



Cutaneous Manifestations of COVID-19: An Evidence-Based Review

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Abstract

Background The coronavirus disease 2019 (COVID-19) pandemic has affected 18 million people and killed over 690,000 patients. Although this virus primarily causes respiratory symptoms, an increasing number of cutaneous manifestations associated with this disease have been reported.

Objective The aim of this review was to collate and categorize the dermatologic findings reported in patients with COVID-19 and identify specific lesions that may facilitate diagnosis and prognostication.

Methods An evidence-based review of the PubMed database was conducted on 14 May, 2020 using the search terms “Covid-19 skin,” “Covid-19 rash,” “Covid-19 exanthem,” and “Covid-19 chilblains.” Peer-reviewed publications containing original COVID-19 patient cases and a discussion of the associated cutaneous findings were included in the analysis.

Results The literature search identified 115 records, of which 34 publications describing 996 patients with dermatologic conditions were included. Case reports ($n = 15$), case series ($n = 13$), and observational prospective studies ($n = 4$) were the most common publication types. Acral lesions resembling pseudo-chilblains were the most frequent lesion identified (40.4% of cases), appearing in young adults (mean age, 23.2 years) after the onset of extracutaneous COVID-19 symptoms (55/100 patients). Erythematous maculopapular rashes affected 21.3% of patients, most frequently impacting middle-aged adults (mean age, 53.2 years) and occurring at the same time as non-cutaneous symptoms (110/187 patients). Vesicular rashes affected 13.0% of patients, appearing in middle-aged adults (mean age, 48.3 years) after the onset of other symptoms (52/84 patients). Urticarial rashes affected 10.9% of patients, appearing in adults (mean age, 38.3 years) and occurring at the same time as non-cutaneous symptoms (46/78 patients). Vascular rashes resembling livedo or purpura were uncommon (4% of cases), appearing in elderly patients (mean age, 77.5 years) and occurring at the same time as non-cutaneous COVID-19 symptoms (18/29 patients). Erythema multiforme-like eruptions, although infrequent (3.7% of cases), affected mostly children (mean age, 12.2 years).

Conclusions Vesicular rashes may suggest an initial diagnosis of COVID-19, acral lesions may be most appropriate for epidemiological uses, and vascular rashes may be a useful prognostic marker for severe disease. As a potential correlate to disease severity, prognosis, or infectibility, it is critical that all healthcare professionals be well versed in these increasingly common cutaneous manifestations of COVID-19.

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Key Points

Acral lesions, urticarial rashes, vesicular rashes, erythematous maculopapular rashes, vascular lesions within the spectrum of livedo/purpura/necrosis, and erythema multiforme-like eruptions are the most commonly reported cutaneous symptoms of COVID-19.

Dermatologists and primary care physicians should be made aware of the cutaneous symptoms linked to COVID-19 as they might be the presenting sign of infection in otherwise asymptomatic or minimally symptomatic patients.

1 Introduction

In December 2019, a new infectious pathogen named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified in Wuhan, China [1]. Transmitted through respiratory droplets, SARS-CoV-2 is the causative pathogen of coronavirus disease 2019 (COVID-19), which has rapidly spread across the globe to infect 188 countries. The combination of its high infectivity and lengthy asymptomatic latency period has culminated in a global pandemic affecting 18 million people and resulting in over 690,000 deaths to date [2]. Although known to primarily cause interstitial pneumonia and respiratory failure, recent reports from around the world have indicated that this novel coronavirus may be associated with specific cutaneous manifestations. These dermatologic symptoms may be useful in identifying otherwise asymptomatic COVID-19 carriers, which may help slow the transmission of this highly infectious and dangerous virus. As such, an evidence-based review of peer-reviewed scientific literature was conducted to collect clinically relevant information on the cutaneous signs and symptoms of patients with COVID-19.

2 Materials and Methods

To identify all peer-reviewed articles reporting on the cutaneous manifestations associated with COVID-19, an evidence-based review of the PubMed database was conducted on 14 May, 2020 using the search terms “Covid-19 skin,” “Covid-19 rash,” “Covid-19 exanthem,” and “Covid-19 chilblains.” Records identified through the electronic database were initially screened by title and abstract content. The full-text articles that remained were assessed for eligibility and inclusion in the evidence-based review. Peer-reviewed publications that contained original patient cases of COVID-19 and a discussion of the associated dermatologic findings were included in the analysis. Review or opinion articles that did not report on original patient cases, observational studies, or case reports that did not discuss cutaneous symptoms, and articles that were published prior to the first COVID-19 case in December 2019 were excluded.

Eligible articles were assessed for study type, location, setting, and Level of Evidence for clinical research according to the Oxford Centre for Evidence-Based Medicine 2011 guidelines [37]. Study type included the following: survey snapshot studies, which reported on data collected through patient- or physician-reported surveys; case reports, which reported on the presentation and management of an individual patient; case series, which reported on the presentation of multiple patients who presented under similar circumstances; and observational prospective studies, which

followed a cohort of patients over a period of time and were thus useful in collecting data on disease prevalence. Demographic characteristics such as patient sample sizes, ages, and sexes was collected. COVID-19 status and diagnostic modality were also noted. Descriptive characteristics of the cutaneous manifestations were recorded, including: rash type, location, duration, associated symptoms, relation to drug intake, and correlation to the onset of other COVID-19 symptoms.

3 Results

3.1 Study Characteristics and Patient Demographics

As depicted in Fig. 1, 115 records were initially identified in the literature search. After screening for eligibility and inclusion criteria, 34 peer-reviewed publications were ultimately included in the evidence-based review [3–36]. Study and demographic characteristics are summarized in Table 1. The majority of publications were case reports ($n = 15$), followed by case series ($n = 13$), observational prospective studies ($n = 4$), and survey-based studies ($n = 2$). All studies included were rated as Level 4 or 5 Evidence for clinical research as detailed in the Oxford Centre for Evidence-Based Medicine 2011 guidelines [37]. Most studies originated from Europe (Italy, $n = 9$; Spain, $n = 9$; France, $n = 7$; Belgium, $n = 2$; joint study from Italy and Spain, $n = 1$), followed by the USA ($n = 3$), the Middle East (Qatar, $n = 1$; Iran, $n = 1$), and Southeast Asia (Thailand, $n = 1$). Patients were identified from dermatology clinics ($n = 19$) and hospitals ($n = 15$). A total of 996 patients with dermatologic symptoms were included in the analysis, of which 54.3% were female and the mean age was 37.3 years (range 1.0–98.0 years).

