Cutaneous findings in SARS-CoV-2-associated Multisystem Inflammatory Disease in Children (MIS-C)

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Abstract:

Rash is a common feature of the multisystem inflammatory syndrome in children (MIS-C), a post-infectious hyperinflammatory disease associated with prior SARS-CoV- 2 infection. Because the differential diagnosis of fever and rash in children is broad, understanding clinical characteristics of MIS-C may assist with diagnosis. Here we describe the cutaneous findings observed in a series of children with MIS-C-associated rash.

Introduction:

In April 2020, a hyperinflammatory condition apparently associated with SARS-CoV-2 was recognized in children. This syndrome, now termed multisystem inflammatory syndrome in children (MIS-C),[4] is characterized by fever, profound systemic inflammation, multi-organ involvement, and often rash.[23] Here, we describe the dermatologic manifestations of MIS-C at a single institution.

Methods:

All children admitted to our tertiary care, academic, pediatric medical center with concern for MIS-C per CDC criteria are routinely evaluated by an expert multidisciplinary committee to reach diagnostic consensus.[5] Skin findings were photographed and included in the secure electronic health record. Clinical characteristics were abstracted through chart review. As of 28 July 2020, a total of 24 children were diagnosed with MIS-C, of whom 18 (75%) exhibited mucocutaneous changes and photographs had been obtained during the course of clinical care for 10 (41.7%). Consent was obtained for 7 patients. Clinical and laboratory findings of patients 1, 2, and 4 have been previously reported.[6]

Patient consent statement:

The design of this work was reviewed by the Institutional Review Board of the Children's Hospital of Philadelphia, who deemed this exempt research. Verbal informed consent for photograph use was obtained from the parents or legal guardians of all children whose images are included in this study.

Results:

Patients with MIS-C exhibited a variety of cutaneous clinical findings (Figure 1, Table 1). Palmar and plantar erythema were observed in 3/7 (43%) patients; no patient exhibited plantar erythema in the absence of palmar erythema. While discrete lesions were noted in all body locations, lesions on the chest and upper extremities were common (4/7, 57%) (Fig. 1A-D) and the lower extremities were uniformly involved (7/7 of patients) (Fig. IE-H). In particular, 5/7 patients (71%) had lesions of the proximal medial thigh. Two patients exhibited rash on or around the ears (2/7, 29%) and neck (Fig1I,J). Although mucosal changes were common (6/7, 86%), including lip changes, the remaining

face was less frequently involved: one patient each had lesions on the forehead/hairline (Fig.1I) and cheek (not shown).

A variety of erythematous lesions were observed, classified as urticarial, morbilliform, and livedoid. These skin changes were observed in patients with diverse skin tones and pigmentation. The most common lesions observed were small-to-medium annular plaques (taking on an urticarial appearance) in 57% (4/7) of patients, although morbilliform eruptions with coalescing papules to plaques (Fig. 1K) and coalescing macules were also noted, each in one patient. Reticulated plaques and patches (taking on a livedoid appearance) were noted in 2 patients (29%) (Fig. 1L, M, N). 29% (2 of 7) of children described the rash as mildly pruritic. In one patient, rash did not occur until the fourth hospital day, following recrudescent fever after IVIG and steroids; the rash resolved with an additional dose of IVIG. Purpura were seen in 4 (57%) of 7 patients. Most commonly (3 of 4), purpura were noted in the center of annular (urticarial) plaques, mimicking the appearance of erythema multiforme-like lesions. All skin findings completely resolved by the time of hospital discharge. In contrast to rashes associated with Kawasaki disease, none of the rashes desquamated.

Discussion:

MIS-C, thought to be a post-infectious complication of SARS-CoV-2 infection, remains largely a diagnosis of exclusion, as its clinical manifestations, including fever, gastrointestinal distress, and rash, are common to many other pediatric infections. Acute COVID-19 has presented with a myriad of cutaneous findings in children, including erythema multiforme, urticaria, vesicular exanthem, polymorphic rash, purpura, and pityriasis rosea-like eruption.[7] The pathophysiology of SARS-CoV-2-associated rashes are poorly understood, and may overlap with that of MIS-C-associated mucocutaneous changes.

We find that no unique, stereotypic rash was observed in patients who were treated for MIS-C, although annular plaques in the proximal medial lower extremities were common, a finding that warrants further study in larger cohorts. We note overlap between cutaneous findings of MIS-C and those observed in rickettsial illness (palmar/plantar involvement), toxic shock syndrome (diffuse rash

and some erythroderma), Kawasaki disease (diffuse rash, mucocutaneous changes, extremity changes), and viral exanthems, which continue to pose a significant diagnostic dilemma.

