





ORIGINAL ARTICLE

Not all that glitters is COVID-19: a case series demonstrating the need for histopathology when skin findings accompany SARS-CoV-2 infection

A. Barrera-Godínez,¹  S. Méndez-Flores,¹ M. Gatica-Torres,¹ A. Rosales-Sotomayor,¹ 
K.I. Campos-Jiménez,¹ D.M. Carrillo-Córdova,¹ M.C. Durand-Muñoz,¹ G.L. Mena-Hernández,¹
Y.K. Melchor-Mendoza,¹ A.L. Ruelas-Villavicencio,¹  A. García-Irigoyen,²  G.A. Acatitla-Acevedo,²
S. Toussaint-Caire,³ J. Domínguez-Cherit^{1,*}

¹Department of Dermatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

²Department of Internal Medicine, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

³Department of Dermatopathology, Hospital General Manuel Gea González, Mexico City, Mexico

*Correspondence: J. Domínguez-Cherit. E-mail: dominguez.judith@gmail.com

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Abstract

Background Descriptions of cutaneous findings associated with COVID-19 have not been consistently accompanied by histopathology or confirmatory testing for SARS-CoV-2.

Objective To describe and classify the cutaneous findings with supporting histopathology of confirmed COVID-19 inpatients.

Methods We included consecutive inpatients with a confirmed diagnosis of COVID-19 for whom a dermatology consult was requested. A skin biopsy was performed in all cases. Skin findings were classified as being compatible with a cutaneous manifestation of COVID-19 or as representing a distinct clinical entity.

Results Twenty-eight patients were studied in whom thirty-one dermatologic diagnoses were made. Twenty-two of the dermatoses were compatible with a cutaneous manifestation of COVID-19; nine entities were not associated with infection by SARS-CoV-2. The most common COVID-19-associated pattern was an exanthematous presentation. In four patients, a new pattern was observed, characterized by discrete papules with varied histopathological findings including a case of neutrophilic eccrine hidradenitis. No cases of pemio-like lesions were identified. Skin findings not associated with COVID-19 represented 29% of diagnoses and included *Malassezia* folliculitis, tinea, miliaria and contact dermatitis.

Limitations There is no gold-standard test to distinguish between viral exanthems and drug reactions.

Conclusion A histopathological study is critical before attributing skin findings to a manifestation of COVID-19.

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Conflict of Interest

All of the authors declare no conflict of interest.

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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causal agent of coronavirus disease 2019 (COVID-19).¹ The first reports² by dermatologists regarding cutaneous findings accompanying COVID-19 described erythematous, urticarial and varicelliform lesions. Since then a broad spectrum of cutaneous manifestations has been described in association with COVID-19,^{3,4,5} but not all of the reported cases have had confirmatory testing for SARS-CoV-2 infection. Skin biopsies have

revealed diverse changes that mirror the clinical gamut,⁶ but they have not been performed consistently throughout reports and descriptive histopathological findings are scarce. An international registry amassed and classified more than 700 cases with cutaneous manifestations of confirmed and probable COVID-19 cases and showcased the varied clinical presentations,⁷ but a lack of diversity in representation was noted by the authors. Different classifications of the COVID-19-associated findings have been proposed.^{7,8}

Herein, we describe a series of inpatients with a confirmed diagnosis of COVID-19 who during their admission developed skin lesions, as well as the accompanying histopathological findings.

Material and methods

This is a cross-sectional study conducted from 1 April to 31 August 2020 in a tertiary care centre (Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán) in Mexico City, Mexico. Through a governmental decree, our institution was converted into a COVID-19-only hospital and during the following months focused exclusively on treating adult inpatients with SARS-CoV-2 infection. We included consecutive hospitalized patients in whom skin findings were reported by the primary team for a Dermatology consult, who had a confirmed diagnosis of COVID-19 by a positive real-time reverse-transcriptase polymerase chain reaction (RT-PCR) for SARS-CoV-2 from nasopharyngeal swab specimens as well as compatible findings in a chest computed tomography (CT). Every single patient was evaluated in person by at least one member of the Dermatology department who donned the required personal protective equipment and obtained clinical photographs. Routine skin punch biopsies were performed, fixed in formalin and evaluated with haematoxylin–eosin staining for the assessment of histopathological characteristics. An electronic medical record review was carried out for each patient to obtain relevant data, including age, sex, body mass index (BMI), comorbidities, labwork at baseline, and medical treatment received before and during the hospital stay. If the patient required admission into a critical care unit because of a need for mechanical ventilatory support, we recorded the maximum value of administered positive end-expiratory pressure (PEEP, cmH₂O).

At this moment, there is no gold standard for the diagnosis of cutaneous manifestations associated with infection by SARS-CoV-2. Therefore, skin findings were classified as being compatible with a cutaneous manifestation of COVID-19 or as representing a distinct clinical entity unrelated to viral infection according to clinical and histopathological findings.

