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ORIGINAL ARTICLE

The spectrum of COVID-19–associated dermatologic manifestations: An international registry of 716 patients from 31 countries

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Boston, Massachusetts; Philadelphia, Pennsylvania; Dallas and Plano, Texas; New York, New York; Munich, Germany; Miami, Florida; Detroit, Michigan; Charleston, South Carolina; St Louis, Missouri; and San Francisco, California

Background: Coronavirus disease 2019 (COVID-19) has associated cutaneous manifestations.

Objective: To characterize the diversity of cutaneous manifestations of COVID-19 and facilitate understanding of the underlying pathophysiology.

Methods: Case series from an international registry from the American Academy of Dermatology and International League of Dermatological Societies.

Results: The registry collected 716 cases of new-onset dermatologic symptoms in patients with confirmed/suspected COVID-19. Of the 171 patients in the registry with laboratory-confirmed COVID-19, the most common morphologies were morbilliform (22%), pernio-like (18%), urticarial (16%), macular erythema (13%), vesicular (11%), papulosquamous (9.9%), and retiform purpura (6.4%). Pernio-like lesions were common in patients with mild disease, whereas retiform purpura presented exclusively in ill, hospitalized patients.

Limitations: We cannot estimate incidence or prevalence. Confirmation bias is possible.

Conclusions: This study highlights the array of cutaneous manifestations associated with COVID-19. Many morphologies were nonspecific, whereas others may provide insight into potential immune or inflammatory pathways in COVID-19 pathophysiology. (J Am Acad Dermatol https://doi.org/10.1016/j.jaad.2020.06.1016.)

Key words: COVID-19; COVID toes; dermatology; global health; macular erythema; morbilliform; pernio; public health; registry; retiform purpura; SARS-CoV-2; urticarial; vesicular.

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IRB approval status: The registry was reviewed by the Partners Healthcare (Massachusetts General Hospital) IRB and was determined to not meet the definition of human subjects research.

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COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has associated cutaneous manifestations.[1] Case series have documented pernio-like lesions,[2-7] erythematous macules or papules,[5,6,8] urticarial,[8,9] morbilliform,[9] varicelliform,[5,6,8-10] papulosquamous,[11] petechial eruptions,[9,12] livedo reticularis-like rashes,[5,9] purpuric lesions,[5] acro-ischemic lesions,[13] and retiform purpura.[14] The timing of eruptions in the disease course and potential associations between morphologic subtypes with different COVID-19–associated syndromes and/or outcomes remain unclear.

Dermatologic manifestations of infectious diseases are important for identifying and treating viral illnesses including HIV, dengue, and chikungunya. Expert guidance in recognizing these signs represents an opportunity to improve diagnosis and management. Identification and characterization of COVID-19 skin lesions, like the well-described association with anosmia, may prompt suspicion for SARS-CoV-2 infection.[15] Thus, dermatologists at Harvard Medical School and Massachusetts General Hospital created the COVID-19 Dermatology Registry and, in collaboration with the American Academy of Dermatology (AAD) and International League of Dermatologic Societies (ILDS), invited health care workers globally to submit data for possible cutaneous manifestations of confirmed or suspected COVID-19.[16]

For this study, we aimed to (1) characterize internationally representative cutaneous manifestations of confirmed/suspected COVID-19 and 2) identify cutaneous manifestations that may provide insight into the pathophysiology and disease course of COVID-19.

CAPSULE SUMMARY

- In this international registry, the most common dermatologic morphologies in 171 COVID-19 laboratory-confirmed cases included morbilliform (22%), pernio-like (18%), urticarial (16%), macular erythema (13%), vesicular (11%), papulosquamous (9.9%), and retiform purpura (6.4%).
- Pernio-like lesions were noted in mild disease, whereas retiform purpura was seen exclusively in critically ill patients.

METHODS

In collaboration with the AAD and ILDS, we established an international registry to collect cases of COVID-19 cutaneous manifestations (www.aad.org/covidregistry); the registry is open to medical professionals only, from any specialty.[7] No protected health information was collected, and all data were deidentified. The registry collected COVID-19 diagnosis type (suspected vs laboratory confirmed), demographics, comorbidities, dermatologic condition details, timing of symptoms, skin biopsy results, COVID-19 symptoms and outcomes, including hospitalization, oxygen and ventilator requirements, and deaths. Providers were prompted by e-mail for case updates.

Suspected or laboratory-confirmed COVID-19 cases with new-onset dermatologic findings were eligible for inclusion in the initial analysis. Patients whose eruptions were identified as drug induced by submitting health care providers were analyzed separately. Additional analysis was performed on the laboratory-confirmed COVID-19 patient subgroup. For patients with pernio-like lesions, we excluded those with prior pernio history. Data were analyzed by using Stata (version 16). The Partners Healthcare institutional review board approved this study, which did not meet the definition of human subjects research.

RESULTS

From April 8 to May 17, 2020, 716 cases of new-onset dermatologic manifestations in the setting of confirmed/suspected COVID-19 were entered into the registry by dermatologists (54%), other physicians (32%), midlevel practitioners (7.3%), nurses (2.8%), and other medical professionals (3.4%). Cases were reported from 31 countries, most (89%) from the United States. Seven cases designated by providers as medication-induced were analyzed separately and excluded from subgroup analysis of laboratory confirmed cases (Supplemental Table I; available via Mendeley at http://doi.org/10.17632/gh945hpwy3.1), and 27 cases with prior pernio history were excluded. A total of 171 cases (25%) were laboratory confirmed: 135 by polymerase chain reaction (PCR), 19 by antibody, and 17 by unspecified testing (positive result on COVID-19 laboratory assay, but the specific test performed was unreported or unknown). The median age of patients with laboratory-confirmed COVID-19 was 44 years (interquartile range [IQR], 28-61), and 54% were female (Table I).