The majority of patients (58.2%) had a laboratory-confirmed diagnosis of COVID-19. Exceptions include De Masson et al. (252 out of 277 patients were suspected to have COVID-19 because of extracutaneous symptoms and/or prior contact with a patient with COVID-19), Fernandez-Nieto et al. (82 out of 132 patients were suspected to have COVID-19 because of prior contact with a patient or healthcare worker with COVID-19), Landa et al. (three out of six patients were not tested for COVID-19), Piccolo et al. (59 out of 63 patients were either not tested or had missing information on COVID-19 status), Recalcati et al. (14 out of 14 patients were COVID-19 negative on a polymerase chain reaction [PCR] analysis), Torres-Navarro et al. (two out of two patients were COVID-19 negative on PCR analysis), and Tosti et al. (four out of four patients were not tested for COVID-19) [9, 18, 20, 33–36]. These non-laboratory confirmed patients all presented during the COVID-19 outbreak and, for those with a negative COVID-19 PCR result,

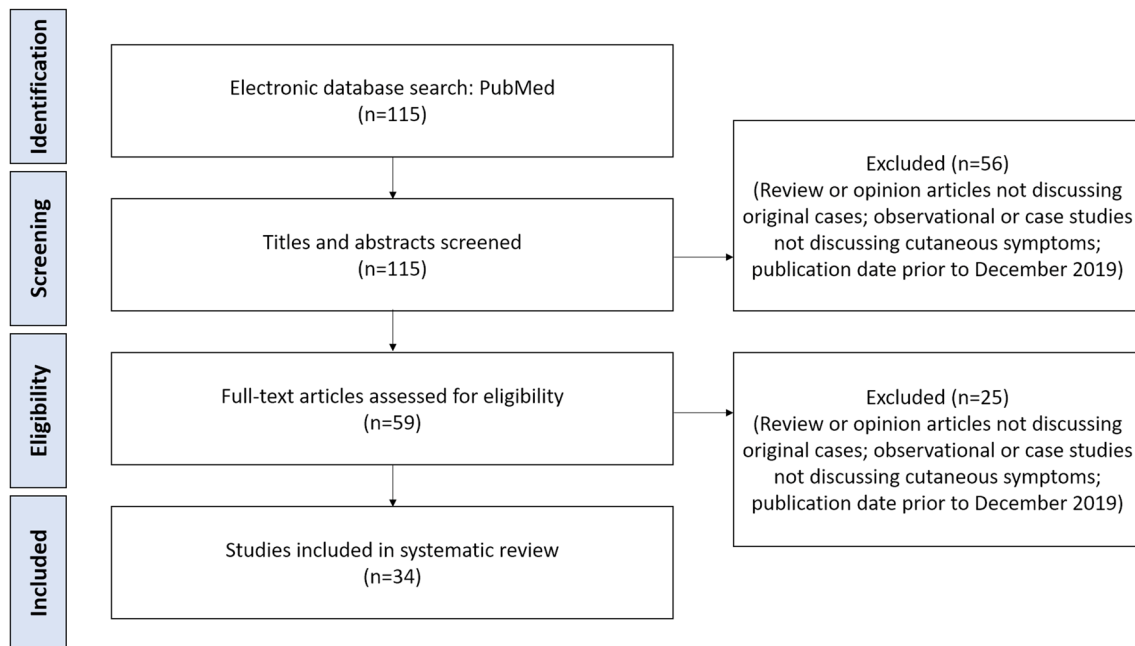


Fig. 1 Flow diagram of the search strategy

antibody testing was not available to establish the possibility of prior infection. The case fatality rate range was 0.0–13.6% [8, 13, 30]. For studies that examined a larger cohort of patients who were COVID-19 positive (both with cutaneous and extracutaneous symptoms), the prevalence range of skin symptoms was 4.9–20.4% [3–12].

3.2 Characteristics of Cutaneous Symptoms

Table 2 summarizes the characteristics of the cutaneous symptoms described in the COVID-19 literature. These dermatologic manifestations were then grouped together into categories using common descriptive terminology and photographic evidence. These categories included: erythema multiforme-like eruptions, erythematous maculopapular rashes, erythematous rashes not otherwise specified, figurate erythema, vascular rashes within the spectrum of livedo/purpura/necrosis, pityriasis rosea-like eruptions, acral lesions resembling pseudo-chilblains, symmetrical drug-related intertriginous and flexural exanthema, urticarial rashes, vesicular rashes, and other rashes.

As seen in Table 3, acral lesions were the most common category identified (40.4% of all cases), followed by erythematous maculopapular rashes (21.3%), vesicular rashes (13.0%), urticarial rashes (10.9%), other rashes (4.3%, including one eruptive cherry angioma, one reactivation of herpes simplex virus-1, and 41 unspecified cases of eczematous, angiomatous, or annular lesions), vascular rashes within the spectrum of livedo/purpura/necrosis (4%), erythema multiforme-like eruptions (3.7%), and unspecified

erythematous rashes (2.1%). Cutaneous manifestations resembling symmetrical drug-related intertriginous and flexural exanthema, pityriasis rosea, and figurate erythema were the least common (0.3% combined).

Mean patient age associated with each dermatologic category was as follows: vascular rashes resembling livedo/purpura/necrosis (77.5 years), unspecified erythematous rashes (67.0 years), erythematous maculopapular rashes (53.2 years), vesicular rashes (48.3 years), other rashes (45.6 years), urticarial rashes (38.3 years), acral lesions (23.2 years), and erythema multiforme-like eruptions (12.2 years). All rashes had a female predominance except for vascular rashes (52.9% male predominance), erythema multiforme-like eruptions (59.5% male predominance), pityriasis rosea (only one case reported and the patient was male), and figurate erythema (only one case reported and the patient was male).