This work was performed per the principles expressed in the Declaration of Helsinki. The study was approved (Reference 3407) by the Ethical Committee from the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, and written informed consent was obtained from patients or their responsible family member.

Due to the current size of the sample, it was not possible to perform comparative statistics. Therefore, descriptive statistics were performed, and continuous variables were dichotomized according to values of clinical significance. Continuous data are expressed as the median, (minimum and maximum), and categorical variables as a percentage.

Results

Twenty-eight patients were included in the study. The median age was 49 years, and males represented 86% of the cases. The most commonly encountered Fitzpatrick skin phototype was IV in 89% of cases (range III to V). The most frequent comorbidities were obesity (54%, with a median BMI of 30.9 for all the patients in the study) and diabetes mellitus type 2 (32%). Two cases of immunosuppression were identified as HIV infection and chronic granulocytic leukaemia. None of the patients had a history of cutaneous pathology. Consults were more frequently requested for patients within a critical care unit (71%). All of the patients evaluated received low-molecular-weight heparin (LMWH) as prophylactic or therapeutic anticoagulation during their stay. Other frequently prescribed medications, including those received before admission, included antibiotics (76%) and

Table 1 Patient characteristics (*N* = 28)

Characteristics	<i>N</i> (%)
Male sex	24 (86%)
Age (median)	49 years
Age (range)	28 to 62 years
Fitzpatrick skin phototype	
III	1 (4%)
IV	25 (89%)
V	7 (8%)
Comorbidities	
Obesity	15 (53%)
Diabetes type 2	9 (32%)
Active or prior tobacco use	8 (28%)
Hypertension	7 (25%)
Immunosuppression	2 (7%)
Critical care	
Admitted to ICU for IMV	20 (71%)
Prone position ventilation	13 (46%)
Medical treatment received before and during the hospital stay	
LMWH	25 (100%)
Antibiotics	22 (76%)
Systemic steroids	10 (35%)
Tocilizumab	2 (7%)
Abnormal laboratory work upon admission	
D-dimer > 500 mg/dL	21 (75%)
hs-CRP > 10 mg/dL	20 (71%)
Lymphocytopenia	20 (71%)
Ferritin > 500 ng/mL	19 (67%)
Fibrinogen > 500 mg/dL	16 (57%)
LDH > 500 UI/L	11 (39%)
Outcomes	
Developed skin findings associated with COVID-19	21 (75%)
Survived disease course	14 (50%)

ICU, intensive care unit; IMV, invasive mechanical ventilation; hs-CRP, high-sensitivity C-reactive protein; LDH, lactate dehydrogenase; LMWH, low-molecular-weight heparin.

