Early Cutaneous Manifestations of COVID-19: A Systematic Review and Public Health Implications

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ABSTRACT

Introduction: Cutaneous manifestations before other symptoms have great potential for early COVID-19 diagnosis to prevent surge.

Methods: We conducted a search of PubMed and Embase databases through April 11, 2021 to include 39 studies reporting skin manifestations occurring prior to any other COVID-19 symptoms in laboratory-confirmed cases.

Results: Ninety-seven patients were included. Urticarial (24.7%) and maculopapular (22.7%) lesions were most common, followed by pernio (17.5%), vesicular (14.4%), papulosquamous (8.2%), and purpuric (5.1%) lesions. Cutaneous to systemic symptom latency ranged from 2 to 20 days in cases that reported it (26%), while skin lesions were the only presentation in 23 cases (23.7%). Skin lesions were the only COVID-19 manifestation in 58.8% of pernio, 40% of vesicular, 16.6% of urticarial, 18.2% of maculopapular, and 12.5% of papulosquamous presymptomatic cases. Although sample size is limited, all purpuric cases developed other symptom(s) later.

Conclusions: Pernio and purpuric lesions have been well-associated with COVID-19, but papulosquamous, vesicular, mild maculopapular, and urticarial lesions can easily be dismissed as unrelated to COVID-19. Pernio lesions are thought to be related to strong immune response and low contagiousness, while purpuric and vesicular cases are speculated to be related to higher SARS-CoV2 viral load, severity, and contagiousness. All rashes, even without other symptoms, should necessitate high level of suspicion for isolation or contact tracing.

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INTRODUCTION

Coronavirus 2019 (COVID-19) vaccination has led to a decrease in cases. However, with the rise of variants of concern and the removal of mask mandates, recent reports have shown increased cases across different countries and concerns about future surges. COVID-19 can have a presymptomatic incubation up to 14 days before common symptoms manifest. Asymptomatic or presymptomatic cases can transmit severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Postvaccination breakthrough cases are possible and could present with longer incubation period and atypical nonrespiratory symptoms. Although fully vaccinated people have less severe symptoms, recent reports show that they are equally capable of spreading SARS-CoV-2.[1,2] Early detection of potential asymptomatic or presymptomatic cases is an important preemptive measure to prevent future surges in this postvaccination variant strain era.

It is now known that SARS-CoV2 has high affinity for angiotensin II converting enzyme (ACE2) receptors. ACE2 receptors are found in various tissues, thereby explaining the wide spectrum of systemic symptoms of COVID-19.[3] High ACE2 receptor expression has been found in keratinocytes, explaining the myriad COVID-19 skin lesions.[4] Cutaneous signs can occur before, concurrent, or after other symptoms.[5,6] Many skin complaints are easily dismissed or overlooked; however, cutaneous features that manifest before any other symptoms have great potential for early COVID-19 diagnosis. Therefore, a systematic review of the litera-

ture was conducted to collate and analyze cutaneous manifestations in laboratory-confirmed COVID-19 patients who presented initially or only with a skin lesion.

METHODS

A primary literature search was conducted using PubMed and Embase on April 1, 2023. Three authors independently screened PubMed with the search terms "covid OR SARS-COV-2" AND "skin OR cutaneous OR dermatology" and Embase with the search terms "coronavirus disease 2019" AND "skin disease." PubMed Medical Subject Headings (MeSH) controlled vocabulary; Embase Emtree terms and text words all were utilized to develop the search terms.

Three reviewers independently screened all article titles and abstracts to include cohort studies, case series, cross-sectional studies, or case reports published in English and Chinese on skin manifestations that occurred prior to any other COVID-19 symptoms in polymerase chain reaction (PCR) laboratory-confirmed cases. Articles that described skin lesions concurrent with other symptom(s) were excluded. Subsequently identified studies were subjected to full-text review. Bias risk and methodological quality were assessed. Rationales for exclusion and article appraisals were recorded at every stage. References of included and excluded studies were reviewed for potential studies not identified through initial search strategy.

Included studies were summarized using a data extraction form. Skin lesions were classified into the categories maculopapular, papulosquamous, pernio, purpuric, urticarial, vesicular, and others, according to a modification of Freeman et al's and Galvan-Casas et al's studies.[7,8] Cutaneous signs are also systemic COVID-19 manifestations; however, for simplicity, in this manuscript, we use the term "presymptomatic" to denote cases that presented initially or only with a skin lesion.

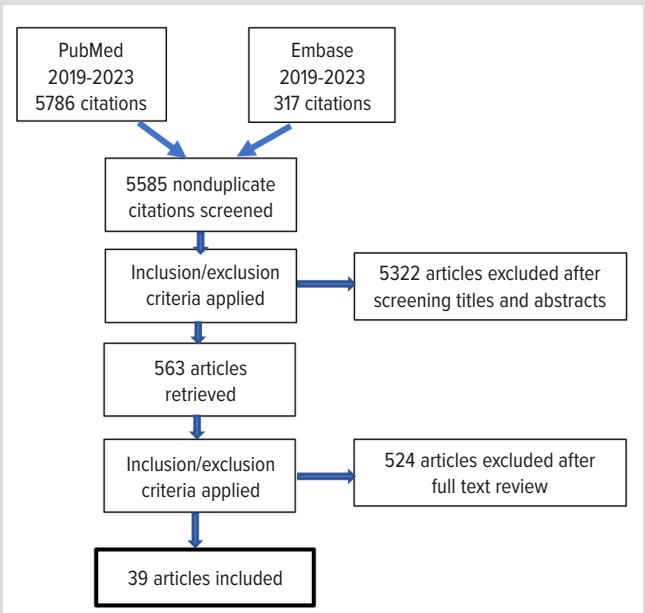
RESULTS

Through full-text screening of 5885 nonduplicate articles, 39 studies including 27 case reports and 12 case series and totaling to 97 patients (6 months to 78 years old; 25 male, 17 female, 55 unknown) were included in this review (Figure).

Cutaneous to systemic symptom latency ranged from 2 to 20 days in 25 patients (2 days in 12 patients, 3-6 days in 3 patients, 7 days in 5 patients, 8-14 days in 4 patients, 20 days in 1 patient, and nondocumented in 49 patients. Skin lesions were the only presentation (no other symptoms) in 23 patients (23.7%) (see Table). COVID-19 symptoms that occurred after cutaneous lesions included anosmia, cough, dyspnea, fever, headache, myalgia, and odynophagia. Skin lesions lasted from 1 to 24 days in cases that reported duration. No cases of mortality were reported; however, mortality/recovery status were unavailable for 28 cases.