Limitations include a small sample size, due in part to the rarity of MIS-C and challenges imposed by isolation precautions, as well as the imprecision of MIS-C diagnostic criteria.

Conclusions:

Cutaneous manifestations are common in MIS-C, although the underlying pathophysiology is not well understood. We anticipate these images and descriptions will aid clinicians in the diagnosis of future cases.

Notes/Acknowledgments:

We thank the Children's Hospital of Philadelphia MIS-C Research Collaborative for its contribution to the work described, especially Hamid Bassiri, Edward M. Behrens, Caroline Diorio, Julie C. Fitzgerald, Therese Giglia, Michele Lambert, Whitney Petrosa, David T. Teachey, Laura A. Vella, and Char Witmer. AB is supported by NIH T32-GM075766. KC is supported by AHRQ K12-HS026393. LSC is supported by the Dermatology Foundation. AOJ is supported by NIH/NIAID R01-AI103280, R21-AI123808, and R21-AI130584, and AOJ is an Investigator in the Pathogenesis of Infectious Diseases (PATH) of the Burroughs Wellcome Fund. *Potential conflicts of interest*: None of the authors (AMB, MO, KC, LCS, or AOJ) report an association that may pose a conflict of interest with the current study.

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Figure legend

Figure 1. Characteristic cutaneous findings in pediatric MIS-C.

Arrows indicate regions of erythema.

Table 1. Clinical and dermatological characteristics of patients with MIS-C

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Figure 1 panel	A, C, D, G, I	B, F	E	H	J	K	L, M, N
Age in years / sex	8 F	5 F	8 F	14 F	11 M	10 M	7 F
BMI (kg/m^2) / comorbidities	15.26 / asthma	16.0 / none	23.8 / none	18.8 / none	ND / autism	35.9 / none	26.2 / none
Presenting symptoms							
Fever	+	+	+	+	+	+	+
Diarrhea	-	+	+	+	+	+	+
Abdominal pain/emesis	+	+	+	-	+	+	+
Rash	+	+	+	+	+	+	-
Conjunctivitis	+	-	+	-	+	+	+
Fissured lips/strawberry tongue	-	+	+	-	+	+	+
Lymphadenopathy	-	-	-	-	-	-	-
Extremity edema	-	+	-	-	-	+	+
Headache	-	-	+	+	-	-	+
Altered mental status/irritability	-	-	-	-	-	-	-
Respiratory failure	-	+	+	+	-	-	+
Shock	+	+	+	+	-	+	+
Key initial findings							
C-reactive protein (mg/dL)	18.9	16.8	8.7	34.3	5.7	23.5	35.3
Procalcitonin (ng/mL)	ND	69.97	22.82	15.29	ND	14.18	27.15
Ferritin (ng/mL)	806.8	512.6	644	1096	857.3	3774	3559.5
Platelets (10^3/mL)	251	98	232	150	96	155	94
Brain type natriuretic peptide (pg/mL)	77	606	72.6	ND	16.2	722.6	291
Absolute lymphocyte count (cells/uL)	1080	910	1310	170	240	1030	400

Troponin (ng/mL)	0.03	0.3	0.19	ND	0.01	0.65	0.04
SARS-CoV-2 testing							
Nasopharyngeal SARS-CoV-2 PCR (Cycle threshold if +)	Negative	Positive (40.21)	Negative	Negative	Positive (40.08)	Negative	Positive (35.17)
Anti-SARS-CoV-2 IgG	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Outcome	**Home**	**Home**	**Home**	**Home**	**Home**	**Home**	**Home**
Key dermatological findings							
Rash details							
Fitzpatrick Phototypes (I - VI)	IV	II	V	V	III	V	II
Morphology	Annular plaques	Annular plaques	Annular plaques	Macules and Patches	Macules and patches	Papules and plaques (some annular, some reticulated)	Reticulated patches
Affected body parts	Neck, Trunk (back, chest), lower extremities (inne	Trunk (chest and abdomen), lower extremities (inner thighs) including skin folds (popliteal fossa), feet	Lower extremities (inner thighs) including skin folds (inguinal crease), palms	Upper and lower extremities (inner/ anterior thighs, knees) including skin folds (poplit	Trunk (back), upper and lower extremities (inner thighs)	Neck and trunk (Back), Upper and lower extremities	Upper extremities (shoulder and hand), lower extremitie

	r thighs) including skin folds (axilla, inguinal crease)			eal fossa), palms and soles			s (knees),
Purpura	-	+	+	+	-	+	-
Classification	Urticarial	Urticarial	Urticarial	Morbilliform	Morbilliform	Urticarial	Lived oid
Mucosal involvement (erythema of the lips, tongue, and/or ocular conjunctivitis)	+	+	+	-	+	+	+
Acral erythema	-	+	+	+	-	-	-