In the 171 patients with laboratory-confirmed COVID-19, the most common morphologies were morbilliform (22%), pernio-like (18%), urticarial (16%), macular erythema (13%), vesicular (11%), papulosquamous (9.9%), and retiform purpura (6.4%) (for clinical photos, see Supplemental Fig 1;

Abbreviations used:

AAD:	American Academy of Dermatology
IQR:	interquartile range
PCR:	polymerase chain reaction
SARS-CoV-2:	severe acute respiratory syndrome coronavirus 2

available via Mendeley at http://doi.org/10.17632/gh945hpwy3.1). A subgroup analysis of patients submitted by dermatologists showed similar distribution (Supplemental Table II; available via Mendeley at http://doi.org/10.17632/gh945hpwy3.1). A minority of patients presented with multiple morphologies, including 4 cases of morbilliform plus urticarial rash, and 2 cases of morbilliform plus pernio. Six reports involved mucous membranes (4 of oral mucosa and 2 of conjunctivae). Of 17 reports of edema, most (71%) were associated with another cutaneous finding.

Skin symptoms and affected body sites varied by morphology (Table II). For example, morbilliform morphologies were often pruritic and involved the trunk, whereas pernio morphologies often caused pain/burning and involved the feet/hands. The face was involved in 21% of morbilliform rashes. Retiform purpura were on the extremities and buttocks. The full course of laboratory-confirmed rashes lasted a median of 7 days (IQR, 3-10). Pernio, however, had a longer course, with a median of 14 days (IQR, 8-24). Full duration could be determined only for resolved lesions. Most patients (72%) had ongoing lesions; therefore, these values may underestimate duration.

Lesions generally occurred after (64%) or concurrent (15%) with other COVID-19 symptoms. In particular, skin lesions occurred after COVID-19 symptoms for morbilliform (76%), pernio-like (48%), urticarial (67%), macular erythema (57%), vesicular (72%), papulosquamous (53%), and retiform purpura (91%) morphologies. A minority occurred before other COVID-19 symptoms (12%).

Many patients with laboratory-confirmed COVID-19 and dermatologic findings had no clear documented COVID-19 exposure (Table III). The most common COVID-19 symptoms among laboratory-confirmed cases included fever (61%) and cough (59%). With respect to Centers for Disease Control and Prevention (CDC)–defined PCR test qualifying symptoms, patients with pernio-like skin lesions met fewer CDC testing criteria, meeting 3 or more criteria in 29%, compared to morbilliform eruptions (55%), urticaria (70%), macular erythema (74%), or vesicular eruptions (61%).[17] An additional 8.8% of patients with laboratory-confirmed COVID-19 were asymptomatic aside from rash. Pernio-like lesions were not associated with other COVID-19 symptoms in 19%.

The most common medical comorbidities included hypertension (16%), diabetes (12%), and smoking (12%). Most patients did not receive COVID-19–specific treatment (60%). For the 69 patients receiving COVID-19 treatment, 55% received antimalarial agents, and 50% received antibiotics including azithromycin (56%), ceftriaxone (37%), vancomycin (37%), piperacillin-tazobactam (29%), and doxycycline (27%). Treatment preceded the COVID-19–associated dermatologic condition in 56%. For morbilliform rashes, 37% received no treatment, 15% received treatment before morbilliform rashes started, and 48% received treatment after morbilliform rash onset.

Hospitalization varied: 16% of patients with pernio-like lesions were hospitalized, compared to 35% for all other COVID-19 dermatologic manifestations. Patients with retiform purpura tended to be sicker; 100% were hospitalized and 82% had acute respiratory distress syndrome (Table III and Fig 1). For the 60 hospitalized patients with laboratory-confirmed COVID-19, 24 (40%) required invasive mechanical ventilation and/or extracorporeal membrane oxygenation, and 17 (28%) required supplemental oxygen. The most common complication was acute respiratory distress syndrome, in 23 (38%). Ten patients died, including those with morbilliform rash and macular erythema (n = 2), urticaria (n = 1), acrocyanosis and pernio-like lesions (n = 1), acrocyanosis (n = 1), livedo-reticularis (n = 1), retiform purpura (n = 2), livedo racemosa (n = 1), retiform purpura and livedo racemosa (n = 1), and pernio-like lesions, acrocyanosis, and petechiae (1).

Dermatopathology (Table IV) was available from 14 laboratory-confirmed cases (15 total biopsies). Six patients with clinical retiform purpura and/or livedo racemosa showed thrombotic vasculopathy. One patient with clinically described buttock pressure injury also showed thrombotic vasculopathy. Another patient with a complicated hospital course also developed buttock pressure injury and retiform purpura, but the biopsy showed only clotting and pressure necrosis. One patient with palpable purpura with ulceration showed leukocytoclastic vasculitis. Two patients with papulosquamous morphologies showed spongiosis and dermal inflammation. One patient with pernio-like lesions had vacuolar interface dermatitis, subepidermal edema, and superficial and deep lymphocytic inflammation. One patient with an acrally distributed petechial, macular, and urticarial eruption showed diffuse vacuolar interface dermatitis with numerous dyskeratotic keratinocytes, sparse perivascular