Twenty-two cases (22.7%) presented with maculopapular lesions, 17 (17.5%) with pernio, 24 (24.7%) with urticarial, 14 (14.4%) with vesicular, 8 (8.2%) with papulosquamous, and 5 (5.1%) with purpuric lesions. Cases are summarized in subsections below. Noncategorizable lesions were grouped under "Others."

Figure 1. Flow Diagram for the Systematic Review of Cutaneous COVID-19 Lesions That Occurred Prior to Other Symptoms



Most of the 14 hospitalized cases (14.4%) were the eldest cases among each lesion category or patients with preexisting chronic conditions, except for a 6-year-old boy with severe cheilitis along erythema multiforme, 22-year-old man with thrombocytopenia along petechial purpura, and 50-year-old man with recurrent periorbital dyschromia along dyspnea. No hospitalization cases were noted among the pernio and papulosquamous lesion categories, while hospitalization was noted highest in the purpuric group. Twenty-eight cases (28.9%, age 10 months–61 years old) remained as outpatient, and 55 (56.7%) had undocumented hospitalization status (Table). Skin was the only COVID-19 manifestation in 58.8% of pernio, 40% of vesicular, 16.6% of urticarial, 18.2% of maculopapular, and 12.5% of papulosquamous presymptomatic cases. Although sample size is limited, all purpuric cases developed other symptom(s) later.

Maculopapular

No predilection of any body area was noted in the 22 patients (age 10 months–74 years old) with maculopapular presymptomatic lesions.

Papulosquamous

Among the 8 papulosquamous cases (age 26-38 years old), there was 1 case of pityriasis rosea (PR). There was no predilection for any body part, but face was spared in all 8 cases.

Pernio

Pernio lesions were noted in 17 cases (age 14-59 years old; 14

acral, 1 nonacral – auricle, 2 unknown). In acral lesions, the feet were 4 times more likely to be involved than the fingers. The auricle pernio[9] was an incidental case of positive PCR found via contact tracing. It is unclear whether auricle pernio occurred during active COVID-19 or as a long-term sequela.

Purpuric

Four cases presented with reticular purpura on the limbs. One 22-year-old previously healthy male had petechial, purpuric lesions in his bilateral lower extremities and dorsal hands and was hospitalized due to thrombocytopenia and buccal bleeding 2 days after. No trunk involvement was noted in all 3 cases.[10]

Urticarial

Twenty-four urticarial cases (age 6 months–61 years old) did not reveal predilection of any body area. Two cases developed angioedema,[11,12] with 1 progressing to odynophagia.[11] A 61-year- old male showed purpuric evolution from initial urticarial lesions.[13]

Vesicular

Among the 14 vesicular cases (age 19-65 years old), 3 involved diffuse papulovesicular lesions that had a predilection for the trunk. One reported hemorrhagic crusted vesicles in a dermatomal distribution[14] that was later clinically diagnosed as herpes zoster. Four cases clinically ruled out herpes zoster. None of the cases performed a Tzanck test nor herpes PCR.

DISCUSSION

In 1966, microbiologist Mims highlighted an existing lack of knowledge about viral rashes. He speculated blood vessel dilation, vascular injury, extravascular spread to cutaneous layers, hypersensitivity, and direct viral damage as possible pathomechanisms.[15] In 2005, French dermatologists Lipsker and Saurat broadly classified viral eruptions into classic viral (direct cytopathogenic viral interactions with skin) or paraviral (viral-triggered immune reactions). They noted that classic viral eruptions (eg, morbilliform measles rash) usually correlate to active viremia and contagiousness, while paraviral eruptions (eg, parvovirus B19 reticular lacy rash) usually indicate immune response against the virus and lower contagiousness.[16] The concept of linking viral rash pathomechanism to disease contagiousness is intriguing—especially during this COVID-19 pandemic—but not always clear-cut, ie, if immune reaction was partial and the virus remains latent in the body, contagiousness cannot be determined confidently. With COVID-19, more studies are needed to determine relationship of viremia load curve, contagiousness, and skin manifestations. Cycle threshold (Ct) numbers can be reported in future studies for contagiousness determination.

Previous publications analyzing laboratory-confirmed COVID-19 skin manifestations (occurring prior, concurrent, and/or after) showed that maculopapular (35.7%-52.1%) were the most frequent lesion type[7,8] Galvan-Casas et al's study (December 2019–April 8, 2020) showed that other common lesion types in laboratory-confirmed patients included urticarial (20.9%) and pernio (12.4%),[8] while Freeman et al's study (April 8, 2020–May 17, 2020) revealed pernio (18.1%) and urticarial (15.8%) lesions.[7] In our review (December 2019-April 2023) that solely studied skin manifestations occurring prior to any other symptom(s), urticarial (24.7%) and maculopapular (22.7%) lesions were the most reported, followed by pernio lesions (17.5%). These differences could be related to overreporting of pernio lesions due to the chilblain debate that started around April 2020.[7,17] Moreover, patients are likely to dismiss or forget skin lesions during history intake. It is also possible that many cases with only cutaneous signs have gone undiagnosed. It is pertinent to note that alopecia and pernio are the most frequent long-term cutaneous manifestations of COVID-19 in contrast to the early cutaneous signs of COVID-19, which may be due to persistent inflammation and stress.[6,18] Our findings also are limited by our small sample size. In the next subsections, we discuss the various lesion categories in relevance to clinical significance, possible pathomechanisms and public health implications.

Maculopapular

Macules are thought to be secondary to virally induced lasting local dilation of subpapillary dermal vessels. As dilation progresses to edema and cell infiltration, papules then result. All individual maculopapular case reports included in our review were pruritic, while included case series were reportedly 61% to 91% pruritic.[7,8] It is possible that nonpruritic maculopapular lesions are reflected less in the literature since patients are less concerned with seeking medical help if the rash is nonitchy.