Although not all studies reported on the mean duration of these cutaneous manifestations, most studies described signs and symptoms that resolved within 2–15 days. One study reported persistent acral lesions that required 2–4 weeks for complete resolution [9]. Of the dermatologic findings that were symptomatic, the majority were pruritic ($n = 295$), followed by painful ($n = 68$) or burning ($n = 24$). Most patients had no new drug intake in the 2 weeks preceding the rash onset. Some studies went into more descriptive detail to characterize the skin findings. Fernandez-Nieto et al. observed two different types of vesicular rashes: a diffuse polymorphic rash at various stages of evolution (observed in 75% of patients) and a

Table 1 Study characteristics and patient demographics

Study ID	Study type	Level of evidence ^a	Location	Setting	COVID-19 status (diagnostic modality)	Sample size ^b	Age (years) and sex (M/F)	Other study notes
Ahouach et al. [16]	Case report	5	France	Derm clinic	Positive (lab)	1	57 F	–
Alramthan et al. [11]	Case series	4	Qatar	Derm clinic	Positive (lab)	2	27 F, 35 F	–
Amatore et al. [26]	Case report	5	France	Derm clinic	Positive (lab)	1	39 M	–
Bouaziz et al. [4]	Case series	4	France	Derm clinic	Positive (lab)	14	N/A	–
De Masson et al. [36]	Case series	4	France	Derm clinic	Positive (lab, <i>n</i> =25) Suspected (contact with COVID-positive case or symptomatic patient, <i>n</i> =252)	277	2–98 (27 median) 50% M	–
Diaz-Guimaraens et al. [22]	Case report	5	Spain	Hospital	Positive (lab)	1	48 M	–
Ehsani et al. [25]	Case report	5	Iran	Derm clinic	Positive	1	27 M	–
Estebanez et al. [7]	Case report	5	Spain	Derm clinic	Positive	1	28 F	–
Fernandez-Nieto et al. [16]	Case series	4	Spain	Derm clinic	Positive (clinical, <i>n</i> =19) Suspected (contact with COVID-positive case or healthcare worker, <i>n</i> =82)	132	1–56 (20 mean) 53.8% M	–
Fernandez-Nieto et al. [30]	Observational prospective	4	Spain	Hospital	Positive (lab)	24	19–65 (45 median) 75% F	0% case fatality
Galvan Casas et al. [13]	Survey snapshot	4	Spain	Derm clinic	Positive (lab or clinical)	375	(49 mean) 66.5% F	1.9% case fatality
Genovese et al. [28]	Case report	5	Italy	Derm clinic	Positive (lab)	1	8 F	–
Gianotti et al. [15]	Case series	4	Italy	Hospital	Positive	3	59 F, 89 F, 57 M	–
Hedou et al. [12]	Observational prospective	4	France	Homes and hospital	Positive (lab)	5	N/A	4.9% prevalence of skin symptoms in 103 patients who were COVID-19 positive 0% case fatality
Henry et al. [6]	Case report	5	France	Hospital	Positive (lab)	1	27 F	–
Hunt et al. [24]	Case report	5	New York	Hospital	Positive (lab)	1	20 M	–
Jimenez Cauhe et al. [14]	Case report	5	Spain	Hospital	Positive	1	84 F	–
Joob et al. [23]	Case report	5	Thailand	Hospital	Positive (lab)	1	N/A	Patient was originally misdiagnosed with dengue fever 48 patients were positive for COVID-19 in all of Thailand at the time of the study

Table 1 (continued)

Study ID	Study type	Level of evidence ^a	Location	Setting	COVID-19 status (diagnostic modality)	Sample size ^b	Age (years) and sex (M/F)	Other study notes
Kolivras et al. [32]	Case report	5	Belgium	Derm clinic	Positive (lab)	1	23 M	-
Landa et al. [34]	Case series	4	Spain	Derm clinic	Positive (lab, n=3) N/A (n=3)	6	15 M, 15 F, 23 F, 24 F, 44 M, 91 M	-
Magro et al. [5]	Case series	4	New York	Hospital	Positive (lab)	3	32 M, 66 F, 40 F	-
Mahe et al. [21]	Case report	5	France	Hospital	Positive (lab)	1	64 F	-
Marzano et al. [8]	Case series	4	Italy	Hospital	Positive (lab)	22	8-83 (60 median) 72.7% M	13.6% case fatality
Najarian et al. [29]	Case report	5	New Jersey	Derm clinic	Positive (lab)	1	58 M	-
Piccolo et al. [33]	Survey snapshot	4	Italy	Derm and peds clinics	Positive (lab, n=4) Suspected (contact with COVID-positive case, n=10) N/A (n=49)	63	12-16 (14 median) 57.4% F	-
Quintana-Castaneda et al. [27]	Case report	5	Spain	Derm clinic	Positive (lab)	1	61 M	-
Recalcati [3]	Observational prospective	4	Italy	Hospital	Positive (lab)	18	N/A	20.4% prevalence of skin symptoms in 88 patients who were COVID-19 positive
Recalcati et al. [9]	Observational prospective	4	Italy	Derm clinic	Negative (lab, antibody testing not performed)	14	13-39 (17.5 mean) 57.1% F	11 patients were children
Sachdeva et al. [31]	Case series	4	Italy	Hospital	Positive (lab)	3	71 F, 77 F, 72 F	-
Tammaro et al. [10]	Case series	4	Italy, Spain	Hospital	Positive	3	N/A	-
Torres-Navarro et al. [35]	Case series	4	Spain	Derm clinic	Negative (lab, antibody testing not performed)	2	16 F, 16 M	-
Tosti et al. [20]	Case series	4	Italy	Derm clinic	Not tested	4	26 M, 16 F, 18 F, 48 M	Patients not tested because of limited testing capacity but all presented during the COVID-19 outbreak
Van Damme et al. [17]	Case series	4	Belgium	Derm clinic	Positive (lab, n=1; clinical, n=1)	2	71 M, 39 F	1 patient died 2 weeks after presentation
Zengarini et al. [19]	Case report	5	Italy	Hospital	Positive (lab)	1	67 F	-

COVID-19 coronavirus disease 2019, Derm dermatologic, F female, ID identification, lab laboratory, M male, N/A not available, peds pediatric

^aLevel of Evidence for clinical research as detailed in the Oxford Centre for Evidence-Based Medicine 2011 guidelines [37]

^bSample size denotes the number of Derm patients discussed in the study

Table 2 Characteristics of cutaneous symptoms of coronavirus disease 2019 (COVID-19)