Table I. Characteristics of cases reported for new-onset dermatologic conditions in the setting of COVID-19

Characteristic	COVID-19 laboratory confirmed* (n = 171)	COVID-19 clinically suspected (n = 511)	Total (N = 682)
Reporter title, n (%)			
Dermatologist	81 (47)	289 (57)	370 (54)
Other physician	63 (37)	157 (31)	220 (32)
Physician assistant	12 (7.0)	16 (3.1)	28 (4.1)
Nurse practitioner	5 (2.9)	17 (3.3)	22 (3.2)
Nurse	8 (4.7)	11 (2.2)	19 (2.8)
Other medical professional	2 (1.2)	21 (4.1)	23 (3.4)
Patient age, y, median (IQR)	44 (28-61)	28 (18-42)	30 (19-49)
Patient sex, female, n (%)	93 (54)	260 (51)	353 (52)
Patient race/ethnicity, n (%)†			
White	115 (67)	428 (84)	543 (80)
Asian	15 (8.8)	34 (6.7)	49 (7.2)
Black/African American	7 (4.1)	6 (1.2)	13 (1.9)
Hispanic/Latino	24 (14)	10 (1.2)	34 (5.0)
Missing	10 (5.8)	33 (6.5)	43 (6.3)
Patient geographic region, n (%)			
North America			
United States	148 (88)	458 (90)	606 (89)
Canada	2 (1.2)	17 (3.3)	19 (2.8)
Europe	10 (5.9)	25 (4.9)	35 (5.1)
Asia	6 (3.6)	6 (1.2)	12 (1.8)
Latin America and the Caribbean	2 (1.2)	4 (0.8)	6 (1.8)
Africa	1 (0.6)	—	1 (0.1)
Oceania	—	1 (0.2)	1 (0.1)
Condition type, n (%)			
Skin	166 (97)	509 (100)	675 (99)
Edema	13 (7.6)	50 (9.8)	63 (9.2)
Mucous membrane	8 (4.7)	10 (2.0)	18 (2.6)
Hair	2 (1.2)	3 (0.6)	5 (0.7)
Nail	1 (0.6)	4 (0.8)	5 (0.7)
Morphology of skin change, n (%)			
Pernio	31 (18)	391 (77)	422 (62)
Morbilliform	38 (22)	25 (4.9)	63 (9.2)
Urticarial	27 (16)	28 (5.5)	55 (8.1)
Macular erythema	23 (14)	29 (5.7)	52 (7.6)
Vesicular	18 (11)	31 (6.1)	49 (7.2)
Acrocyanosis	7 (4.1)	41 (8.0)	48 (7.0)
Acral desquamation	7 (4.1)	29 (5.7)	36 (5.3)
Papulosquamous	17 (9.9)	15 (2.9)	32 (4.7)
Livedo reticularis-like	9 (5.3)	15 (2.9)	24 (3.5)
Erythroderma	4 (2.3)	17 (3.3)	21 (3.1)
Grover-like	9 (5.3)	10 (2.0)	19 (2.8)
Retiform purpura	11 (6.4)	7 (1.4)	18 (2.6)
Petechial	5 (2.9)	11 (2.2)	16 (2.3)
Bullous	3 (1.8)	11 (2.2)	14 (2.1)
Palpable purpura/vasculitis	5 (2.9)	7 (1.4)	12 (1.8)
Dengue-like	6 (3.5)	5 (1.0)	11 (1.6)
Pressure injury	8 (4.7)	2 (0.4)	10 (1.5)
Pustular	—	5 (1.0)	5 (0.7)
Erythema nodosum	2 (1.2)	3 (0.6)	5 (0.7)
Livedo racemosa	4 (2.3)	—	4 (0.6)
Miliaria rubra	2 (1.2)	1 (0.2)	3 (0.4)
Multisystem inflammatory syndrome	1 (0.6)	1 (0.2)	2 (0.3)
Acneiform	1 (0.6)	—	1 (0.1)

IQR, Interquartile range.

*Confirmed by polymerase chain reaction test, antibody test, or unspecified laboratory assay.

†Question not asked of all participants.