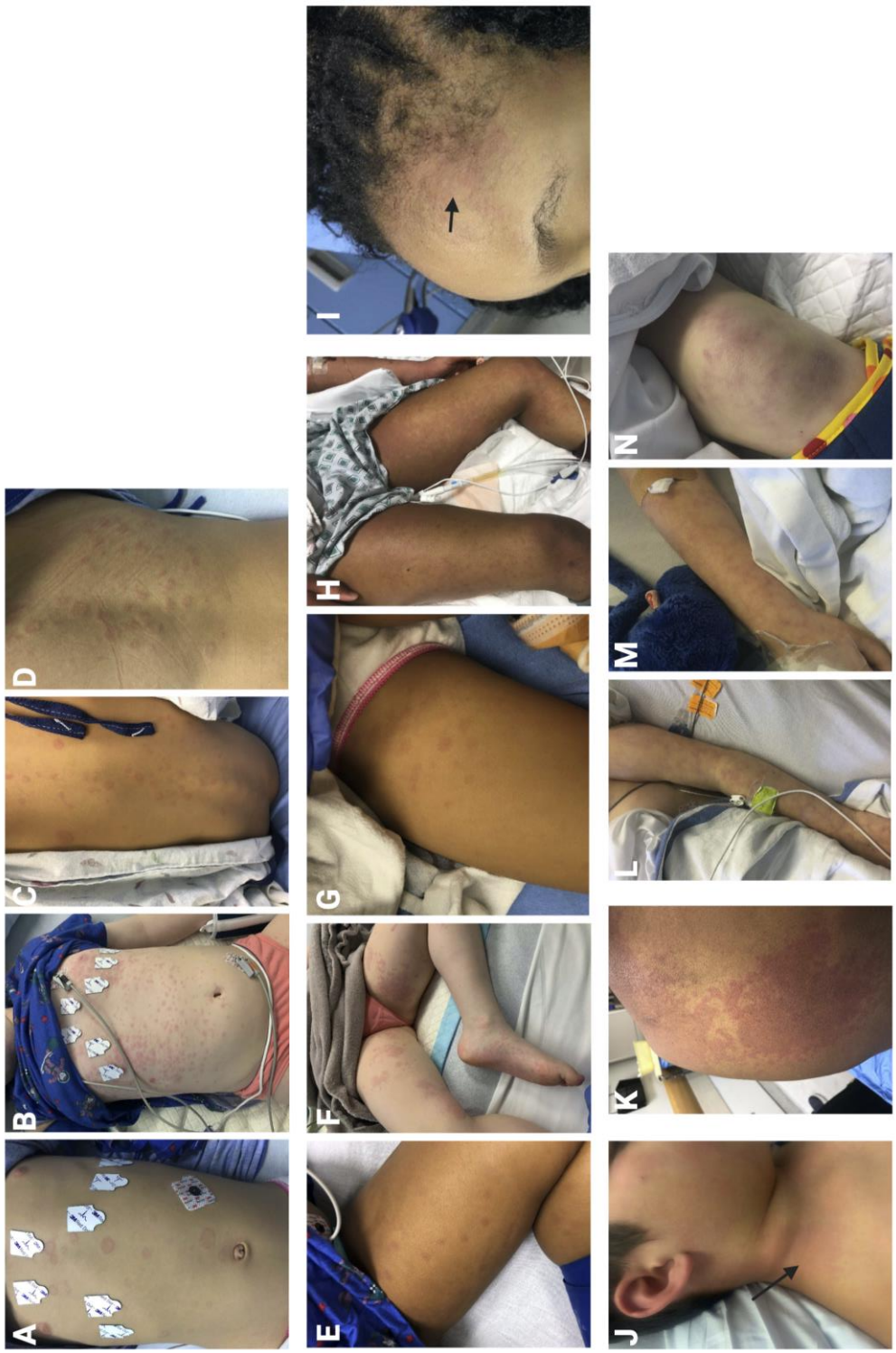

Figure1