Study ID	Rash type, <i>n</i>	Rash location, <i>n</i>	Rash duration	Associated cutaneous symptoms, <i>n</i>	Relation to new drug intake	Relation to onset of other COVID-19 symptoms, <i>n</i>	Other rash notes
Ahouach et al. [16]	Maculopapular (1)	Trunk and limbs	9 days	Burning	No new drug intake	Before	Perivascular lymphocytic infiltrate on skin biopsy
Alramithan et al. [11]	Acral (2)	Dorsal fingers (1) Subungual region (1)	–	–	No new drug intake	Before (2)	–
Amatore et al. [26]	Figurate erythema (1)	Arms (including palms), neck, chest, and abdomen	7 days	–	No new drug intake	At onset	Perivascular lymphocytic infiltrate on skin biopsy
Bouaziz et al. [4]	Erythema-NOS (4) Maculopapular (1) Urticaria (1) Vesicular (2) Vascular (3) Acral (2) Other (1)	Trunk Limbs Feet	–	–	–	After (14)	Other rash was an eruptive cherry angioma Acral lesions were also seen in close contacts of patients (<i>n</i> =40, contacts did not have confirmatory testing for COVID-19)
De Masson et al. [36]	Maculopapular (25) Urticaria (26) Vesicular (41) Vascular (11) Acral (142) Other (41)	Trunk and limbs (103) Face (12) Limbs (2) Hands/feet (56)	–	–	–	–	Other rashes included eczematous, angiomatous, and annular lesions No relation to cold exposure or comorbidities Perivascular mononuclear infiltrate with vascular microthrombi on skin biopsy
Diaz-Guimaraens et al. [22]	Maculopapular (1)	Buttocks and legs	5 days	Pruritis	No new drug intake	After	Perivascular lymphocytic infiltrate on skin biopsy
Ehsami et al. [25]	Pityriasis rosea (1)	Trunk and arms	–	Pruritis	No new drug intake	After	–
Estebanez et al. [7]	Urticaria (1)	Heels	–	Pruritis	No new drug intake	After	–
Fernandez-Nieto et al. [16]	Acral (95) Erythema multiforme (37)	Digits (Acral) Hands and feet (erythema multiforme)	9 days	–	No new drug intake	At onset (3) After (16)	Statistically, acral lesions were associated with a greater patient age and erythema multiforme was associated with more ventrally distributed lesions

Table 2 (continued)

Study ID	Rash type, <i>n</i>	Rash location, <i>n</i>	Rash duration	Associated cutaneous symptoms, <i>n</i>	Relation to new drug intake	Relation to onset of other COVID-19 symptoms, <i>n</i>	Other rash notes
Fernandez-Nieto et al. [30]	Vesicular (24)	Head (4) Chest (21) Trunk (14) Arms (8) Legs (10) Palms/soles (2)	10 days	Pruritis (20)	7 patients had prior drug intake	Before (2) At onset (3) After (19)	75% of patients had a diffuse polymorphic rash at various stages of evolution, 25% had a localized monomorphic rash at the same stage of evolution 4 patients' lesions were tested and were negative for COVID-19 PCR
Galvan Casas et al. [13]	Acral (71) Vesicular (34) Urticaria (73) Maculopapular (176) Vascular (21)	Hands and feet (Acral) Trunk or limbs (Vesicular) Trunk or palms (Urticaria) Limbs (Maculopapular) Trunk or digits (Vascular)	6–13 days	Pruritis (213) Pain (32) Burning (22)	Many patients had prior drug intake (unable to ascertain exact number)	Before (22) At onset (212) After (139)	More HSV reactivation noted in cohort Some maculopapular rashes were described as resembling pityriasis rosea or erythema multiforme Statistically, vascular lesions were associated with the greatest patient age and the worst outcomes, followed by maculopapular rashes, urticaria, vesicular rashes, and finally acral lesions
Genovese et al. [28]	Vesicular (1)	Trunk	7 days	–	No new drug intake	After	–
Gianotti et al. [15]	Maculopapular (3)	Trunk (3) Arms (2) Legs (1)	5–10 days	Pruritis (1)	–	Before (1) After (2)	Superficial perivascular dermatitis with small-vessel thrombosis on skin biopsy
Hedou et al. [12]	Erythema-NOS (2) Urticaria (2) Other (1)	Face and arms (3)	2–6 days	Pruritis (5)	–	Before (1) At onset (4)	Other rash was a reactivation of HSV-1
Henry et al. [6]	Maculopapular (1)	Forehead, hand, and foot	–	Pruritis	No new drug intake	Before	–
Hunt et al. [24]	Maculopapular (1)	Trunk and limbs	–	–	–	At onset	–
Jimenez Cauhe et al. [14]	Vascular (1)	Axilla	–	Mild pruritis	Had prior drug intake	After	–
Joob et al. [23]	Vascular (1)	–	–	–	–	Before	–

Table 2 (continued)

Study ID	Rash type, <i>n</i>	Rash location, <i>n</i>	Rash duration	Associated cutaneous symptoms, <i>n</i>	Relation to new drug intake	Relation to onset of other COVID-19 symptoms, <i>n</i>	Other rash notes
Kolivras et al. [32]	Acral (1)	Feet and toes	–	Pain	No new drug intake	After	No relation to cold exposure or comorbidities Perivascular lymphocytic infiltrate on skin biopsy
Landa et al. [34]	Acral (6)	Toes (5) Soles (1)	–	Mild pruritus (2) Mild pain (3)	–	Before (1) After (5)	No relation to cold exposure or comorbidities
Magro et al. [5]	Vascular (3)	Buttocks (1) Chest, arms, and legs (1) Palms and soles (1)	–	–	2 patients had prior drug intake	After (3)	Thrombogenic vasculopathy with deposition of C4d and C5b-9 on skin biopsy
Mahe et al. [21]	SDRIFE (1)	Trunk and arms	5 days	–	Had prior drug intake	After	The rash both appeared and disappeared while taking new oral drug
Marzano et al. [8]	Vascular (22)	Trunk (22) Limbs (4)	4–15 days	Mild pruritus (9)	No new drug intake	Before (1) At onset (2) After (16)	7 patients' skin biopsies showed viral infection 6 patients had a diffuse exanthem
Najararian et al. [29]	Maculopapular (1)	Limbs, shoulders, trunk, chest, and abdomen	4 days	Pruritus	Had prior drug intake	After	Patient was taking azithromycin when rash developed but had previously taken it without complications
Piccolo et al. [33]	Acral (63)	Hands/feet (63)	–	Pruritus (30) Pain (30)	–	After	No relation to cold exposure or comorbidities Two different patterns of lesions were observed: erythematous-edematous and blistering types
Quintana-Castaneda et al. [27]	Urticaria (1)	Limbs	7 days	Mild pruritus	No new drug intake	Before	–
Recalcati [3]	Erythema-NOS (14) Urticaria (3) Vesicular (1)	Trunk	"A few days"	Minimal pruritus	No new drug intake	At onset (8) After (10)	–
Recalcati et al. [9]	Acral (14)	Feet (10) Hands (6)	14–28 days	Minimal pruritus	No new drug intake	Before (11) After (3)	No relation to cold exposure or comorbidities
Sachdeva et al. [31]	Maculopapular (2) Vesicular (1)	Trunk (3) Legs (2) Chest (1)	10 days	Pruritus (2)	1 patient had prior drug intake	At onset (1) After (2)	One of the rashes resembled Grover's disease
Tammaro et al. [10]	Vesicular (3)	Trunk (3)	–	Mild pruritus (3)	–	After (3)	Rash appeared to belong to Herpesviridae family