Table II. Dermatologic findings in patients with laboratory-confirmed COVID-19

Characteristics	Laboratory-confirmed COVID-19						
	Morbilliform (n = 38)*	Pernio (n = 31)	Urticarial (n = 27)	Macular erythema (n = 23)	Vesicular (n = 18)	Papulosquamous (n = 17)	Retiform purpura (n = 11)
Age, y, median (IQR)	52 (36-66)	35 (22-59)	42 (29-54)	31 (27-55)	55 (36-58)	28 (27-38)	66 (51-73)
Female sex, n (%)†	19 (50)	16 (52)	21 (78)	16 (70)	10 (56)	7 (41)	2 (18)
Body site affected, n (%)							
Face	8 (21)	—	8 (30)	6 (26)	6 (33)	4 (24)	—
Head (excluding face)	2 (5.3)	—	4 (15)	1 (4.3)	1 (5.6)	—	—
Neck	10 (26)	—	5 (19)	6 (26)	1 (5.6)	4 (24)	—
Chest	19 (50)	—	8 (30)	8 (35)	6 (33)	8 (47)	—
Abdomen	24 (63)	—	11 (41)	9 (39)	8 (44)	11 (65)	—
Back	23 (61)	—	11 (41)	11 (48)	6 (33)	11 (65)	—
Arm	21 (55)	—	13 (48)	11 (48)	8 (44)	11 (65)	2 (18)
Hand	7 (18)	10 (32)	7 (48)	4 (18)	7 (39)	3 (18)	3 (27)
Genitals	2 (5.3)	—	1 (3.7)	—	2 (11)	2 (12)	—
Legs/buttocks‡	22 (58)	—	14 (52)	10 (44)	8 (44)	11 (65)	7 (64)
Foot	7 (18)	26 (84)	6 (22)	5 (22)	3 (17)	2 (12)	2 (18)
Entire body	4 (11)	—	4 (15)	1 (4.3)	—	—	—
Dermatologic symptoms, n (%)							
Asymptomatic	8 (21)	3 (9.7)	1 (3.7)	4 (17)	2 (11)	—	8 (73)
Pain/burning	6 (16)	22 (71)	6 (22)	6 (26)	9 (50)	5 (29)	1 (9.1)
Pruritus	23 (61)	11 (36)	20 (74)	14 (61)	13 (72)	16 (94)	—
Timing of dermatologic changes, n (%)							
Before COVID-19 symptoms	3 (7.9)	5 (16)	2 (7.4)	2 (8.7)	1 (5.6)	3 (17.6)	1 (9.1)
After COVID-19 symptoms	29 (76)	15 (48)	18 (67)	13 (57)	13 (72)	9 (53)	10 (91)
At the same time as COVID-19	5 (13)	3 (9.7)	6 (22)	7 (30)	4 (22)	4 (24)	—
No other COVID-19 symptoms	1 (2.6)	6 (19)	1 (3.7)	1 (4.3)	—	1 (5.9)	—
Most likely etiology, as determined by health care provider, n (%)§							
COVID-19 related	27 (71)	28 (90)	20 (74)	21 (91)	16 (89)	13 (77)	9 (82)
Related to another virus	4 (11)	2 (6.5)	4 (15)	—	—	2 (12)	—
Postviral rash	6 (16)	—	3 (11)	1 (4.3)	2 (11)	2 (12)	—
Unsure	1 (2.6)	1 (3.2)	—	1 (4.3)	—	—	2 (18)
Comorbid dermatologic condition							
Contact dermatitis	1 (2.6)	—	—	1 (4.3)	—	3 (18)	—
Alopecia areata	—	—	1 (3.7)	1 (4.3)	—	2 (12)	—
Melanoma	2 (5.3)	1 (3.2)	—	—	—	—	—
Hidradenitis suppurativa	—	1 (3.2)	—	—	1 (5.6)	—	—

IQR, Interquartile range.

*Because providers could select more than 1 rash morphology, some patients are double counted (ie, patient had both morbilliform rash and pernio).

†Defined as sex assigned at birth.

‡Legs and buttocks were combined because of the questionnaire design, which changed slightly over the course of the study.

§Cases determined to be due to a drug have been excluded from this table and are included in the Supplemental Materials (available via Mendeley at http://doi.org/10.17632/gh945hpwy3.1).

lymphohistiocytic inflammation, and rare dermal eosinophils.

DISCUSSION

This study highlights the wide variety of cutaneous manifestations of COVID-19 reported concurrently with or after COVID-19 diagnosis. The most common morphologies in laboratory-confirmed cases in our registry include morbilliform, pernio-like, urticarial, macular erythematous, vesicular, papulosquamous, and retiform purpura. Many of these morphologies occur with different viral infections and, thus, may not provide specific insight into pathophysiology or treatment targets. However, others may suggest potential immune or inflammatory pathways involved in COVID-19 pathogenesis. Furthermore, by documenting this constellation of

Table III. COVID-19–related characteristics of patients with laboratory-confirmed COVID-19 and new-onset dermatologic conditions