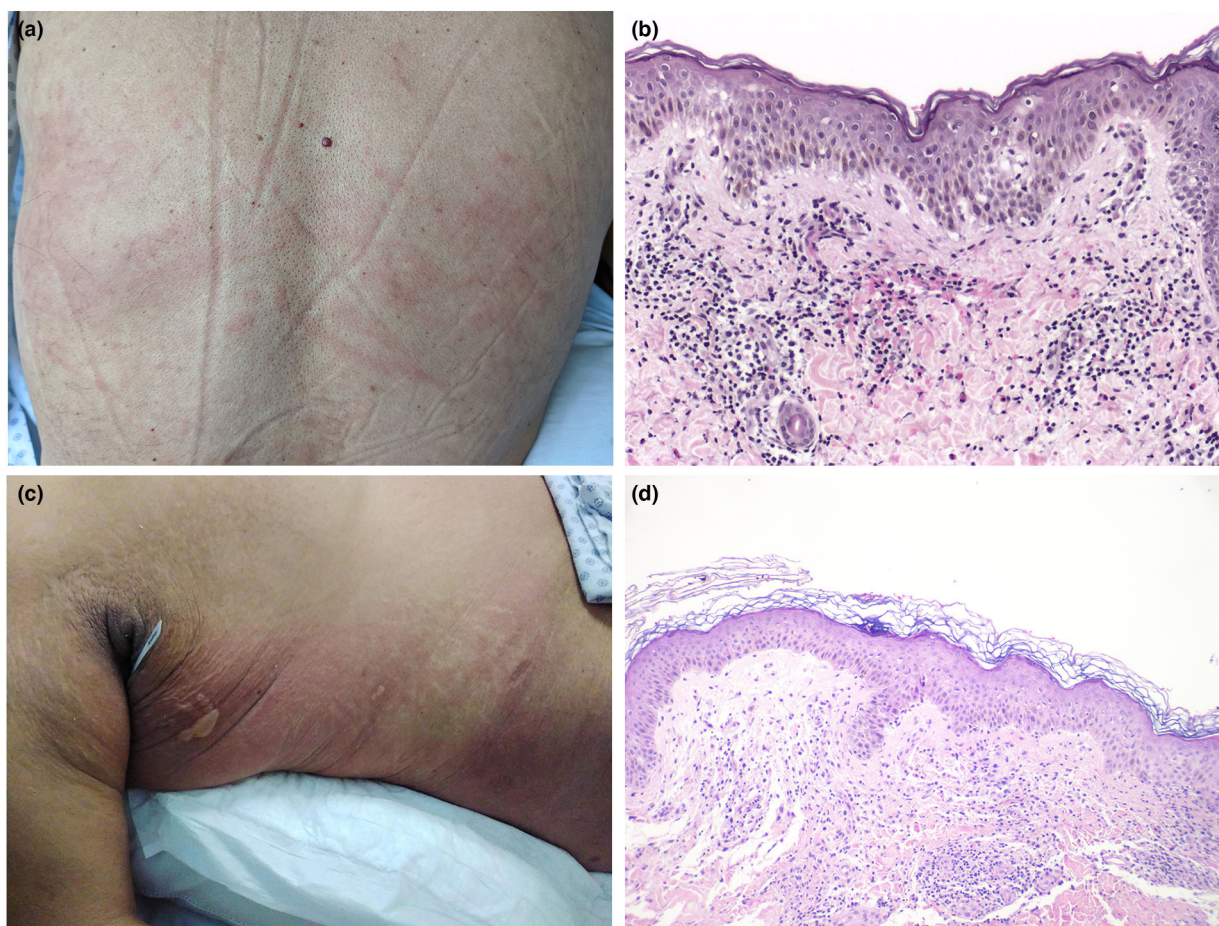


Figure 1 COVID-19-associated exanthems. Figure shows cases 12 (a,b) and 15 (c,d) with side-to-side clinical and histopathological findings. (a) An urticarial exanthema with a flagellate appearance that resolved with postinflammatory hyperpigmentation. (b) Vacuolar interface dermatitis, superficial perivascular infiltrate, lymphocytic predominance with some eosinophils and scarce neutrophils. (c) An erythematous and bullous plaque with a flexural predominance. (d) Confluent epidermal necrosis with a vacuolar interface dermatitis, with superficial and mid perivascular infiltrate with lymphocytes, eosinophils and mast cells. Endothelial oedema can be seen.

systemic steroids (35%). Common laboratory work anomalies upon initial presentation are presented in Table 1.

In these patients, thirty-one dermatologic diagnoses were made. Twenty-two of the dermatoses (71%) were deemed compatible with a cutaneous manifestation of COVID-19. The remaining nine entities (29%) were not associated with infection by SARS-CoV-2.

Of the dermatoses compatible with a manifestation of COVID-19, the most common patterns of presentations included exanthems in seventeen patients (77%), discrete papules in four cases (18%) and retiform purpura in one (5%). The most frequently encountered morphologies of the exanthems were morbilliform (56%), urticariform (25%), vesiculobullous (19%) and reticulated (13%). Two patients with exanthems presented more than one morphology. In six patients (27%), we observed a predominance of lesions in recumbent

areas, most evident on the flanks (Fig. 1). No cases of pernio-like lesions were observed. The median time to presentation was 21 days since symptom onset (range, 5 to 32 days) and 11 days from admission (range, 1 to 22 days). Figures 1 and 2 compile the clinical images of representative patients with their accompanying histopathological findings. The mean duration for the exanthematous pattern (including only those patients in whom the full duration is known) was 6 days (2 to 12 days range).

Histopathological findings are explicitly described in Table 2 for each of the COVID-19-associated dermatosis. An interface dermatitis was documented in 13 of the 17 exanthems (76%), including all of those that featured an urticarial morphology. The cells composing the inflammatory infiltrate were generally mixed but frequently showed a lymphocyte predominance, occasionally combined with neutrophils and eosinophils. Sporadically, mast cells were observed. No viral cytopathic changes, such