Table 2 (continued)

Study ID	Rash type, n	Rash location, n	Rash duration	Associated cutaneous symptoms, n	Relation to new drug intake	Relation to onset of other COVID-19 symptoms, n	Other rash notes
Torres-Navarro et al. [35]	Acral (2)	Fingers	-	-	-	-	-
Tosti et al. [20]	Acral (4)	Heels (2) Toes (2)	-	Pain (2) Burning (1) Pruritis (1)	1 patient had prior drug intake	Before (2) After (2)	No relation to cold exposure or comorbidities
Van Damme et al. [17]	Urticaria (2)	Trunk and legs (2)	-	Pruritis (1)	No new drug intake	At onset	-
Zengarini et al. [19]	Erythema-NOS (1)	Neck and trunk	7 days	Mild pruritis	Had prior drug intake	After	Perivascular lymphocytic infiltrate on skin biopsy

HSV herpes simplex virus, ID identification, NOS not otherwise specified, PCR polymerase chain reaction, SDRIFE symmetrical drug-related intertriginous and flexural exanthema

localized monomorphic rash at the same stage of evolution (observed in 25% of patients) [30]. The single case of a vesicular rash reported by Sachdeva et al. was described as resembling Grover’s disease [31]. Piccolo et al. observed two different lesion patterns for acral lesions: erythematous-edematous types and blistering types. A few articles also described skin biopsy findings, which almost uniformly revealed a perivascular mononuclear/lymphocytic infiltrate with occasional small-vessel thrombosis [8, 15, 16, 19, 22, 26, 32, 36]. One study in particular revealed a complement-mediated thrombogenic vasculopathy with deposition of C4d and C5b-9 on histopathology [5].

The association and time relationship between each dermatologic manifestation and the non-cutaneous symptoms of COVID-19 (such as fever, cough, shortness of breath, malaise, and myalgia) are depicted in Table 3. The appearance of nearly half of the cutaneous findings coincided with the onset of other COVID-19 symptoms (46.1% of all cases). Other rashes appeared shortly after (44.3%) or before (9.6%) the onset of non-cutaneous COVID-19 manifestations. Erythematous maculopapular rashes were more likely to present concurrently with other symptoms (58.8%) compared with before (5.9%) or after (35.3%). Urticarial rashes also frequently coincided with the onset of non-cutaneous symptoms (59.0%) compared with before (6.4%) or after (34.6%). The same trend was observed for vascular rashes, with the majority of cases appearing alongside other COVID-19 symptoms (62.1%) compared with before (6.9%) or after (31.0%). Of the cases reported, otherwise unspecified erythematous rashes presented most frequently after other symptoms of COVID-19 (71.4%) rather than before (0%) or at the same time (28.6%). Acral lesions also more commonly appeared after (55.0%) compared with before (21.0%) or at the same time (24.0%) as extracutaneous symptoms. Vesicular rashes were also more likely to present after other symptoms (61.9%) compared with before (9.5%) or at the same time (28.6%).

A breakdown of COVID-19 skin symptoms by location is depicted in Table 4. Hands and feet were the most frequently reported site for dermatologic findings (55.1% of cases), followed by a mixed location pattern (26.8%), trunk alone (10.2%), limbs alone (3.3%), face and neck (3.0%), palms and soles (1.2%), and chest and abdomen (0.4%).

4 Discussion

The repercussions of the SARS-CoV-2 pandemic is substantial, impacting millions of patients medically, financially, and socially. Unfortunately, this highly virulent pathogen is extremely difficult to contain given its prolonged asymptomatic latency period and respiratory droplet transmission pattern. Cutaneous manifestations of COVID-19 may help

Table 3 Summary of rashes by type, patient characteristics, and onset characteristics

Rash type	Sample size, <i>n</i> (%)	Age, mean years ^a	Female ^a , <i>n</i> (%)	Relation to onset of other COVID-19 symptoms ^b		
				Before (%)	At onset (%)	After (%)
Acral lesions	402 (40.4)	23.2	211 (54.1)	21 (21.0)	24 (24.0)	55 (55.0)
Erythematous maculopapular rashes	212 (21.3)	53.2	115 (55.6)	11 (5.9)	110 (58.8)	66 (35.3)
Vesicular rashes	129 (13.0)	48.3	61 (50.8)	8 (9.5)	24 (28.6)	52 (61.9)
Urticarial rashes	109 (10.9)	38.3	59 (59.0)	5 (6.4)	46 (59.0)	27 (34.6)
Other rashes ^c	43 (4.3)	45.6	25 (69.4)	0 (0)	1 (50.0)	1 (50.0)
Vascular rashes	40 (4.0)	77.5	16 (47.1)	2 (6.9)	18 (62.1)	9 (31.0)
Erythema multiforme-like eruptions	37 (3.7)	12.2	15 (40.5)	–	–	–
Erythematous rash (not otherwise specified)	21 (2.1)	67	1 (100)	0 (0)	2 (28.6)	5 (71.4)
Symmetrical drug-related intertriginous and flexural exanthema	1 (0.1)	64	1 (100)	0 (0)	0 (0)	1 (100)
Pityriasis rosea	1 (0.1)	27	0 (0)	0 (0)	0 (0)	1 (100)
Figurate erythema	1 (0.1)	39	0 (0)	0 (0)	1 (100)	0 (0)
	Total 996 (100)	Mean 37.3	Total 504 (54.3)	Total 47 (9.6)	Total 226 (46.1)	Total 217 (44.3)