	Laboratory-confirmed COVID-19						
Characteristics	**Morbilliform (n = 38)***	**Pernio (n = 31)**	**Urticarial (n = 27)**	**Macular erythema (n = 23)**	**Vesicular (n = 18)**	**Papulosquamous (n = 17)**	**Retiform purpura (n = 11)**
COVID-19 diagnosis, n (%)							
PCR	32 (84)	16 (52)	23 (85)	19 (83)	16 (89)	14 (82)	10 (91)
Antibody	—	11 (35)†	—	2 (8.7)	1 (5.5)	3 (18)	—
Unspecified laboratory assay	6 (16)	4 (13)	4 (15)	2 (8.7)	1 (5.5)	—	1 (9)
COVID-19 exposure, n (%)							
None	9 (24)	11 (36)	9 (33)	7 (30)	4 (22)	6 (35)	6 (55)
Unknown	13 (34)	7 (23)	6 (22)	5 (22)	5 (28)	4 (24)	3 (27)
Close contact with a laboratory-confirmed case of COVID-19 infection	9 (24)	5 (16)	7 (26)	7 (30)	3 (17)	4 (24)	1 (9.1)
Close contact with a probable case of COVID-19 infection	5 (13)	7 (23)	4 (15)	3 (13)	3 (17)	3 (18)	—
Presence in a health care facility where COVID-19 infections have been managed	8 (21)	1 (3.2)	5 (19)	2 (8.7)	3 (17)	1 (5.9)	1 (9.1)
COVID-19 symptoms, n (%)							
Fever	28 (74)	11 (35)	19 (70)	15 (65)	13 (72)	10 (59)	7 (64)
Cough	25 (66)	11 (35)	16 (59)	12 (52)	11 (61)	9 (53)	8 (73)
Shortness of breath	17 (45)	9 (29)	11 (41)	9 (39)	5 (28)	5 (29)	8 (73)
Sore throat	15 (40)	8 (26)	11 (41)	9 (39)	9 (50)	7 (41)	3 (27)
Headache	14 (37)	7 (23)	13 (48)	7 (30)	6 (33)	7 (41)	—
Diarrhea, vomiting, or nausea	15 (40)	7 (23)	10 (37)	9 (39)	5 (28)	5 (29)	—
Malaise	12 (32)	5 (16)	8 (30)	9 (39)	6 (33)	2 (12)	3 (27)
Myalgia	8 (21)	10 (32)	9 (33)	2 (8.7)	4 (22)	2 (12)	—
Irritability/confusion	5 (13)	3 (9.7)	5 (19)	4 (17)	6 (33)	4 (24)	—
Chest pain	2 (5.3)	2 (6.5)	7 (26)	5 (22)	4 (22)	5 (29)	—
Abdominal pain	1 (2.6)	1 (3.2)	7 (26)	5 (22)	5 (28)	4 (24)	—
Anosmia	3 (7.9)	3 (9.7)	2 (7.4)	3 (13)	5 (28)	2 (12)	—
Dysgeusia	1 (2.6)	2 (6.5)	5 (19)	—	2 (11)	2 (12)	—
Arthralgia	7 (18)	1 (3.2)	3 (11)	1 (4.3)	3 (17)	—	1 (9.1)
Rhinorrhea	3 (7.9)	5 (16)	4 (15)	1 (4.3)	1 (5.6)	—	—
Asymptomatic	1 (2.6)	6 (19)	2 (7.4)	—	—	2 (12)	—
COVID-19 testing criteria, n (%)‡							
Does not meet CDC testing criteria	2 (5.3)	9 (29)	2 (7.4)	1 (4.3)	—	2 (12)	—
1 or 2 CDC testing criteria	15 (40)	13 (42)	6 (22)	5 (22)	7 (39)	8 (47)	6 (55)
3 or more CDC testing criteria	21 (55)	9 (29)	19 (70)	17 (74)	11 (61)	7 (41)	5 (46)
COVID-19 treatment, n (%)							
Supportive care only	19 (50)	21 (68)	16 (59)	14 (61)	11 (61)	15 (88)	—
Antimalarial agents	13 (34)	3 (9.7)	6 (22)	4 (17)	4 (22)	1 (5.9)	10 (91)
Antibiotics	11 (29)	4 (13)	6 (22)	6 (26)	4 (22)	—	9 (82)
Bevacizumab	5 (13)	—	4 (15)	1 (4.3)	2 (11)	—	—
Remdesivir	2 (5.3)	1 (3.2)	2 (7.4)	1 (4.3)	1 (5.6)	1 (5.9)	1 (9.1)
Serpin inhibitors	1 (2.6)	1 (3.2)	1 (3.7)	—	1 (5.6)	2 (12)	—
IL-6 inhibitors	—	—	1 (3.7)	—	1 (5.6)	—	2 (18)
Lopinavir/ritonavir	1 (2.6)	—	1 (3.7)	—	—	—	—
JAK inhibitors	—	2 (6.5)	—	—	—	—	—
COVID-19 level of care, n (%)							
Outpatient care only	21 (55)	26 (84)	18 (67)	14 (61)	14 (78)	16 (94)	0
Hospitalized							
No supplemental oxygen	5 (13)	2 (6.5)	5 (19)	1 (4.3)	3 (17)	1 (5.9)	0
Supplemental oxygen only	6 (16)	—	2 (7.4)	4 (17)	—	—	1 (9.1)

Continued

Table III. Cont'd

Characteristics	Laboratory-confirmed COVID-19						
	Morbilliform (n = 38)*	Pernio (n = 31)	Urticarial (n = 27)	Macular erythema (n = 23)	Vesicular (n = 18)	Papulosquamous (n = 17)	Retiform purpura (n = 11)
Noninvasive ventilation or high flow oxygen	—	1 (3.2)	0	—	—	—	0
Ventilator and/or ECMO required	6 (16)	1 (3.2)	2 (17.4)	4 (17)	1 (5.6)	—	10 (91)
COVID-19 complications, n (%)							
None	27 (71)	26 (84)	24 (89)	17 (74)	17 (94)	17 (100)	—
ARDS	4 (11)	1 (3.2)	1 (3.7)	4 (17)	1 (5.6)	—	9 (82)
Thrombotic event	3 (7.9)	2 (6.5)	—	1 (4.3)	—	—	7 (64)
Other infection	1 (2.6)	1 (3.2)	2 (7.4)	1 (4.3)	—	—	6 (55)
Sepsis	4 (11)	—	0	2 (8.7)	—	—	2 (18)
Acute kidney injury	3 (7.9)	—	—	2 (8.7)	—	—	2 (18)
Death	1 (2.6)	2 (6.5)	1 (3.7)	1 (4.4)	—	—	3 (27)
Comorbid medical conditions, n (%)							
None	21 (55)	21 (68)	17 (63)	13 (57)	12 (67)	13 (77)	2 (18)
Hypertension	8 (21)	4 (13)	3 (11)	4 (17)	3 (17)	3 (18)	7 (64)
Diabetes	7 (18)	—	4 (15)	1 (4.3)	2 (11)	1 (5.9)	4 (36)
Obstructive lung disease	3 (7.9)	—	1 (3.7)	2 (8.7)	1 (5.6)	1 (5.9)	6 (55)
Other lung disease	3 (7.9)	1 (3.2)	3 (11)	1 (4.3)	1 (5.6)	—	—
Rheumatologic disease	1 (2.6)	2 (6.5)	—	—	1 (5.6)	—	1 (9.1)
Cardiovascular disease	2 (5.3)	1 (3.2)	—	1 (4.3)	—	—	1 (9.1)
Kidney disease	1 (2.6)	—	—	2 (8.7)	—	2 (12)	—

ARDS, Acute respiratory distress syndrome; *CDC,* Centers for Disease Control and Prevention; *ECMO,* extracorporeal membrane oxygenation; *IL,* interleukin; *JAK,* Janus kinase; *PCR,* polymerase chain reaction.