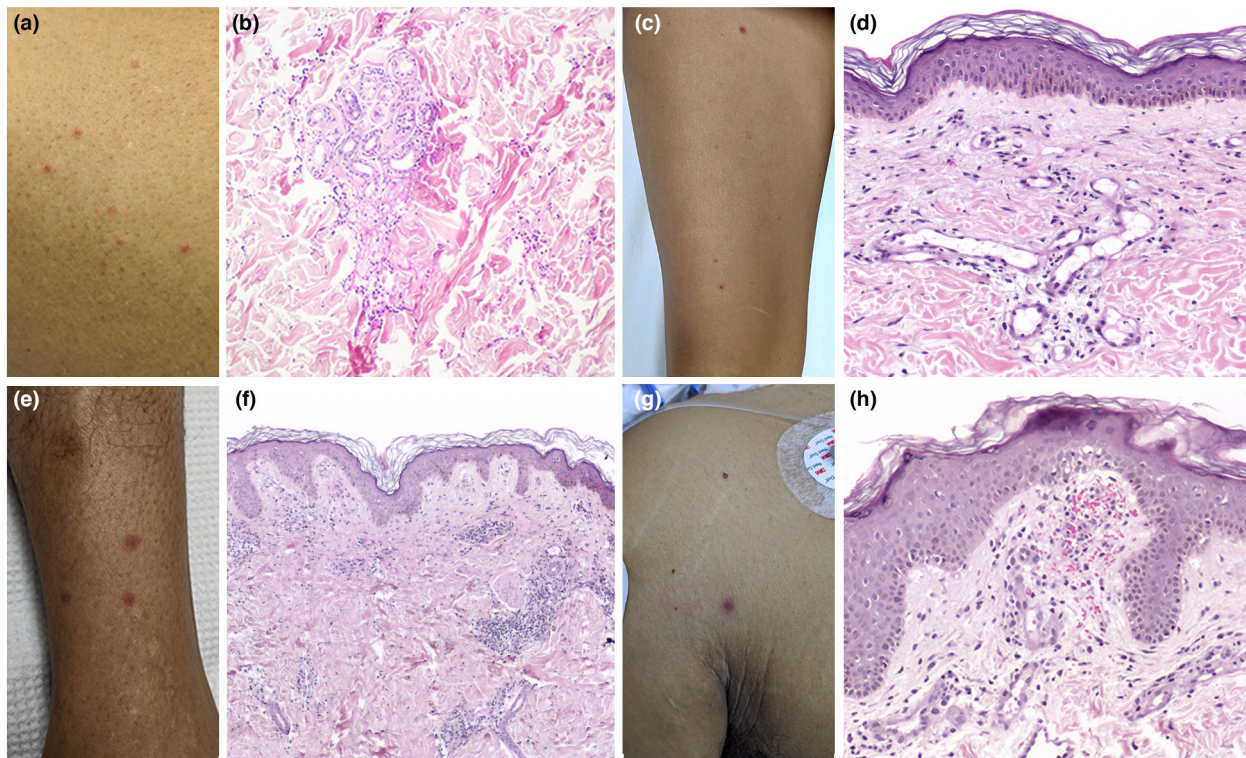


Figure 2 COVID-19-associated papular pattern. Figure shows cases 18 (a,b), 19 (c,d), 20 (e,f) and 21 (g,h) with side-to-side clinical and histopathological findings. (a) Discrete millimetric bright red papules. (b) Neutrophils dissecting collagen bundles and surrounding eccrine structures. (c) Discrete purpuric papules with surrounding pale halo. (d) There is a sparse superficial perivascular inflammatory cell infiltrate containing lymphocytes and histiocytes and vacuolar alteration. (e) Dull red papules in the lower leg. (f) A denser superficial and deep perivascular inflammatory cell infiltrate with lymphocytes. (g) Two purpuric papules near the axilla. (h) Subtle vacuolar interface dermatitis with endothelial oedema and extravasated erythrocytes.

as multinucleation or ballooning degeneration, were documented.

The final diagnoses of dermatoses not associated with COVID-19 were *Malassezia* folliculitis (4), tinea (2), miliaria crystallina (1), urticaria pigmentosa (1) and irritant contact dermatitis (1). Both cases of tinea presented in a flexural topography (axilla and gluteal sulcus), and all the *Malassezia* folliculitis lesions had a truncal distribution. The vesicles of miliaria crystallina overlaid a morbilliform exanthem presented by one of the patients. Figure 4 assembles clinical images of these cases with accompanying histopathological findings.

Discussion

This case series demonstrates the broad scope of cutaneous findings in inpatients with COVID-19. We intend to contribute to the delineation of COVID-19-associated patterns by describing dermatoses in confirmed cases with supporting histopathological characteristics in Mexican cases featuring skin of colour.

A high proportion of the cases in this series were male and more than half of the patients had a BMI compatible with

obesity. Rather than suggesting an increased risk of developing skin manifestations, this mirrors the increased severity of COVID-19 cases in male and obese patients who are more likely to require hospital admission. The observed laboratory abnormalities also replicate those commonly observed in moderate to severe cases of COVID-19.

The timing of rash onset is strikingly variable, suggesting that skin findings may present at any stage of the infection. However, approximately 55% of the skin lesions compatible with a COVID-19-associated manifestation occurred within 14 days after hospital admission.