COVID-19 coronavirus disease 2019

^aStudies by Bouaziz et al., Hedou et al., Joob and Wiwanikit, Recalcati et al., and Tammaro et al. excluded because of inability to extract exact data [3, 4, 10, 12, 23]

^bStudies by De Masson et al., Fernandez-Nieto et al., Piccolo et al., Recalcati et al., and Torres-Navarro et al. excluded because of inability to extract exact data [3, 16, 33, 35, 36]

^cOther rashes included: eruptive cherry angioma (*n* = 1), reactivation of herpes simplex virus-1 (*n* = 1), and unspecified cases of eczematous, angiomatous, or annular lesions (*n* = 41)

Table 4 Summary of rashes by location

Rash location	Sample size ^a , <i>n</i> (%)
Face/neck	15 (3.0)
Chest/abdomen	2 (0.4)
Trunk/back	52 (10.2)
Arms/legs	17 (3.3)
Hands/feet	280 (55.1)
Palms/soles	6 (1.2)
Mixed ^b	136 (26.8)
Total	508 (100)

^aStudies by Bouaziz et al. and Galvan Casas excluded because of inability to extract exact data [4, 13]

^bMost common mixed pattern was trunk and limbs

assist in the identification of carriers, enabling healthcare officials to implement appropriate measures to stem the spread and, if appropriate, provide earlier COVID-19-specific care to these individuals.

Reports of the dermatologic signs and symptoms associated with COVID-19 are mounting in the literature, but these studies have yet to be comprehensively evaluated. This article presents an extensive evidence-based review of the COVID-19 scientific literature to identify and present

the cutaneous manifestations of SARS-CoV-2. Thirty-four studies on 996 patients with dermatologic conditions from eight different countries and four different continents were included in this report.

The most commonly reported dermatologic findings included acral lesions resembling pseudo-chilblains, erythematous maculopapular rashes, vesicular rashes, urticarial rashes, other rashes including eruptive cherry angioma and herpes simplex virus-1 reactivation, vascular rashes within the spectrum of livedo/purpura/necrosis, erythema multiforme-like eruptions, and otherwise unspecified erythematous rashes. Most of these rashes may be attributable to a COVID-19-specific viral exanthem; however, some dermatologic manifestations may be by-products of the thrombogenic and immune deregulatory effects of SARS-CoV-2, as evidenced by the cutaneous reaction patterns and histopathological findings [38].

Acral lesions, also described as pseud-chilblains or pernio-like lesions in the literature, were the most common type of rash presented in the literature, primarily affecting young adult patients and presenting after the onset of non-cutaneous COVID-19 symptoms [40]. According to Galvan Casas et al., acral lesions were significantly associated with younger aged patients and with a milder disease course. Patients with acral lesions typically required fewer

treatments than those with vascular rashes, erythematous maculopapular rashes, urticarial rashes, and vesicular rashes [13]. Of note, these acral lesions were largely unrelated to cold exposure (secondary to social isolation and stay-at-home orders) or a prior history of Raynaud's disease [9, 20, 32–34, 36]. Moreover, many of the patients who presented with acral lesions did not have a laboratory-confirmed diagnosis of COVID-19 and were instead suspected of having the disease because they had known infected contacts. As previously reported, many children presenting with acral lesions during the COVID-19 pandemic actually had laboratory-negative SARS-CoV-2 PCR [41]. This could in part be explained by the rapid decrease in viral loads after initial symptomatology, particularly in children who were not tested immediately because of country-wide lockdown measures. As such, although these cutaneous findings are likely COVID-19-induced acral lesions rather than primary pernio disease, their association with SARS-CoV-2 is not irrefutable. The majority of acral lesion cases were associated with milder disease, resolving disease, or negative laboratory testing. In one study, acral lesions were found in many close patient contacts [4]. As this rash affected a large number of patients, it may be useful for detecting individuals more likely to unknowingly transmit the disease. As such, acral lesions may be most appropriate for epidemiologic uses rather than diagnostic applications.

Erythematous maculopapular rashes were the second most common skin manifestation, affecting mostly middle-aged patients and presenting at the same time as other symptoms. Vesicular rashes and urticarial rashes were the next most frequent dermatologic findings. Both rash types affected adults, but vesicular rashes typically presented after the onset of extracutaneous COVID-19 manifestations while urticarial rashes occurred simultaneously. Urticarial rashes and erythematous maculopapular rashes are often drug induced, which lessens the ability of these cutaneous reactions to serve as a COVID-19 diagnostic marker. Vesicular lesions, however, tend to be more specific to viral exanthemas. As such, vesicular lesions may be a more useful COVID-19 diagnostic tool. Unfortunately, the pattern of vesicular lesions varies amongst COVID-19 studies, from diffuse polymorphic to localized monomorphic distributions. Further studies evaluating the type of vesicular rash most strongly associated with COVID-19 are warranted prior to determining the diagnostic utility of this particular cutaneous lesion.

Vascular rashes belonging to the spectrum of livedo/purpura/necrosis, while relatively uncommon, were primarily seen in elderly patients at the onset of non-dermatologic COVID-19 symptoms. According to Galvan Casas et al., vascular rashes were significantly correlated with more advanced age and/or severe symptomatology. Unsurprisingly, these vascular rashes were then associated with higher

rates of hospital admission and mechanical ventilation compared with erythematous maculopapular rashes, urticarial rashes, vesicular rashes, and acral lesions [13]. Given their correlation to disease severity, these vascular rashes might represent a COVID-19-specific complication in which the virus-induced pro-thrombotic state provokes vascular occlusion and ischemia [38]. Consequently, these rashes may be a useful prognostic marker that can help guide medical management.

Erythema multiforme-like eruptions were infrequent and typically occurred in young patients, particularly children. Other rashes (including one herpes simplex virus-1 reactivation and one eruptive cherry angioma), erythema multiforme-like eruptions, pityriasis rosea, and symmetrical drug-related intertriginous and flexural exanthema were also rarely observed. As such, these cutaneous manifestations may not be directly correlated to the COVID-19 virus. However, the true incidence of erythema multiforme-like eruptions and pityriasis rosea may be under-reported, as some studies grouped many unspecified rashes of annular or angiomatous appearance into the other rash category [36]. The frequency of pityriasis rosea in particular warrants further investigation, as this rash has previously been linked to other viruses [39].