Papulosquamous

From dermal vessels, viruses can affect the dermis then epidermis, leading to epidermal changes, such as scales and vesicles.[15] Papulosquamous lesions, such as PR, can be triggered by various viruses, especially Herpesviridae.[19,20] This raises the question on whether PR was triggered by COVID-19 infection or due to co-infection with other viruses. Abadías-Granado et al's study suggested that SARS-CoV-2 could cause reactivation of human herpesvirus 6 (HHV-6), leading to PR; however, authors also highlighted the need for more investigation due to limited sample size and serology limitations.[21]

Vesicular

Similarly, it is interesting to investigate whether vesicles were caused by COVID-19 or by other etiologies, such as varicella, herpes zoster, or pseudovesicular Grover disease.[22] Our review included 1 clinically diagnosed herpes zoster case in a male patient with a positive COVID-19 PCR.[14] It has been speculated that COVID-19-related lymphopenia could predispose to herpesvirus recurrence.[23,24] Some authors have suggested that herpes zoster (reflecting immunosuppression) in an otherwise immunocompetent patient should raise suspicion for subclinical COVID-19 coinfection, especially if lesions are present in various stages of

development at the same time.[24,25] Histologically, Mahé et al reported that SARS-CoV-2 vesicles appear with acantholysis and dyskeratosis with unilocular intraepidermal suprabasal vesicle, distinct from the large multinucleated cells and ballooning degeneration in the basal layer seen in herpes zoster.[26]

Vesicular viral lesions (eg, varicella, herpes zoster) are generally thought to be contagious19 through airborne respiratory droplets and vesicular fluid contact 1 to 2 days prior to the lesions up until the vesicles are crusted.[27] The same questions exist with COVID-19 vesicles. Fernandez-Nieto et al found negative vesicular PCR in 2 patients with nasopharyngeal PCR-confirmed COVID-19; however, more studies are needed.[25] Apart from the systemic vessel-dermis-epidermis route, concerns have been raised on whether SARS-CoV2 can enter through the skin, cause epidermal changes (such as vesicles or scales), then spread into the systemic circulation;[28] however, no studies have been done in this area.

Urticarial

Vesicles and urticarial lesions also can result from hypersensitivity reactions to viral components.[15] Urticaria can be easily overseen and disregarded as idiopathic;[12] however, infections are known triggers for acute and chronic urticaria.[29] Urticaria results from a combination of Types I-IV hypersensitivity reactions.[30] Increased bradykinin production due to activation of contact coagulation cascade and decreased bradykinin breakdown due to viral-ACE2 binding also are implicated in COVID-19-related urticaria and dry cough.[31-33] Coagulation factors also are thought to activate mast cell release of histamine.[34] As with all urticaria, angioedema development must be cautioned.

Pernio

Several scientific groups hypothesize that pernio is due to high production of type I interferon related to innate immune response against COVID-19.[19,35] In fact, in his 1966 review, Mims noted that interferons are likely related to recovery from primary virus infection, while antibodies confer resistance to reinfection.[15] Immune inflammation could then lead to microthromboses.[28] Microangiopathy reflecting COVID-19-related endothelitis[17] has been noted in nailfold capillaroscopy of fingers and toes of COVID-19 patients, even when lesions are visible only in the toes,[36] reflecting a systemic process. The nonacral auricle pernio case included in our review[9] also supports the systemic microcirculatory alterations that underlie pernio development in COVID-19.

Pernio is thought to be associated with younger patients and milder cases.[7,37] Our review reflects the same – presymptomatic pernio cases were found in the age range 22 to 59 years old and all outpatients. The strong innate immune response also explains the mild course in these patients[19,35] and the lack of other systemic symptoms in 58.8% of pernio cases included in this review. Some authors also believe that due to the strong innate immune response, patients with pernio lesions are no longer contagious,[17] which supports Lipsker and Saurat's theory of paraviral eruptions.[19]

Purpuric

Parallel to viral-induced vasodilation, viruses also can cause vessel injury leading to purpura.[15,19] Specifically, retiform purpura is due to vessel occlusion,[8] while petechiae is due to red blood cell extravasation and hemorrhage into the dermis. Purpuric COVID-19 lesions were usually found in elderly, more severe cases.[8,38] Our review included limited purpuric cases (n = 5, 22–66 years old) but did not reflect a more elderly population. In contrast to the strong innate immune reaction that could lead to microthromboses in pernio cases, purpura reflects COVID-19-related macrothrombotic hypercoagulability, possibly due to ineffective defense against the virus,[17,28,38] which supports why increased severity was noted with purpuric cases. Histologic findings of the petechial purpura case included in our review were consistent with viral exanthem,[10] possibly reflecting active viremia alongside the vascular phenomena.

Others

Cutaneous hyperesthesia, along with hyposmia and dysgeusia, belong to viral-induced subjective neurological symptoms found frequently with neurotropic viruses, such as the Herpesviridae.[39] Subjective neurological symptoms in SARS-COV2 are thought to be related to the presence of ACE2 receptors in sensory neurons.[40] Smell and taste abnormalities – often considered as early specific symptoms – frequently have been reported in COVID-19 patients, while cutaneous hyperesthesia, such as that included in our review, rarely has been reported.[41]

Periorbital dyschromia and the subsequent fever and cough in 2 cases recurred for the second time after initial resolution. The authors speculated that periorbital dyschromia was due to coagulation dysfunction of periocular vessels.[42] It is, therefore, intriguing to investigate the pathogenesis of COVID-19 more in depth.

Polymorphic Evolution

Patel et al's case[33] that reported multiple morphologies evolving from concurrent maculopapular, vesicular, and urticarial lesions to purpuric lesions is a good material to explore the sequential pathogenesis of COVID-19 cutaneous manifestations. As the virus proliferates in the bloodstream, dermal vascular dilatation and inflammation-related cell infiltration leads to maculopapular lesions. From dermal vessels, viruses can affect the dermis then epidermis, leading to epidermal vesicular (and papulosquamous) eruptions. Continued viral proliferation brings upon early coagulation dysfunction and hypersensitivity reactions to viral components, leading to urticaria and facial angioedema. Purpura forms as coagulation dysfunction progresses. Patel et al also pointed out the possibility of coinfection with other viruses or multiple viral strains leading to polymorphic presentation,[33] which is supported by reports of coinfection with herpes zoster or HHV-6.[14,21]

Table 1. Summary of Studies Reporting Skin Lesions Prior to Any Other COVID-19 Symptoms

