manifestations of postacute sequelae of “long” COVID-19, constellation and timing of clinical features suggested a distinct presentation consistent with MIS-A. It is also possible that patients may be misclassified as the MIS-A criteria evolve. Given the complexity in the clinical course of these patients, medication reactions or concomitant diagnoses may have contributed to the findings. Nonetheless, our initial observations will support further development of the MIS-A criteria regarding the presence and type of mucocutaneous disease. The study team in collaboration with the Centers for Disease Control and Prevention is undertaking a study to evaluate MIS-A criteria, including specific morphologic characteristics of mucocutaneous manifestations.

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Table I. Clinical characteristics of 6 patients with probable multisystem inflammatory syndrome in adults at 2 New York health centers between March 23, 2020, and December 18, 2020

Characteristic	Patients					
	1	2	3	4	5	6
Age (years); sex (M/F)	43; M	56; F	76; M	57; F	83; M	59; M
Comorbidities	Former alcohol abuse, fatty liver disease	Diabetes mellitus	Tobacco use, COPD, hypertension, congestive heart failure	Obesity, rheumatic heart disease	None	None
Days from onset of acute COVID-19 symptoms to MIS symptoms	16	32	19	32	27	49
Morphology of mucocutaneous findings	Morbilloform eruption of chest, extremities, and back; nonexudative conjunctivitis	Purpura of the neck; necrosis of the cheeks	Purpura of the arms and hands	Petechiae of the trunk, arms, and thighs	Retiform purpura of bilateral legs	Morbilloform eruption of the arms; retiform purpura of the arms and hands
Abdominal symptoms	Diarrhea	Diarrhea	Diarrhea	Diarrhea, abdominal pain	Diarrhea, abdominal pain, nausea and vomiting	None
Neurologic signs/symptoms	Encephalopathy	Encephalopathy	Encephalopathy	Encephalopathy, new-onset upper and lower extremity weakness	Seizures	Encephalitis
Severe cardiac illness	LV systolic dysfunction, RV strain, pericardial effusion	Pericarditis, RV enlargement, RV systolic dysfunction	Ventricular tachycardia, LV systolic dysfunction, pericardial effusion	Diastolic dysfunction, RA enlargement, pulmonary hypertension	Global hypokinesia, cardiomyopathy, atrioventricular conduction abnormalities	RV enlargement, PE
Hypotension/shock requiring vasopressors	Yes	Yes	Yes	Yes	Yes	Yes
Minimum platelet count (reference, 150-400 K/uL)	145	129	147	150	66	467
Maximum D-dimer (reference <229 ng/mL)	1086	1914	1077	3228	2434	4452
Outcome	Discharged	Expired	Expired	Discharged	Expired	Expired

COPD, Chronic obstructive pulmonary disease; LV, left ventricular; MIS, multisystem inflammatory syndrome; PE, pulmonary embolism; RA, right atrial; RV, right ventricular.

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Conflicts of interest

Dr Garg has received honoraria from AbbVie, Amgen, Boehringer Ingelheim, Incyte, Janssen, Novartis, Pfizer, UCB, and Viela Bio and has served as an advisor for AbbVie, Amgen, Boehringer Ingelheim, Janssen, Pfizer, Incyte, InfalRx, Viela Bio, and UCB. Authors Tannenbaum, Strunk, Burshtein, Grbic, Nazir, and Norden and Drs Rekhtman, Birabaharan, Shaigany, Godfred-Cato, Belay, and Patel do not have any conflicts of interest to disclose.

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