As with any cutaneous eruption, one must consider that it may have been triggered by a medication. Drugs used to treat COVID-19, such as antimalarials, azithromycin, remdesivir, antiretrovirals, corticosteroids, and biologics, are known to cause acute urticaria, vasculitis, and other pruritic lesions. The rashes included in this evidence-based review that coincided with a recent medication intake were determined to be non-drug induced, as most authors reported that, for each questionable patient, the administered drug had either previously been taken without complication or was not known to cause the specific rashes observed. Of note, some patients with COVID-19 with previous skin conditions such as rosacea, acne, eczema, and atopic dermatitis experienced a flare during the course of their disease [42].

Finally, the case fatality rate reported by the studies included in this analysis had a range of 0.0–13.6%. This span encompasses the most recent and accurate estimation of the overall COVID-19 mortality rate of 3.8% [2]. As a rapidly evolving situation, COVID-19 peer-reviewed reports are rarely in the form of high-powered, strictly controlled clinical trials. As such, one of the limitations of this study was the inability to collect complete and standardized data sets to allow for in-depth comparisons between rash subgroups. Given the novelty of COVID-19 and the scientific literature's still limited understanding of the symptomatology of this disease, another limitation is the distinct possibility that many of the articles included in this review do not reflect the entire spectrum and variability of cutaneous lesions of

COVID-19. This can only be improved upon with continued observation and detailed reporting. Additionally, not all studies included in this analysis reported on patients with a laboratory-confirmed diagnosis of COVID-19; however, this may also be attributable to the unprecedented turmoil induced by this novel coronavirus, as testing is often limited or inaccessible.

5 Conclusions

A study of 552 hospitals in mainland China initially indicated a 0.2% prevalence of COVID-19 skin symptoms [43]. However, the prevalence suggested by this evidence-based analysis implies that the true rate is much greater, affecting up to 20.4% of patients with COVID-19. As a potential correlate to disease severity, prognosis, or infectibility, it is critical that all healthcare professionals be well versed in these increasingly common cutaneous manifestations of COVID-19. Hand surgeons and podiatrists must be even more aware of these lesions, as they most often appear on the hands and feet. Additional standardized studies of the COVID-19 rashes are warranted to further establish the diagnostic validity and utility of these visible findings.

Declarations

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References

- Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med*. 2020;382(8):727–33. <https://doi.org/10.1056/NEJMoa2001017>.
- Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis*. 2020;20(5):533–53.
- Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. *J Eur Acad Dermatol Venereol*. 2020. <https://doi.org/10.1111/jdv.16387>.
- Bouaziz JD, Duong T, Jachiet M, et al. Vascular skin symptoms in COVID-19: a French observational study. *J Eur Acad Dermatol Venereol*. 2020. <https://doi.org/10.1111/jdv.16544>.
- Magro C, Mulvey JJ, Berlin D, et al. Complement associated microvascular injury and thrombosis in the of severe COVID-19 infection: a report of five cases. *Transl Res*. 2020. <https://doi.org/10.1016/j.trsl.2020.04.007>.
- Henry D, Ackerman M, Sancelme E, et al. Urticarial eruption in COVID-19 infection. *J Eur Acad Dermatol Venereol*. 2020. <https://doi.org/10.1111/jdv.16472>.
- Estebanez A, Perez-Santiago L, Silva E, et al. Cutaneous manifestations in COVID-19: a new contribution. *J Eur Acad Dermatol Venereol*. 2020. <https://doi.org/10.1111/jdv.16474>.
- Marzano AV, Genovese G, Fabbrocini G, et al. Varicella-like exanthem as a specific COVID-19-associated skin manifestation: multicenter case series of 22 patients. *J Am Acad Dermatol*. 2020. <https://doi.org/10.1016/j.jaad.2020.04.044>.
- Recalcati S, Barbagallo T, Frasin LA, et al. Acral cutaneous lesions in the time of COVID-19. *J Eur Acad Dermatol Venereol*. 2020. <https://doi.org/10.1111/jdv.16533>.
- Tammaro A, Adebajo GAR, Parisella FR, et al. Cutaneous manifestations in COVID-19: the experiences of Barcelona and Rome. *J Eur Acad Dermatol Venereol*. 2020. <https://doi.org/10.1111/jdv.16530>.
- Alramthan A, Aldaraji W. A case of COVID-19 presenting in clinical picture resembling chilblains disease: first report from the Middle East. *Clin Exp Dermatol*. 2020. <https://doi.org/10.1111/ced.14243>.
- Hedou M, Carsuzaa F, Chary E, et al. Comment on “Cutaneous manifestations in COVID-19: a first perspective” by Recalcati S. *J Eur Acad Dermatol Venereol*. 2020. <https://doi.org/10.1111/jdv.16519>.
- Galvan Casas C, Catala A, Carretero Hernandez G, et al. Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases. *Br J Dermatol*. 2020. <https://doi.org/10.1111/bjd.19163>.
- Jimenez Cauhe J, Ortega Quijano D, Prieto Barrios M, et al. Reply to “COVID-19 can present with a rash and be mistaken for Dengue”: petechial rash in a patient with COVID-19 infection. *J Am Acad Dermatol*. 2020. <https://doi.org/10.1016/j.jaad.2020.04.016>.
- Gianotti R, Veraldi S, Recalcati S, et al. Cutaneous clinicopathological findings in three COVID-19-positive patients observed in the Metropolitan area of Milan, Italy. *Acta Derm Venereol*. 2020. <https://doi.org/10.2340/00015555-3490>.
- Ahouach B, Harant S, Ullmer A, et al. Cutaneous lesions in a patients with COVID-19: are they related? *Br J Dermatol*. 2020. <https://doi.org/10.1111/bjd.19168>.
- Van Damme C, Berlingin E, Saussez S, Accaputo O. Acute urticaria with pyrexia as the first manifestations of a COVID-19 infection. *J Eur Acad Dermatol Venereol*. 2020. <https://doi.org/10.1111/jdv.16523>.
- Fernandez-Nieto D, Jimenez-Cauhe J, Suarez-Valle A, et al. Characterization of acute acro-ischemic lesions in non-hospitalized patients: a case series of 132 patients during the COVID-19 outbreak. *J Am Acad Dermatol*. 2020. <https://doi.org/10.1016/j.jaad.2020.04.093>.
- Zengarini C, Orioni G, Cascavilla A, et al. Histological pattern in COVID-19 induced viral rash. *J Eur Acad Dermatol Venereol*. 2020. <https://doi.org/10.1111/jdv.16569>.
- Tosti G, Barisani A, Queirolo P, et al. Skin signs resembling vascular acroyndromes during the COVID-19 outbreak in Italy. *Clin Exp Dermatol*. 2020. <https://doi.org/10.1111/ced.14267>.