Author(s), Year	Study Design	Age (y), Sex	Comorbidities	Skin Lesion Location and Clinical Features	Latency (days)	Inpatient
Maculopapular (22/97 = 22.7%); 9.1% hospitalized, 72.7% unknown hospitalization status; **18.2% cutaneous symptoms only**						
Altayeb et al, 2020[44]	Case report (n = 1), extracted from n = 2	74, M	AF, FL	Neck, back, and chest; pruritic	-10 (D)	Yes
Hunjan et al, 2020[45]	Case report (n = 1)	64, F	NR	From trunk that rapidly spread to upper thighs and inner arms with associated facial edema; pruritic	-7 (DF)	Yes
Dertlioğlu, 2020[46]	Case report (n = 1), extracted from n = 5	10 mo, M	NR	Widespread: trunk and arm; pruritic	Skin only	No
Freeman et al, 2020[7]	n = 3 out of case series (n = 23)	31 (27–55); 7 M, 16 F	N/A	Macular erythema: back (48%), arms (48%); 61% pruritic, 26% painful/burning	-x (n = 2), skin only (n = 1)	NR (n = 3)
Freeman et al, 2020[7]	n = 4 out of case series (n = 38)	52 (36–66); 19 M, 19 F	N/A	Morbilliform: abdomen (63%), back (61%); 61% pruritic, 61% painful/burning	-x (n = 3), skin only (n = 1)	NR (n = 4)
Galván Casas et al, 2020[8]	n = 4 out of case series (n = 122)	60 (45–77); 63 M, 59 F	N/A	N/A; 91% pruritic, 6% burning, 3% painful	-x (n = 4)	NR (n = 4)
Gianotti et al, 2020[47]	Case report (n = 1), extracted from n = 3	57, M	None	Widespread; pruritic	-2 (CF)	No
Serafini et al, 2020[48]	case report (n = 1)	32, F	None	Sparing face, scalp, and abdomen; pruritic	-7 (C)	No
Ghafoor et al, 2022[49]	n = 5 out of case series (n = 23)	38.9 ± 11.5	None	N/A	-x (n = 5)	NR (n = 5)
Assaf et al, 2021[50]	Case report (n = 1)	26, M	None	Initially appeared on legs, then progressed to affect trunk and arms, sparing the face; pruritic	Skin only	No
Papulosquamous (8/97 = 8.2%); 0% hospitalized, 75% unknown hospitalization status; **12.5% cutaneous symptoms only**						
Chu et al, 2020[51]	Case report (n = 1)	52, M	DM, HTN	Bilateral palms, forearms, and legs; pruritic	-4 (DF)	No
Freeman et al, 2020[7]	n = 4 out of case series (n = 17)	28 (27–38); 10 M, 7 F	N/A	Abdomen (65%), arms (65%), back (65%), legs/buttocks (65%); 94% pruritic, 29% painful/burning	-x (n = 3), skin only (n = 1)	NR (n = 4)
Merhy et al, 2020[20]	Case report (n = 1)	26, F	None	Christmas tree pityriasis rosea pattern preceded by herald annular plaque on right thigh	-9 (CFM)	No
Ghafoor R et al, 2022[49]	n = 2 out of case series (n = 5)	31.4 ± 8.3	None	N/A	-x (n = 2)	NR (n = 2)
Pernio (17/97 = 17.5%); 0% hospitalized, 70.5% unknown hospitalization status; **58.8% cutaneous symptoms only**						
Altayeb et al, 2020[44]	Case report (n = 1) extracted from n = 2	29, M	NR	Fingertips; also had symmetrical painless desquamation	-4 (CF)	No
Freeman et al, 2020[7]	n = 11 out of case series (n = 31)	35 (22–59); 15 M, 16 F	N/A	Feet (84%), hands (32%); 36% pruritic, 71% painful/burning	-x (n = 5), skin only (n = 6)	NR (n = 11)
Galván Casas et al, 2020[8]	n = 1 out of case series (n = 29)	44 (21–67) 11 M, 18 F	N/A	N/A; 47% pruritic, 42% painful, 11% burning	-x (n = 1)	NR) (n = 1)
Guarneri et al, 2021[52]	Case report (n = 1), extracted from n = 3	14, M	NR	Dorsum of toes; progressed to small ulcer on left 5th toes after 7 day	Skin only	No
Guarneri et al, 2021[52]	Case report (n = 1), extracted from n = 3	14, M	NR	Dorsum of toes; some progressed to necrotic blackish crusts	Skin only	No
Proietti et al, 2020[9]	Case report (n = 1)	35, F	None	Lateral right auricle; extremely painful	Skin only	No
Paparella et al, 2022[53]	Case report (n = 1)	14, M	None	Left toes; swollen erythematous; itching	Skin only	No
Purpuric (5/97 = 5.1%); **80% hospitalized; 40% cutaneous symptoms only**						
Freeman et al, 2020[7]	n = 1 out of case series (n = 11)	66 (51–73); 9 M, 2 F	NR	Legs/buttocks (64%), trunk and face spared; 9% painful/burning	-x (n = 1)	Yes
Lobos et al, 2020[10]	Case report (n = 1)	22, M	None	Petechiae in bilateral lower limbs and dorsal hands; gingival bleeding and buccal hematoma after dental	-5 (H)	Yes
Khalil et al, 2020[54]	Case report (n = 1)	34, F	None	Livedo reticularis of bilateral arms and thighs	-2 (M)	No
Brito Caldeira et al, 2021[55]	Case report (n = 1)	44, M	None	Both thighs; large (>15 cm)	Skin only	Yes
McBride JD et al, 2021 [56]	Case report (n = 1)	66, F	HTN, DM, COPD	Bilateral buttocks; nonindurated, retiform purpuric patch	Skin only	Yes

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Abbreviations: M, male; F, female; y, years; mo, months; NR, not reported; ICU, intensive care unit; N/A, not applicable; AF atrial fibrillation, FL, follicular lymphoma, DM, diabetes mellitus; HTN, hypertension; PHTN, pulmonary hypertension; OSA, obstructive sleep apnea; CKD, chronic kidney disease; VE, vascular epilepsy; HF, heart failure; HSV, herpes simplex virus; A, anosmia; C, cough; D, dyspnea; F, fever; M, myalgia; O, odynophagia; COPD, chronic obstructive pulmonary disease.