The morphological patterns observed in the cases compatible with a COVID-19-associated cutaneous manifestation partially reinforce what has been reported by other groups. The most frequent morphologies include morbilliform and urticariform exanthems, and the only case of retiform purpura was observed in a patient who required critical care. Notable differences with other series are the complete absence of pernio-like lesions, varicelliform exanthems, petechial or pustular morphology. Although a vesiculobullous morphology was observed in four of

Table 2 Description of cases with COVID-19-associated skin manifestations

Case	Sex (Age in years)	Days (Since symptom onset/since admission)	Affected regions	Morphology	Histopathology	Duration (days)	Outcome
Exanthems							
1	M (43)	11/5	Trunk and extremities, flexural	Morbilliform/vesicular	Vacuolar interface, spongiosis, mild superficial perivascular lymphocytic infiltrate.	At least [†] 2 days	Deceased
2	M (46)	23/19	Trunk and extremities	Morbilliform	Vacuolar interface dermatitis with superficial perivascular lymphocytic infiltrate. Oedematous endothelial cells.	9	Alive
3	F (51)	14/9	Trunk and extremities	Morbilliform [‡]	Superficial mixed perivascular inflammatory cell infiltrate with eosinophils, lymphocytes and histiocytes. Subcorneal spongiotic vesicle.	11	Deceased
4	M (62)	26/12	Trunk and extremities	Morbilliform	Vacuolar interface, spongiosis, superficial perivascular infiltrate composed of lymphocytes with neutrophils and some eosinophils.	4	Alive
5	M (59)	29/21	Trunk and extremities	Morbilliform	Focal vacuolar interface dermatitis, superficial and mid perivascular and periadnexal infiltrate lymphocyte predominance, with mast cells and some neutrophils and eosinophils. Oedematous endothelial cells.	At least [†] 3	Deceased
6	F (57)	20/18	Trunk and extremities, periflexural	Morbilliform	Superficial perivascular inflammatory cell infiltrate with eosinophils, lymphocytes, some neutrophils, with red blood cell extravasation.	5	Alive
7	M (56)	25/21	Trunk and extremities, flexural	Morbilliform [‡]	Vacuolar interface dermatitis, superficial perivascular and periadnexal infiltrate, lymphocyte predominance, some eosinophils. Focal spongiosis.	At least [†] 3	Deceased
8	M (48)	32/17	Trunk and extremities	Morbilliform	Superficial perivascular and periadnexal infiltrate with lymphocyte predominance. Pigment incontinence.	2	Alive
9	M (62)	15/10	Trunk and extremities	Urticiform	Vacuolar interface dermatitis, superficial perivascular infiltrate composed of lymphocytes and neutrophils. Prominent endothelium.	At least [†] 5	Deceased
10	F (28)	22/14	Trunk and extremities	Urticiform	Vacuolar interface dermatitis with superficial perivascular infiltrate composed of lymphocytes and neutrophils.	5	Alive
11	M (40)	24/17	Trunk and extremities	Urticiform [‡]	Vacuolar interface dermatitis with necrotic keratinocytes, superficial perivascular and periadnexal infiltrate with lymphocyte predominance and scarce eosinophils.	6	Alive
12	M (58)	8/3	Trunk	Urticiform, flagellate	Vacuolar interface dermatitis, superficial perivascular infiltrate, lymphocytic predominance with some eosinophils, and scarce neutrophils. Red blood cell extravasation.	5	Alive
13	M (40)	21/13	Trunk and extremities	Bullous, erosions [‡]	Vacuolar interface dermatitis with confluent epidermal necrosis, inflammatory cell infiltrate with eosinophils and lymphocytes.	At least [†] 5	Deceased
14	M (31)	14/11	Trunk and extremities	Bullous, targetoid [‡]	Confluent epidermal necrosis with a vacuolar interface dermatitis, superficial and mid perivascular and periadnexal infiltrate mainly composed of eosinophils and lymphocytes.	At least [†] 10	Deceased
15	M (50)	24/7	Trunk	Morbilliform, bullous	Confluent epidermal necrosis with a vacuolar interface dermatitis, superficial and mid perivascular infiltrate, endothelial oedema, with lymphocytes, mast cells and eosinophils.	12	Alive
16	M (40)	11/3	Trunk	Reticulated	Focal interface dermatitis, superficial perivascular lymphocytic infiltrate, congestive blood vessels.	8	Alive

Table 2 Continued

Case	Sex (Age in years)	Days (Since symptom onset/since admission)	Affected regions	Morphology	Histopathology	Duration (days)	Outcome
17	M (52)	5/1	Trunk and extremities	Reticulated	Focal spongiosis, superficial perivascular lymphocytic infiltrate.	7	Alive
Discrete, disseminated papules							
18	M (34)	8/5	Trunk and extremities	Bright red papules	Neutrophilic eccrine hidradenitis with interstitial neutrophils.	3	Alive
19	M (50)	12/4	Extremities	Dull red papules	Superficial and deep perivascular lymphocytic infiltrate, erythrocyte extravasation, pigment incontinence.	5	Alive
20	F (50)	22/5	Extremities	Bright red papules	Vacuolar interface dermatitis with necrotic keratinocytes, superficial perivascular lymphocytic infiltrate, telangiectasias.	21	Alive
21	M (35)	13/7	Extremities	Dark red papule	Vacuolar interface dermatitis, endothelial oedema, red blood cell extravasation.	8	Alive
Retiform purpura							
22	M (46)	28/22	Trunk	Purpura, bullae	Intraluminal microthrombosis with pale dermis and absence of epidermis.	At least [†] 3	Deceased

F, female; M, male.