*Because providers could select more than 1 rash morphology, some patients are double counted (ie, a patient had both morbilliform rash and pernio).

†Immunoglobulin (Ig) M positive, IgG negative: n = 5; IgM negative, IgG positive: n = 1; IgM unknown, IgG positive: n = 1; unknown type of antibodies tested: n = 4.

‡CDC testing criteria reviewed as of May 15, 2020, included fever, cough, sore throat, shortness of breath, myalgia, dysgeusia, anosmia, and vomiting/diarrhea.

cutaneous manifestations, we hope to help providers more accurately identify signs of COVID-19. Cutaneous COVID-19 manifestations generally presented simultaneous to or after other COVID-19 symptoms. However, 12% occurred before other COVID-19 signs, highlighting their importance in assisting COVID-19 detection.

Similar to previous reports, pernio-like lesions were reported more than other dermatologic manifestations.[1,7,9] The high frequency of these reports may reflect the media attention pernio-like lesions received, especially in April/May 2020, with providers potentially sensitized to enter cases even without laboratory confirmation.[18,19] However, when restricted to laboratory-confirmed subgroup analysis, morbilliform and/or macular erythema presentations were more common. Similarly, a Spanish case series reported half of laboratory-confirmed COVID-19 dermatologic manifestations as maculopapular, 19% as pernio-like, and 19% as urticarial.[6]

Thirty-one patients with pernio-like lesions had laboratory-confirmed COVID-19—including 16 who had positive results on PCR—and, therefore, were possibly infectious. Given public health risks posed by COVID-19, new onset of pernio-like lesions should prompt patient-provider discussions regarding both testing with PCR and/or antibody assays and the role of self-isolation in concordance with local and national guidelines. Reassuringly, pernio-like lesions usually appeared in patients with relatively mild COVID-19 disease courses; these patients had fewer other COVID-19 symptoms and lesser severity (5/31 hospitalized, 2 deaths). How this relates to immune response to the virus and likelihood for complications remains unclear. If not coincidental, perhaps the underlying mechanism that predisposed patients to pernio-like lesions is protective, suggesting that pernio may be a marker of a robust, effective host antiviral response limiting COVID-19 complications.[7] Although we cannot completely exclude epiphenomena, because patients may notice foot lesions more and be more likely to seek care, this cluster is unusual. New cases appeared in geographies where winter temperatures remained >10°C and continue even during late spring's warmer weather.

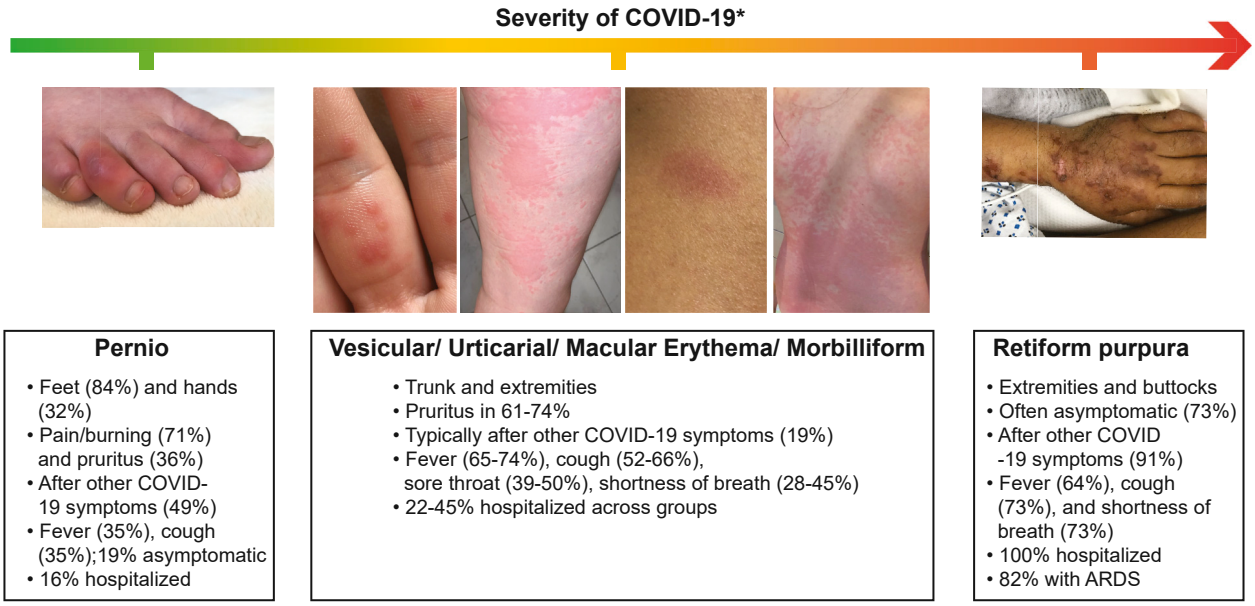

Fig 1. The spectrum of COVID-19 dermatologic manifestations in all patients, with severity of disease calculated based on the percentage of patients with each condition who were hospitalized. *ARDS,* Acute respiratory distress syndrome.