Table 1 continued. Summary of Studies Reporting Skin Lesions Prior to Any Other COVID-19 Symptoms

Author(s), Year	Study Design	Age (y), Sex	Comorbidities	Skin Lesion Location and Clinical Features	Latency (days)	Inpatient
Urticarial (24/97 = 24.7%); 10.7% hospitalized, 58.3% unknown hospitalization status; **16.6% cutaneous symptoms only**						
Naziroğlu et al, 2020[57]	Case report (n = 1)	53, M	Previous smoker	Generalized; pruritic	Skin only	Yes
Pagali and Parikh, 2021[58]	Case report (n = 1)	54, F	Obesity, PHTN, OSA, AF, CKD	Upper/lower limbs and trunk; pruritic, burning	-2 (DM)	Yes
Chen et al, 2020[59]	Case report (n = 1)	6 mo, M	None	Generalized; pruritic	-11 (F)	No
Dertlioğlu, 2020[46]	Case report (n = 1), extracted from n = 5	42, M	NR	Trunk	-7 (CM)	No
Galván Casas et al, 2020[8]	n = 2 out of case series (n = 49)	53 (32–74); 17 M, 32 F	N/A	N/A; 98% pruritic, 2% burning	-x (n = 2)	NR (n = 2)
Freeman et al, 2020[7]	n = 3 out of case series (n = 27)	42 (29–54); 6 M, 21 F	NR	Legs/buttocks (52%), arms (48%), hands (48%); 74% pruritic, 22% painful/burning	-x (n = 2), skin only (n = 1)	NR (n = 3)
Hassan et al, 2020[12]	Case report (n = 1)	46, F	Asthma, hay fever	Upper/lower limbs and trunk, after a day involved face and angioedema of lips; pruritic	-2 (CF)	No
Mendes and Pimenta, 2020[60]	Case report (n = 1)	18, F	None	Trunk, inguinal zone, distal upper/lower limbs, forehead; asymptomatic	-2 (F)	No
Palomo-Pérez et al, 2021[11]	Case report (n = 1), extracted from n = 4	43, F	NR	Gace, progressed to odynophagia	-2 (OM)	No
Quintana-Castanedo et al, 2020[13]	Case report (n = 1)	61, M	NR	Thighs, arms, and forearms; pruritic	Skin only	No
van Damme et al, 2020[61]	Case report (n = 1), extracted from n = 2	39, F	None	Generalized (started from forearms); pruritic	-2 (F), -5 (A)	No
Pangburn J et al, 2023[62]	Case report (n = 1) extracted from n = 2	46, M	None	Bilateral upper and lower exctremities	Skin only	Yes
Ghafoor et al, 2022[49]	Case series (n = 9) extracted from n = 15	40.4 ± 11.5	None	N/A	-x (n=9)	NR (n = 9)
Vesicular (14/97 = 14.4%); 14.2% hospitalized, 42.8% unknown hospitalization status; **0% cutaneous symptoms only**						
Goyal et al, 2021[14]	Case report (n = 1), extracted from n = 3	60s, M	NR	Left T6 dermatome; hemorrhagic	-2 (AFM)	Yes
Marzano et al, 2020[63]	Case report (n = 1), extracted from n = 22	65, M	NR	Trunk, no facial/mucosal involvement; pruritic	-2 (CF)	Yes
Fernandez-Nieto et al, 2020[25]	n = 2 out of case series (n = 24)	45 (19-65), 6 M, 18 F	NR	Widespread: trunk; different stages of the lesions appeared simultaneously	-10 (n = 1), -20 (n = 1)	NR (n = 2)
Freeman et al, 2020[7]	n = 1 out of case series (n = 18)	55 (36-58), 8 M, 10 F	N/A	Abdomen (44%), arms (44%), legs/buttocks (44%); 72% pruritic, 50% painful/burning	-x (n = 1)	NR (n = 1)
Galván Casas et al, 2020[8]	n = 2 out of case series (n = 17)	56 (43-70), 11 M, 6 F	N/A	N/A; 85% pruritic, 15% burning	-x (n = 2)	NR
Ghafoor et al, 2022[49]	n = 1 out of case series (n = 15)	46.7 ± 7.8	None	N/A	-x (n = 1)	NR (n = 1)
Sil et al, 2022[64]	Case series n = 6	58 (34–76) 4 M, 2 F	Diabetes (n = 1)	Facial vesicles; painful; burning sensation	-x (n = 6)	no
Others						
Labé et al, 2020[65]	Case report (n = 1), extracted from n = 2	6, M	None	Severe erosive cheilitis, bilateral conjunctivitis, multiple erythema multiforme target lesions (HSV and *Mycoplasma pneumoniae* ruled out by serology)	-7 (F)	Yes
Patel et al, 2020[33]	Case report (n = 1)	78, F	VE, HF, hypothyroid	Widespread maculopapules with vesicles and urticaria on trunk and malar region; facial angioedema with drooling; progressed to purpuric rash; nonpruritic	-7 (F)	Yes
Kalner and Vergilis, 2020[42]	Case report (n = 1), extracted from n = 3	50, M	None	Dusky red, nonpruritic, nonblanching periorbital dyschromia; skin and systemic symptoms recurred after resolution	-2 (DMF)	Yes
Kalner and Vergilis, 2020[42]	Case report (n = 1), extracted from n = 3	43, F	None	Dusky red, nonpruritic, nonblanching periorbital dyschromia; skin and systemic symptoms recurred after resolution	-2 (CFM)	No
Krajewski et al, 2020[41]	Case report (n = 1), extracted from n = 9	62, F	NR	Cutaneous hyperesthesia	-2 (FM)	NR (n = 1)
Andina-Martínez et al, 2021[66]	Case series (n = 2), extracted from n = 6	5, F; 9, M	None	Hands; mild erythema and desquamation of the fingertips	Skin only	No

Abbreviations: M, male; F, female; y, years; mo, months; NR, not reported; ICU, intensive care unit; N/A, not applicable; AF atrial fibrillation, FL, follicular lymphoma, DM, diabetes mellitus; HTN, hypertension; PHTN, pulmonary hypertension; OSA, obstructive sleep apnea; CKD, chronic kidney disease; VE, vascular epilepsy; HF, heart failure; HSV, herpes simplex virus; A, anosmia; C, cough; D, dyspnea; F, fever; M, myalgia; O, odynophagia; COPD, chronic obstructive pulmonary disease.