[†]Days of duration preceded by 'at least' implies the patient perished with the skin lesions and therefore full duration is not known.

[‡]Represents cases where an alternate diagnosis with a drug reaction was possible.

our patients, no cytopathic changes were observed in the cases. Rather, histopathological findings included prominent spongiosis and signs of interface dermatitis. A vesicular morphology was also observed in those dermatoses that were not related to COVID-19, such as miliaria crystallina and irritant contact dermatitis.

We hypothesize the lack of pernio-like lesions can be attributed to several factors. Our series does not include the patient population in whom these lesions have been typically described because of the characteristics of the inpatients. Pernio-like lesions are reported more frequently in paediatric outpatients and our report only includes adult inpatients. Likewise, pernio-like findings have been associated with a milder course of COVID-19, and we featured moderate and severe cases that required admission. Some authors have explained the development of pernio-like lesions as a parallel phenomenon to a robust antiviral response mediated by type I interferon.⁹ A competent immune response could theoretically lead to rapid SARS-CoV-2 clearance before complications developed. The lack of pernio-like lesions in our series supports the hypothesis that it is a cutaneous manifestation associated with mild COVID-19 cases. However, it should also be noted that some studies¹⁰ challenge the association between COVID-19 and chilblain-like lesions because serological and RT-PCR tests can yield negative results. Furthermore, microthrombosis has been a histopathological finding in some of the reports of skin biopsies from pernio-like lesions.¹¹ All of the patients in our series received

anticoagulation with LMWH in both prophylactic and therapeutic doses which lead us to hypothesize that anticoagulation could prevent the development of clinically evident pernio-like lesions by inhibiting thrombus formation. Conversely, chilblain-like lesions can be more common in outpatients because anticoagulation is not routinely prescribed in that setting.

An interesting finding in six of our patients was the predominance of skin lesions in recumbent regions (Fig. 3). This was more evident when patients were switched from a supine to a prone position as a manoeuvre for the management of severe acute respiratory distress syndrome (ARDS) and the full rear side was visible. In those patients who remained in the supine position, the recumbent predominance was observed in the posterior half of the flanks. We hypothesize that the associated skin findings can be due, in part, to the known haemodynamics effect of PEEP inducing a rise in intrathoracic pressure and a reduction in venous return,¹² possibly resulting in systemic venous congestion that is more prominent in recumbent regions. Slower blood flow could lead to a higher local concentration of inflammatory mediators. In this group of patients, histopathology showed a vacuolar interface dermatitis with an inflammatory cell infiltrate predominantly by lymphocytes, eosinophils and neutrophils. These microscopic findings do not suggest an exogenous factor was the cause of this manifestation.

Four of the patients with COVID-19-associated skin findings manifested a clinical pattern of disseminated discrete papules with strikingly different histopathological findings (Fig. 2). This

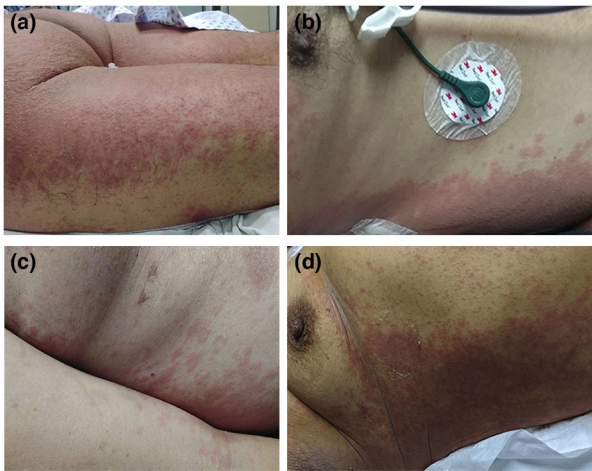


Figure 3 COVID-19-associated exanthems. Cutaneous lesion predominance in the posterior or recumbent regions, most evident on the flanks featuring cases 1 (a), 4 (b), 5 (c) and 6 (d).

pattern is distinct from previous reports of COVID-19-associated exanthems that featured a maculopapular morphology: in our cases, non-confluent papules, with no macular component, were observed. One patient developed neutrophilic eccrine hidradenitis (NEH). NEH is typically described in patients receiving antineoplastic drugs,¹³ but there are reports of biopsy-confirmed NEH in children that carried a self-limited course.¹⁴ In our case, the papules resolved without treatment during the following 3 days. We hypothesize that NEH can develop during viral infections and carry a benign course. This suggests a possible link between neutrophilic eccrine hidradenitis and COVID-19, where the highly metabolically active sweat gland epithelium could be susceptible to the hypoxia induced by the infection. Interestingly, a recent publication¹⁵ has demonstrated the presence of SARS-CoV-2 spike proteins within sweat gland epithelium accompanied by a lymphocytic infiltrate in skin autopsy samples. Two other patients presented similarly with disseminated pseudoangiomatous red papules but with histopathologic findings of a vacuolar interface and superficial perivascular dermatitis, endothelial oedema, and necrotic keratinocytes that waxed and waned during the following weeks leaving residual hyperpigmentation. We believe this also represents an atypical cutaneous manifestation of COVID-19 that initially suggested a diagnosis of eruptive pseudoangiomatosis but showed a different histological picture. A similar case was reported as eruptive angiomas in a French series but no histopathological analysis was described.¹⁶ Finally, the papules in the fourth patient were self-limited and showed a periadnexal and perivascular superficial and deep lymphocytic infiltrate with erythrocyte extravasation. The clinical presentation and biopsy findings are both non-