Of patients with other dermatologic manifestations of COVID-19, including morbilliform eruptions, macular erythema, urticaria, and vesicular rashes, 22% to 45% were hospitalized, with 3 deaths. However, fixed livedo racemosa, retiform purpura, and true acral ischemia appeared in critically ill patients, corroborating others' findings.[6,14] Given the occurrence on acral surfaces, these morphologies should be distinguished from pernio-like lesions. In acral livedo racemosa, retiform purpura, and acro-ischemia, the histopathologic findings presented here show noninflammatory to pauci-inflammatory thrombi without other findings often associated with pernio, such as vacuolar interface changes with associated necrotic keratinocytes, papillary derma edema, and a superficial and deep dermal lymphocytic infiltrate. This suggests that thrombotic disease in critically ill patients with COVID-19 may extend to the skin in patients with livedo racemosa/retiform purpura/acro-ischemia, with a morphology distinct from pernio.[14] One study implicated activation of the alternative complement pathway cutaneous thrombosis pathophysiology.[14] Placentas in mothers with mild COVID-19 showed no viral infection but abnormal thrombus formation in the absence of complement activation, suggesting that systemic coagulopathy may not involve complement pathway activation in all patients.[20] Why some patients develop severe coagulopathy but others do not remains under active investigation.

Accurate evaluation and morphologic descriptions of subtle physical examination findings, including consideration of whether lesions are appropriate for skin biopsy, are important in evaluating acral lesions in patients with known/suspected COVID-19. This nuance is especially true in patients with skin of color, for whom the examination of frank erythema and pernio-like lesions may be challenging. In darker skin types (Fitzpatrick IV-VI), more assiduous examination is important because erythema may clinically manifest as subtler dark purple/brown hyperpigmentation.

Beyond assisting with clinical examination, we sought to identify dermatologic manifestations of COVID-19 to improve understanding of SARS-CoV-2 pathophysiology. Previously, Suchonwanit et al[21] proposed that cutaneous manifestations in COVID-19 may present in 2 mechanistic patterns: (1) clinical features similar to viral exanthems, an immune response to viral nucleotides and (2) cutaneous eruptions secondary to COVID-19 systemic consequences, especially vasculitis and thrombotic vasculopathy. Although this suggested dichotomy is a loose framework, it may prove a good starting point to consider our findings.

For instance, pernio-like lesions may offer an opportunity for deeper understanding of both the

Table IV. Histologic findings of dermatologic conditions in patients with laboratory-confirmed COVID-19*

	Laboratory-confirmed COVID-19		
Clinical lesion morphology	**Additional clinical details**	**Type of COVID-19 testing**	**Histologic findings**
Thrombotic vasculopathy			
Retiform purpura	Patient required invasive mechanical ventilation. His course was complicated by ARDS, pulmonary embolism, and retiform purpura on the hands, legs, and feet.	PCR positive	Thrombotic vasculopathy
Retiform purpura and livedo reticularis	Patient required invasive mechanical ventilation. His course was complicated by ARDS, pulmonary embolism, and retiform purpura and livedo reticularis of the arm.	PCR positive	Thrombotic vasculopathy
Retiform purpura	Patient was hospitalized and required invasive mechanical ventilation. Course was complicated by ARDS, DVT, and retiform purpura of the buttocks.	PCR positive	Pauci-inflammatory thrombotic vasculopathy
Livedo reticularis	Patient was hospitalized and required invasive mechanical ventilation. Eight days later, she developed livedo reticularis.	PCR positive	Pauci-inflammatory thrombotic vasculopathy
Livedo racemosa	Patient required invasive mechanical ventilation, and her course was complicated by ARDS, pulmonary embolism, secondary infection, and livedo racemosa of the hand.	PCR positive	Thrombotic vasculopathy
Livedo racemosa	Patient required invasive mechanical ventilation. Hospital course was complicated by ARDS, pulmonary embolism, secondary infection, and asymptomatic livedo racemosa of the arm.	PCR positive	Pauci-inflammatory thrombotic vasculopathy
Morbilliform rash, macular erythema, and pressure injury	At the same time as COVID-19 symptoms, patient developed morbilliform rash and macular erythema over the trunk. The patient required invasive mechanical ventilation and developed what appeared to be pressure injury on the buttocks.	PCR positive	Biopsy 1 (abdomen): interface dermatitis; differential diagnosis includes a drug eruption and viral exanthem. Biopsy 2 (buttock): thrombotic vasculopathy