Public Health Implications

Somehow similarly with Lipsker and Saurat, Kolivras et al echoed that specific cutaneous lesions develop in specific stages of COVID-19 and reflect different prognosis and contagiousness. For instance, pernio eruptions due to strong innate immune response eradicating the virus are thought to be less contagious,[17,19] while vesicular and purpuric lesions can be speculated to have a higher viral load and thus more contagious. Findings in our review support these hypotheses. Although sample size is limited, all the purpuric and vesicular cases developed a systemic symptom later, while 58.8% of pernio cases did not develop systemic symptoms. Moreover, hospitalization was also noted highest with purpuric cases.

Our review included 6 pediatric cases (6 months, 10 months, 5 years, 6 years, 9 years, and 14 years old), one of which only presented with maculopapular lesions and no further symptoms. At this writing, COVID-19 vaccines were not yet available for children below 12 years old,[43] making them and their caretakers vulnerable, along with the rest of the unvaccinated population. With the opening of daycares, schools, restaurants and large events—along with removal of mask mandates—cluster outbreaks are highly possible, thereby further highlighting the need for early detection of COVID-19 cases.

CONCLUSIONS

In patients who presented initially or only with cutaneous lesions, urticarial and maculopapular were most common, followed by pernio. Skin lesions were the only COVID-19 manifestation in 23.7% of all included cases in this review. Skin lesions were the only manifestation in 58.8% of pernio-like, 16.6% of urticarial, 18.2% of maculopapular, and 12.5% of papulosquamous presymptomatic cases. Pernio and purpuric lesions have been well-associated with COVID-19, but papulosquamous, vesicular, mild maculopapular and urticarial lesions can be easily overlooked and dismissed as unrelated to COVID-19. Pernio lesions are thought to be related to strong immune response and low contagiousness, while purpuric and vesicular cases are speculated to be related to higher SARS-CoV2 viral load, severity, and contagiousness. However, more studies are needed to better understand the link between viral pathogenesis, gross morphology, and contagiousness. Regardless, all presymptomatic skin lesions could serve as a valuable tool for early case identification and spread control. Rashes should necessitate a high level of suspicion, especially if possible COVID-19 contact history is present. Even when skin lesions occur after the patient is no longer contagious (eg, pernio), contact tracing should still be done to minimize asymptomatic spread that potentially could have happened prior to development of skin lesions

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REFERENCES

1. Clinical care considerations: clinical considerations for care of children and adults with confirmed COVID-19. Centers for Disease Control and Prevention. Accessed May 3, 2021. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html

2. Brown CM, Vostok J, Johnson H, et al. Outbreak of SARS-CoV-2 infections, including COVID-19 vaccine breakthrough infections, associated with large public gatherings - Barnstable County, Massachusetts, July 2021. *MMWR Morb Mortal Wkly Rep.* 2021;70(31):1059-1062. doi:10.15585/mmwr.mm7031e2

3. Grover A, Oberoi M. A systematic review and meta-analysis to evaluate the clinical outcomes in COVID-19 patients on angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. *Eur Heart J Cardiovasc Pharmacother.* 2021;7(2):148-157. doi:10.1093/ehjcvp/pvaa064

4. Xue X, Mi Z, Wang Z, Pang Z, Liu H, Zhang F. High expression of ACE2 on keratinocytes reveals skin as a potential target for SARS-CoV-2. *J Invest Dermatol.* 2021;141(1):206-209.e1. doi:10.1016/j.jid.2020.05.087

5. COVID toes, rashes: how the coronavirus can affect your skin. American Academy of Dermatology Association. Published 2021. Accessed May 3, 2021. https://www.aad.org/public/diseases/coronavirus/covid-toes

6. Grover A, Choi F, Pei-Wang S. 33624 Long-term cutaneous manifestations in COVID-19 patients: a systematic review. *J Am Acad Dermatol.* 2022;87(3):AB76. 10.1016/j.jaad.2022.06.339

7. Freeman EE, McMahon DE, Lipoff JB, et al. The spectrum of COVID-19-associated dermatologic manifestations: an international registry of 716 patients from 31 countries. *J Am Acad Dermatol.* 2020;83(4):1118-1129. doi:10.1016/j.jaad.2020.06.1016

8. Galván Casas C, Català A, Carretero Hernández 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;183(1):71-77. doi:10.1111/bjd.19163

9. Proietti I, Tolino E, Bernardini N, et al. Auricle perniosis as a manifestation of COVID-19 infection. *Dermatol Ther.* 2020;33(6):e14089. doi:10.1111/dth.14089

10. Lobos P, Lobos C, Aravena P. Immune thrombocytopenic purpura associated with coronavirus disease 2019 infection in an asymptomatic young healthy patient. *JAAD Case Rep.* 2020;6(11):1129-1131. doi:10.1016/j.jdcr.2020.08.037

11. Palomo-Pérez JC, Vega-Memije ME, Aguilar-Blancas D, González-Martínez E, Rangel-Gamboa L. Cutaneous manifestations of COVID-19 in Mexican patients: a case series and review of literature. *SAGE Open Med Case Rep*. 2021;9:2050313X21997194. doi:10.1177/2050313X21997194

12. Hassan K. Urticaria and angioedema as a prodromal cutaneous manifestation of SARS-CoV-2 (COVID-19) infection. *BMJ Case Rep*. 2020;13(7):e236981. doi:10.1136/bcr-2020-236981

13. Quintana-Castanedo L, Feito-Rodríguez M, Valero-López I, Chiloeches-Fernández C, Sendagorta-Cudós E, Herranz-Pinto P. Urticarial exanthem as early diagnostic clue for COVID-19 infection. *JAAD Case Rep*. 2020;6(6):498-499. doi:10.1016/j.jdcr.2020.04.026

14. Goyal S, Prabhu S, U S, Pai SB, Mohammed A. Cutaneous manifestations of COVID-19 in skin of color: a firsthand perspective of three cases in a tertiary care center in India. *Postgrad Med*. 2021;133(3):307-309. doi:10.1080/00325481.2020.1852784

15. Mims CA. Pathogenesis of rashes in virus diseases. *Bacteriol Rev*. 1966;30(4):739-760. doi:10.1128/br.30.4.739-760.1966

16. Lipsker D, Saurat JH. A new concept: paraviral eruptions. *Dermatology*. 2005;211(4):309-311. doi:10.1159/000088498

17. Kolivras A, Thompson CT, Richert B. Reply to Pernio during the COVID-19 pandemic and review of inflammation patterns and mechanisms of hypercoagulability. *JAAD Case Rep.* 2020;6(9):954-955. doi:10.1016/j.jdcr.2020.06.003