specific and could represent a cutaneous manifestation of COVID-19, or can also be observed in a dermal hypersensitivity reaction or arthropod bites. All of the patients that presented this papular pattern survived.

No clear association between clinical patterns and histopathological findings was observed. A vacuolar interface pattern was the most commonly observed in skin biopsies from the morbilliform, urticariform, vesiculobullous and papular clinical presentations. We underscore that all of the urticarial exanthems demonstrated an interface dermatitis which is contrary to what would be normally expected in acute urticaria. Therefore, a skin biopsy is useful in differentiating urticariform viral exanthems from acute urticaria in the setting of COVID-19. Likewise, in both cases with bullous morphology, a prominent interface dermatitis was present, but we did not observe other findings that have been described in the literature, such as herpes-like cytopathic changes. The setting in which our study took place, and focused solely on inpatients, could have impacted this: the descriptions of varicelliform exanthems that can present these findings usually begin 3 days after symptom onset.⁵ COVID-19 severity usually develops during the second week of the disease's course, which is when patients usually arrive at the emergency department. Microthrombosis is another finding that has been reported in COVID-19-associated cutaneous lesions and it was not widely observed, save for the patient with retiform purpura. This could have been potentially prevented by the widespread use of anticoagulation in our group of patients.

The histopathological study was paramount to exclude cutaneous manifestations independent of COVID-19. During the earliest phase of the pandemic, every cutaneous finding seen in patients affected by COVID-19 was considered to have a possible association with SARS-CoV-2 infection. Initially, this was in part due to a general lack of knowledge regarding the possible cutaneous manifestations, as well as a natural human tendency to find associations and attribute causation. Due to the routine use of histopathology, we can demonstrate that a morphological and/or a topographical approach is insufficient to characterize COVID-19-associated skin findings. For example, vesicles can be seen in varicelliform exanthems and miliaria, papulovesicles can be seen in viral exanthems and widespread contact dermatitis, and flexures can be affected in exanthems and tinea. In this series, an association with COVID-19 was discarded in almost one-third of the dermatoses observed because of the supporting histopathological findings.

The cutaneous findings diagnosed as a distinct clinical entity not related to COVID-19 exemplify the role that external factors play during the stay of an inpatient and are summarized in Fig. 4. Four cases of *Malassezia* folliculitis were documented in patients who had received systemic steroids as management of COVID-19 and presented with a truncal acneiform eruption. We foresee this to be a common entity in COVID-19 inpatients after robust evidence¹⁷ has been published that supports the use