Continued

Table IV. Cont'd

	Laboratory-confirmed COVID-19		
Clinical lesion morphology	**Additional clinical details**	**Type of COVID-19 testing**	**Histologic findings**
Skin necrosis			
Retiform purpura and pressure injury	Patient required invasive mechanical ventilation. Hospital course was complicated by ARDS, secondary infection, and then retiform purpura plus pressure injury on the buttocks.	PCR positive	Clotting and pressure-induced necrosis
LCV			
Palpable purpura and acral desquamation	Patient developed red itchy rash after COVID-19 symptoms, which worsened with erosions and painful ulceration	IgM positive	LCV
Spongiosis			
Papulosquamous	Patient developed unilateral rash on anterior shin. Patient was not hospitalized and required no treatment.	PCR positive	Spongiosis with hyperkeratosis, edema, perivascular lymphocytes, neutrophils, extravasated erythrocytes
Papulosquamous	Patient presented to dermatology 30 days after onset of COVID-19 symptoms with a papulosquamous eruption.	PCR positive	Favor pityriasis rosea; histologic differential diagnosis includes viral exanthem, contact dermatitis, or eczema
Other			
Pernio-like	Patient presented with painful pernio-like lesions of the fingers and toes.	PCR positive	Mild vacuolar interface dermatitis, subepidermal edema, and superficial/deep lymphocytic inflammation. Differential diagnosis: perniosis, autoimmune CTD such as dermatomyositis, and SLE
Morbilliform, urticarial, and petechial	Patient was hospitalized, was intubated, and developed acral distributed petechial, macular, and urticarial rash 3 to 4 weeks after COVID-19 symptoms.	PCR positive	Diffuse vacuolar interface dermatitis with numerous dyskeratotic keratinocytes predominantly localized to the basal layer, with lymphocyte exocytosis and sparse superficial perivascular lymphohistiocytic inflammation with rare eosinophils
Pernio and Grover-like	Two weeks after COVID-19 symptoms, patient developed Grover-like rash and pernio	IgM positive; PCR negative	Granulomatous dermatitis (colloidal iron showed increased mucin deposition within the center of the granuloma)

ARDS, Acute respiratory distress syndrome; *CTD,* connective tissue disease; *DVT,* deep vein thrombosis; *Ig,* immunoglobulin; *LCV,* leukocytoclastic vasculitis; *PCR,* polymerase chain reaction; *SLE,* systemic lupus erythematosus.
*The cases have been grouped in the table by predominant histologic finding.

pathophysiology of SARS-CoV-2 and pernio as a reaction pattern with multiple etiologies. The underlying cause of pernio-like lesions from the pathology collected suggests a primary inflammatory process. Pernio-like lesions are generally nonischemic and, thus far, do not suggest systemic intravascular thromboses, unlike retiform purpura and acral ischemia. Interferonopathies, genetic conditions with overproduction of type I interferons, may present with pernio-like lesions, suggesting a robust interferon response in the pathogenesis of perniosis.[22] Type I interferon is critical for antiviral immunity, and thus, its heightened production in young, healthy people exposed to SARS-CoV-2 is expected and would lead to successful viral control but also, hypothetically, could trigger pernio.[23] Indeed, a low/delayed interferon response might allow for uncontrolled viral replication and a subsequent cytokine storm leading to severe illness and low incidence of pernio.[23] SARS-CoV-2–infected Chinese patients with interferon-induced transmembrane protein 3 gene polymorphism may develop worsening disease in an age-dependent fashion, suggesting that an interferon-driven antiviral response could be necessary for early viral control.[24]

Our study is limited by the constraints of a case series, which cannot accurately estimate the prevalence or incidence of these findings. The incidence of COVID-19 dermatologic manifestation remains unclear, with studies reporting 0.2% to 20%.[8,25,26] There also remains the possibility of bias due to attribution error, given the reliance on providers' judgment in entering data regarding whether findings were virus related, were from a medication, or were from other causes. Although providers were prompted for case updates, most reports represent a single snapshot, preventing full observation of dermatologic manifestations, disease complications, and follow-up testing. Limited testing of COVID-19 remains a persistent issue. Only 25% of our patients had laboratory-confirmed disease. It is difficult to parse the effects of poor test access and false negative tests on our data. Furthermore, this registry represents a small sample of global dermatologic manifestations; US dermatology networks received the most promotion, as our results reflect. Additionally, providers may have been more likely to enter more severe cases.

The lack of a clear definition for COVID-19–associated skin findings may restrict extrapolation from these data, such as, the nonspecific term *COVID toes*, which may incorporate a variety of acral lesions. Only half of medical professionals entering cases were dermatologists, making morphologic misclassification possible; without photographs to confirm, we cannot ensure consistent description. As more data emerge, we should examine specific subsets (eg, angulated distal purpura, erythema multiforme-like lesions, and true pernio-like lesions) that may have distinct clinical morphologies, histologic patterns, and pathophysiology. Nevertheless, we believe that better recognition of these manifestations, whether from the disease itself or from medications for COVID-19, will provide insight into disease characterization and management.[27]

Our cases lacked diversity in representation, with only 34 Hispanic/Latino and 13 Black/African American patients. This poor racial/ethnic diversity in the classification of COVID-19 dermatologic manifestations is problematic, especially given that photos of these lesions in darker skin types may help patients and providers identify early signs of COVID-19.[28] Disparities in the number of COVID-19 hospitalizations and outcomes show a disproportionate impact on these populations.[29] Lack of race and ethnicity data reporting in state health department registries of COVID-19 cases has complicated this issue.[30] Early recognition, diagnosis, and management of cutaneous manifestations of COVID-19 in patients with skin of color provides an additional way in which health care providers can help care for underrepresented minority populations, thereby reducing the health care disparities seen with COVID-19.

In conclusion, we show a spectrum of COVID-19–related dermatoses. These cutaneous manifestations may present with other COVID-19 symptoms, and others may represent postviral inflammatory responses. Our study highlights that pernio-like lesions are associated with milder COVID-19 disease courses, whereas retiform purpura is associated with severe disease in critically ill patients. Further investigation is needed to precisely ascertain the timing of findings, the pathophysiology behind different morphologies, and potential antibody response in patients who may have only mild COVID-19 symptoms.[31-35] Dermatologic findings should not be overlooked as signs of COVID-19 and should prompt discussions between physicians and patients regarding isolation and possible testing.

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