18. McMahon DE, Gallman AE, Hruza GJ, et al. Long COVID in the skin: a registry analysis of COVID-19 dermatological duration. *Lancet Infect Dis*. 2021;21(3):313-314. doi:10.1016/S1473-3099(20)30986-5

19. Lipsker D. Paraviral eruptions in the era of COVID-19: do some skin manifestations point to a natural resistance to SARS-CoV-2? *Clin Dermatol*. 2020;38(6):757-761. doi:10.1016/j.clindermatol.2020.06.005

20. Merhy R, Sarkis AS, Stephan F. Pityriasis rosea as a leading manifestation of COVID-19 infection. *J Eur Acad Dermatol Venereol*. 2021;35(4):e246-e247. doi:10.1111/jdv.17052

21. Abadías-Granado I, Navarro-Bielsa A, Morales-Callaghan AM, et al. COVID-19-associated cutaneous manifestations: does human herpesvirus 6 play an aetiological role? *Br J Dermatol*. 2021;184(6):1187-1190. doi:10.1111/bjd.19806

22. Llamas-Velasco M, Chicharro P, Rodríguez-Jiménez P, et al. Comment on 'Clinical and histological characterization of vesicular COVID-19 rashes: a prospective study in a tertiary care hospital'. Pseudoherpetic Grover disease seems to occur in patients with COVID-19 infection. *Clin Exp Dermatol.* 2020;45(7):896-898. doi:10.1111/ced.14305

23. Llamas-Velasco M, Rodríguez-Jiménez P, Chicharro P, De Argila D, Muñoz-Hernández P, Daudén E. Reply to "Varicella-like exanthem as a specific COVID-19-associated skin manifestation: Multicenter case series of 22 patients": to consider varicella-like exanthem associated with COVID-19, virus varicella zoster and virus herpes simplex must be ruled out. *J Am Acad Dermatol*. 2020;83(3):e253-e254. doi:10.1016/j.jaad.2020.04.180

24. Lopez-Trujillo E, Rodriguez Mercader S, Güerri-Fernández R, Arrieta Aldea I, Pujol RM, Martin-Ezquerra G. Varicella complicated with pneumonia in a patient infected by COVID-19: the need to rule out other viral coinfections in SARS-CoV-2 patients with vesicular eruptions. *Int J Dermatol*. 2021;60(7):886-888. doi:10.1111/ijd.15515

25. 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;45(7):872-875. doi:10.1111/ced.14277

26. Mahé A, Birckel E, Merklen C, et al. Histology of skin lesions establishes that the vesicular rash associated with COVID-19 is not 'varicella-like'. *J Eur Acad Dermatol Venereol.* 2020;34(10):e559-e561. doi:10.1111/jdv.16706

27. Chickenpox and shingles (varicella / herpes zoster). State of Victoria. Reviewed October 8, 2015. Accessed January 2, 2023. https://www2.health.vic.gov.au/public-health/infectious-diseases/disease-information-advice/chickenpox-and-shingles

28. Ciechanowicz P, Lewandowski K, Szymańska E, Kaniewska M, Rydzewska GM, Walecka I. Skin and gastrointestinal symptoms in COVID-19. *Prz Gastroenterol.* 2020;15(4):301-308. doi:10.5114/pg.2020.101558

29. Imbalzano E, Casciaro M, Quartuccio S, et al. Association between urticaria and virus infections: a systematic review. *Allergy Asthma Proc*. 2016;37(1):18-22. doi:10.2500/aap.2016.37.3915

30. Hennino A, Bérard F, Guillot I, Saad N, Rozières A, Nicolas JF. Pathophysiology of urticaria. *Clin Rev Allergy Immunol*. 2006;30(1):3-11. doi:10.1385/CRIAI:30:1:003

31. Kroumpouzos G. Cutaneous manifestations of COVID-19: an unusual presentation with edematous plaques and pruritic, erythematous papules, and comment on the role of bradykinin storm and its therapeutic implications. *Dermatol Ther.* 2021;34(2):e14753. doi:10.1111/dth.14753

32. Cohen AJ, DiFrancesco MF, Solomon SD, Vaduganathan M. Angioedema in COVID-19. *Eur Heart J.* 2020;41(34):3283-3284. doi:10.1093/eurheartj/ehaa452

33. Patel N, Kho J, Smith KE, et al. Polymorphic cutaneous manifestations of COVID-19 infection in a single viral host. *Int J Dermatol.* 2020;59(9):1149-1150. doi:10.1111/ijd.15072

34. Asero R, Tedeschi A, Marzano AV, Cugno M. Coagulation in chronic urticaria. *Curr Treat Options Allergy.* 2015;2(4):287-293. doi:10.1007/s40521-015-0062-0

35. Battesti G, El Khalifa J, Abdelhedi N, et al. New insights in COVID-19-associated chilblains: a comparative study with chilblain lupus erythematosus. *J Am Acad Dermatol.* 2020;83(4):1219-1222. doi:10.1016/j.jaad.2020.06.1018

36. El Hachem M, Diociaiuti A, Concato C, et al. A clinical, histopathological and laboratory study of 19 consecutive Italian paediatric patients with chilblain-like lesions: lights and shadows on the relationship with COVID-19 infection. *J Eur Acad Dermatol Venereol.* 2020;34(11):2620-2629. doi:10.1111/jdv.16682

37. Freeman EE, McMahon DE, Lipoff JB, et al. Pernio-like skin lesions associated with COVID-19: a case series of 318 patients from 8 countries. *J Am Acad Dermatol.* 2020;83(2):486-492. doi:10.1016/j.jaad.2020.05.109

38. Kolivras A, Dehavay F, Delplace D, et al. Coronavirus (COVID-19) infection-induced chilblains: a case report with histopathologic findings. *JAAD Case Rep*. 2020;6(6):489-492. doi:10.1016/j.jdcr.2020.04.011

39. Yamada K, Kubota Y, Shimizu Y, et al. Sleep shortage is associated with postherpetic neuralgia development through hyperesthesia and acute pain intensity: a community-based prospective cohort study. *Pain Pract*. 2019;19(5):476-483. doi:10.1111/papr.12766