21. Mahe A, Birckel E, Krieger S, et al. A distinctive skin rash associated with coronavirus disease 2019? *J Eur Acad Dermatol Venereol*. 2020. <https://doi.org/10.1111/jdv.16471>.
22. Diaz-Guimaraens B, Dominguez-Santas M, Suarez-Valle A, et al. Petechial skin rash associated with severe acute respiratory syndrome coronavirus 2 infection. *JAMA Dermatol*. 2020. <https://doi.org/10.1001/jamadermatol.2020.1741>.
23. Joob B, Wiwanikit V. COVID-19 can present with a rash and be mistaken for dengue. *J Am Acad Dermatol*. 2020. <https://doi.org/10.1016/j.jaad.2020.03.036>.
24. Hunt M, Koziatek C. A case of COVID-19 pneumonia in a young male with full body rash as a presenting symptom. *Clin Pract Cases Emerg Med*. 2020. <https://doi.org/10.5811/cpcem.2020.3.47349>.
25. Ehsani AH, Nasimi M, Bigdelo Z. Pityriasis rosea as a cutaneous manifestation of COVID-19 infection. *J Eur Acad Dermatol Venereol*. 2020. <https://doi.org/10.1111/jdv.16579>.
26. Amatore F, Macagno N, Mailhe M, et al. SARS-CoV-2 infection presenting as a febrile rash. *J Eur Acad Dermatol Venereol*. 2020. <https://doi.org/10.1111/jdv.16528>.
27. Quintana-Castaneda L, Feito-Rodriguez M, Valero-Lopez I, et al. Urticarial exanthem as early diagnostic clue for COVID-19 infection. *JAAD Case Rep*. 2020. <https://doi.org/10.1016/j.jdcr.2020.04.026>.
28. Genovese G, Colonna C, Marzano AV. Varicella-like exanthem associated with COVID-19 in an 8-year-old girl: a diagnostic clue? *Pediatr Dermatol*. 2020. <https://doi.org/10.1111/pde.14201>.
29. Najarian DJ. Morbilliform exanthem associated with COVID-19. *JAAD Case Rep*. 2020. <https://doi.org/10.1016/j.jdcr.2020.04.015>.
30. Fernandez-Nieto D, Ortega-Quijano D, Jimenez-Cauhe J, et al. Clinical and histological characterization of vesicular COVID-19 rashes: a prospective study in a tertiary care hospital. *Clin Exp Dermatol*. 2020. <https://doi.org/10.1111/ced.14277>.
31. Sachdeva M, Gianotti R, Shah M, et al. Cutaneous manifestations of COVID-19: report of three cases and a review of the literature. *J Dermatol Sci*. 2020. <https://doi.org/10.1016/j.jderm.2020.04.01>.
32. Kolivras A, Dehavay F, Delplace D, et al. Coronavirus (COVID-19) infection-induced chilblains: a case report with histopathologic findings. *JAAD Case Rep*. 2020. <https://doi.org/10.1016/j.jdcr.2020.04.011>.
33. Piccolo V, Neri I, Filippeschi C, et al. Chilblain-like lesions during COVID-19 epidemic: a preliminary study on 63 patients. *J Eur Acad Dermatol Venereol*. 2020. <https://doi.org/10.1111/jdv.16526>.
34. Landa N, Mendieta-Eckert M, Fonda-Pascual P, et al. Chilblain-like lesions on feet and hands during the COVID-19 pandemic. *Int J Dermatol*. 2020;59(6):739–43. <https://doi.org/10.1111/ijd.14937>.
35. Torres-Navarro I, Abril-Perez C, Roca-Gines J, et al. Comment on ‘Two cases of COVID-19 presenting with a clinical picture resembling chilblains: first report from the Middle East’: pernio unrelated to COVID-19. *Clin Exp Dermatol*. 2020. <https://doi.org/10.1111/ced.14255>.
36. De Masson A, Bouaziz J, Sulimovic L, et al. Chilblains are a common cutaneous finding during the COVID-19 pandemic: a retrospective nationwide study from France. *J Am Acad Dermatol*. 2020. <https://doi.org/10.1016/j.jaad.2020.04.161>.
37. OCEBM Levels of Evidence Working Group. “The Oxford 2011 Levels of Evidence”. Oxford Centre for Evidence-Based Medicine. <https://www.cebm.net/index.aspx?o=5653>. Accessed 18 Aug 2020.
38. Bikdeli B, Madhavan MV, Jimenez D, et al. COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antithrombotic therapy, and follow-up. *J Am Coll Cardiol*. 2020. <https://doi.org/10.1016/j.jacc.2020.04.031>.
39. Chuh AA, Zawar V. Pityriasis rosea. In: Hoeger P, Kinsler V, Yan A, Harper J, Oranje A, Bodemer C, Larralde M, Luk D, Mendiratta V, Purvis D, editors. *Harper’s textbook of pediatric dermatology*. Wiley-Blackwell, Hoboken: New Jersey; 2019. p. 416–21.
40. Piccolo V, Neri I, Manunza F, Mazzatenta C, Bassi A. Chilblain-like lesions during the COVID-19 pandemic: should we really worry? *Int J Dermatol*. 2020. <https://doi.org/10.1111/ijd.14993>.
41. Piccolo V, Bassi A. Acral findings during the COVID-19 outbreak: chilblain-like lesions should be preferred to acro-ischemic. *J Am Acad Dermatol*. 2020. <https://doi.org/10.1016/j.jaad.2020.05.077>.
42. Zheng Y, Lai W. Dermatology staff participate in fight against Covid-19 in China. *J Eur Acad Dermatol Venereol*. 2020. <https://doi.org/10.1111/jdv.16390>.
43. Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020. <https://doi.org/10.1056/NEJMoa2002032>.