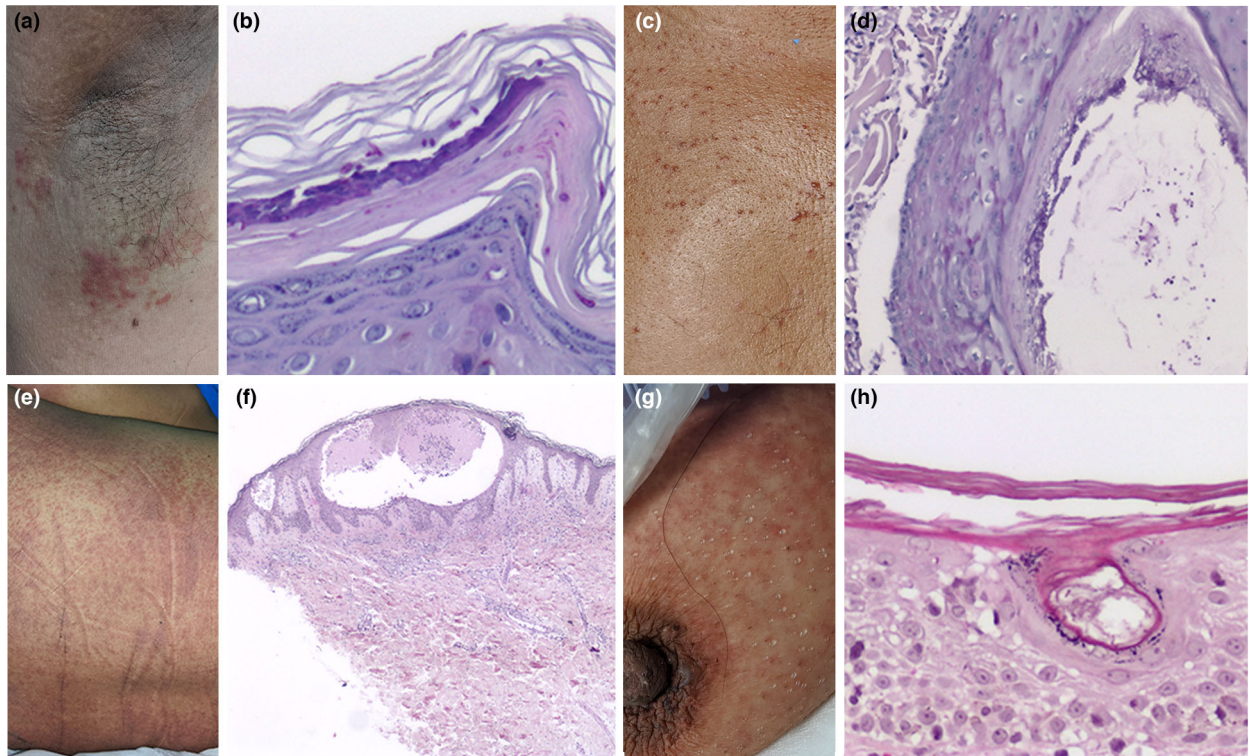


Figure 4 Cutaneous findings not associated with COVID-19. Figure shows side-to-side comparison, including tinea (a,b), *Malassezia* folliculitis (c,d), contact dermatitis (e,f) and miliaria (g,h). (a) Confluent red papules with minimal scale. (b) There are hyphae within the cornified layer. (c) Multiple follicular papules and pustules in the anterior trunk. (d) PAS stain showing numerous spores within the hair follicle. (e) Confluent papules and vesicles. (f) There is spongiosis with intraepidermal vesicles and a superficial perivascular inflammatory cell infiltrate with lymphocytes, histiocytes and eosinophils. (g) Translucent superficial vesicles overlying a morbilliform exanthem. (h) Spongiosis surrounding the acrosyringium.

of systemic corticosteroids in this population. In our series, all of the patients who developed fungal folliculitis had previously received systemic corticosteroids. Likewise, an irritant contact dermatitis that predominated in occluded regions (back and skin folds) was attributed to the use of chlorhexidine for bathing. Miliaria crystallina was observed in the anterior trunk of a woman, who had been persistently febrile, after being switched from the prone to the supine position. We believe the cases of tinea that were observed in a flexural topography could have been exacerbated by the humidity associated with fever and occlusion in these regions. Finally, we consider the case of urticaria pigmentosa to have been an incidental finding completely unrelated to COVID-19. Unfortunately, the patient expired soon after admission, and no further work-up for systemic mastocytosis was performed.

This case series highlights the need for a histopathological study before establishing an association between skin findings and COVID-19. The pandemic led dermatologists to resort to telemedicine for the evaluation of patients, therefore limiting the ease of performing skin biopsies. This series's strength

relies on presenting only confirmed cases with cutaneous lesions and accompanying histopathological findings. However, we cannot overlook that skin lesions in inpatients are frequently secondary to medical treatment (e.g. drug reactions) or a manifestation of systemic complications. We must therefore be cautious in attributing all rashes seen in patients with COVID-19 to the direct effects of SARS-CoV-2. We recognize that several of the exanthems presented can represent drug reactions, which is why we presented cutaneous findings as compatible rather than asserting a definite association. Those patients that presented this diagnostic challenge were all found in the intensive care unit, had a morbilliform morphology, had received multiple medications (piperacillin–tazobactam, meropenem, ceftriaxone and vancomycin were common culprit drugs) and developed the exanthem 4 to 8 days after starting on the medication. These cases are identified in Table 2.

We also wish to draw attention to the fact that none of the members of the Dermatology team who actively participated in this study contracted COVID-19 despite closely evaluating

patients and performing skin biopsies. We recognize that this was due to the guaranteed availability of adequate personal protective equipment in our institution, as well as strict adherence to donning and doffing protocols.

Conclusion

The spectrum of cutaneous manifestations of COVID-19 is broad and a histopathological study is critical before attributing skin findings to a manifestation of the disease. As is expected in viral diseases, exanthems with varied morphology remain the most commonly associated presentation. In our series, the complete absence of pernio-like lesions was striking and probably related to the characteristics of the population studied. New cutaneous findings not previously reported in other series included a case of neutrophilic eccrine hidradenitis, two patients with an atypical rash reminiscent of eruptive pseudoangiomatosis and four cases of *Malassezia* folliculitis that developed after the administration of systemic glucocorticoids for the management of COVID-19. Further research is needed to properly attribute skin findings to COVID-19.

Acknowledgment

The patients in this manuscript (or responsible family members) have given written informed consent to the publication of their case details.

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