40. Moutal A, Martin LF, Boinon L, et al. SARS-CoV-2 spike protein co-opts VEGF-A/neuropilin-1 receptor signaling to induce analgesia. *Pain*. 2021;162(1):243-252. doi:10.1097/j.pain.0000000000002097

41. Krajewski PK, Maj J, Szepietowski JC. Cutaneous hyperaesthesia in SARS-CoV-2 infection: rare but not unique clinical manifestation. *Acta Derm Venereol*. 2021;101(1):adv00366. doi:10.2340/00015555-3729

42. Kalner S, Vergilis IJ. Periorbital erythema as a presenting sign of COVID-19. *JAAD Case Rep.* 2020;6(10):996-998. doi:10.1016/j.jdcr.2020.05.001

43. COVID-19 vaccine safety in children and teens. Centers for Disease Control and Prevention. Updated July 20, 2022. Accessed January 2, 2023. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/vaccine-safety-children-teens.html

44. Altayeb A, Cordaro A, Caesar J, Vyas J, Ingram J. Two cases of skin manifestations prior to the onset of COVID-19 respiratory symptoms. *Int J Dermatol.* 2020;59(12):1541-1542. doi:10.1111/ijd.15247

45. Hunjan MK, Zuzarte L, Bardhan A, Karim S, Heagerty AHM. Toxic erythema as the first sign of COVID-19 infection. *Clin Exp Dermatol.* 2021;46(4):756-758. doi:10.1111/ced.14571

46. Dertlioğlu SB. Skin manifestations in COVID-19: a case series of five patients from Elazığ, Turkey. *Dermatol Ther.* 2020;33(6):e13932. doi:10.1111/dth.13932

47. Gianotti R, Veraldi S, Recalcati S, et al. Cutaneous clinico-pathological findings in three COVID-19-positive patients observed in the metropolitan area of Milan, Italy. *Acta Derm Venereol.* 2020;100(8):adv00124. doi:10.2340/00015555-3490

48. Serafini A, Kurotschka PK, Bertolani M, Riccomi S. An itchy erythematous papular skin rash as a possible early sign of COVID-19: a case report. *J Med Case Rep.* 2020;14(1):216. doi:10.1186/s13256-020-02538-y

49. Ghafoor R, Ali SM, Goldust M. Cutaneous manifestations of coronavirus disease 2019. *J Cosmet Dermatol*. 2022;21(9):3667-3672. doi:10.1111/jocd.15258

50. Assaf J, Sarkis J, Merhy R, Jabbour R, Zeinaty P, Helou-Mallat J. Cutaneous maculopapular and vesicular lesions as the only presentation of COVID-19. *Int J Dermatol.* 2021;60(11):e467-e469. doi:10.1111/ijd.15876

51. Chu S, Christensen LF, Vidmar D. Skin eruption and gastrointestinal symptoms as presentation of COVID-19. *Cutis*. 2020;106(6):309-310. doi:10.12788/cutis.0129

52. Guarneri C, Rullo EV, Pavone P, et al. Silent COVID-19: what your skin can reveal. *Lancet Infect Dis.* 2021;21(1):24-25. doi:10.1016/S1473-3099(20)30402-3

53. Paparella R, Tarani L, Properzi E, et al. Chilblain-like lesions onset during SARS-CoV-2 infection in a COVID-19-vaccinated adolescent: case report and review of literature. *Ital J Pediatr.* 2022;48(1):93. doi:10.1186/s13052-022-01296-5

54. Khalil S, Hinds BR, Manalo IF, Vargas IM, Mallela S, Jacobs R. Livedo reticularis as a presenting sign of severe acute respiratory syndrome coronavirus 2 infection. *JAAD Case Rep*. 2020;6(9):871-874. doi:10.1016/j.jdcr.2020.07.014

55. Brito Caldeira M, Pestana M, João AL, Fernandes C, João A, Cunha N. Retiform purpura and extensive skin necrosis as the single manifestation of SARS-CoV-2 infection. *J Eur Acad Dermatol Venereol.* 2021;35(12):e839-e841. doi:10.1111/jdv.17562

56. McBride JD, Narang J, Simonds R, et al. Development of sacral/buttock retiform purpura as an ominous presenting sign of COVID-19 and clinical and histopathologic evolution during severe disease course. *J Cutan Pathol.* 2021;48(9):1166-1172. doi:10.1111/cup.14038

57. Naziroğlu T, Sözen S, Özkan P, Şeker S, Aksu K. A case of COVID-19 pneumonia presenting with acute urticaria. *Dermatol Ther.* 2020;33(4):e13575. doi:10.1111/dth.13575

58. Pagali S, Parikh RS. Severe urticarial rash as the initial symptom of COVID-19 infection. *BMJ Case Rep*. 2021;14(3):e241793. doi:10.1136/bcr-2021-241793

59. Chen V, Escandon Brehm J, Bellodi Schmidt F. Acute urticaria preceding other COVID-19-associated manifestations-a case report. *Pediatr Dermatol*. 2021;38(2):455-457. doi:10.1111/pde.14505

60. Mendes CC, Pimenta R. Urticaria multiforme-like: a COVID-19 infection. *Pan Afr Med J.* 2020;37:286. doi:10.11604/pamj.2020.37.286.26740

61. 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;34(7):e300-e301. doi:10.1111/jdv.16523

62. Pangburn J, Gibbs J. Two cases of COVID-19 patients with associated purpura fulminans. *J Burn Care Res.* 2023;44(2):485-486. doi:10.1093/jbcr/irac176

63. 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;83(1):280-285. doi:10.1016/j.jaad.2020.04.044

64. Sil A, Bhanja DB, Sarkar AD, Chandra A. Herpes zoster involving trigeminal nerve: an early cutaneous predictor of COVID-19-a case series and review of the literature. *J Cosmet Dermatol.* 2022;21(4):1371-1373. doi:10.1111/jocd.14679

65. Labé P, Ly A, Sin C, et al. Erythema multiforme and Kawasaki disease associated with COVID-19 infection in children. *J Eur Acad Dermatol Venereol.* 2020;34(10):e539-e541. doi:10.1111/jdv.16666

66. Andina-Martínez D, Villaizán-Perez C, Pavo-García MR, et al. Acral peeling as the sole skin manifestation of COVID-19 in children. *Pediatr Dermatol.* 2021;38(3):664-666. doi:10.1111/pde.14599

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