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Cutaneous Manifestations of COVID-19: A Review

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Abstract

Background: COVID-19 is the infectious disease caused by a novel coronavirus which was first identified in Wuhan city, China. It is hypothesized that the virus has originated in a large animal and seafood market and then spread from person to person. Symptoms range in severity from asymptomatic/mild to severe illness and mortality with fever and cough being the most common clinical findings. Some cases of cutaneous manifestations have been reported which were mostly nonspecific. However, it is important to be aware of those manifestations to avoid missing COVID-19 cases.

Objectives: Explaining the cutaneous manifestations associated with COVID-19 and finding their possible clinical correlation.

Methods: databases including google scholar and PubMed have been searched for any case reports and researches regarding skin manifestations associated with COVID-19 with no language restrictions. One retrospective study was excluded as only 12% of the sample size were tested for SARS-COV2 (33/277).

Results: eleven published articles were found including 2 perspective studies, 1 retrospective study, 1 cross sectional, 1 case series, and 10 case reports with various skin manifestations of COVID-19 ranging from nonspecific generalized exanthem to acro-ischemia; one study demonstrated a specific varicella like lesions.

Conclusion: Being aware of what dermatological signs might be caused by COVID-19 could potentially prevent misdiagnosis. However, this is currently limited as further studies are needed to better understand how specific those changes are. Taking pictures, biopsy, and a detailed description of the diagnosed cases would definitely be of a great importance.

Keywords: COVID-19 • Skin manifestations • Exanthem • Cutaneous

Introduction

On the 31st of December 2019, pneumonia of unknown cause was detected in Wuhan, china. On the 12th of March 2020, the WHO announced COVID-19 outbreak a pandemic. To date, 6.47 million cases were diagnosed all over the world with 382.921 deaths reported. The most common presenting symptoms of COVID-19 are fever, dry cough, and tiredness. Some patients may have aches and pains, nasal congestion, anosmia, sore throat or diarrhoea. About 80% of those who get COVID-19 recover from the disease without treatment; 20% become seriously ill and develops difficulty breathing [1]. Over the past three months, several cases of associated skin manifestations were reported ranging from asymptomatic skin rash to acro-ischemia. Understanding the cutaneous manifestations of COVID-19 is crucial as they can be easily mistaken for other conditions.

Literature Review

PubMed and Google scholar were searched using the keywords “COVID-19” “SARS-COV2" and “coronavirus” in combination with cutaneous, rash, skin. Available researches, case reports, and case series that were published from January to the 7th of May and in which the included patients had a confirmatory RT-PCR were included. Data extracted including study type, region, number of patients, age & gender, type of skin manifestations, associated clinical symptoms, rash duration, and clinical outcome.

Results and Discussion

A total of 15 articles were found including 2 perspective studies, 1 retrospective study, 1 cross sectional, 1 case series, and 10 case reports. Total number of cases with cutaneous manifestations was 438 of which, 290 were confirmed cases using RT-PCR. The most common types of dermatological manifestations included: maculopapular rash 177 (40.4%), chilblains like 74 (16.8%), urticarial 76 (17.3%), vesicular rash 57 (13%), livedo/necrotic or acro-ischemia 30 (6.8%), and other lesions including dengue like, SDRIFE like and non-specific or non-described rash 24 (5.47%).

24 (5.47%) cases had the rash before any other symptom and two patients did not develop any symptoms other than chilblain like lesion. Associated cutaneous symptoms included: Itching in 224 (55.2%) patient, pain in 32 (7%), and burning in 23 (4.5%). Chilblains like lesions were noted in younger patients while patients with livedo/necrotic and maculopapular tend to be older (Table 1) [2-16].

Table 1: A summary of the characteristics of the reported case

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Author	Region	Study type	Sample size	Mean age, sex	RT-PCR	Description	Site	Associated symptoms	Temporal relationship	Biopsy	Duration	Clinical outcome
Recalcati[2]	Italy	Perspective	18 out of 88 (20%)had skin manifestations	NR	+ve	14 erythematous rash	Trunk	Mild itching	8(44%)at onset	Not done	-	Unknown
						3 urticaria			10 after hospitalization			
						1 chickenpox like						
Casas [3]	Spain	Prospective	375	222(59.2%) F	62.4% confirmed	47%maculopapulr		Itching: 210	22(5.8%) before	Not done	10.4 days	Case fatality rate 1.9%
						19%pseudochilibls		-56.80%	212(56%)same time			
						9%monovesicular		Pain: 8.5%	139(37%) after			
						Urticarial 19%		Burning: 5.8%				
						Livedo/necrotic 6%						
						Other						
Marzano[4]	Italy	Case series	22	60;	+ve	Varicella like	Trunk; limb in 4 patients	9(40.9%) ild itching	3days after systemic symptoms (-2-15)	Consistent with viral infection	8 days (4-15)	Resolution in 48%
				16 M 6 F								Death in 13.6%
Hunt[5]	Newyork.	Case report	1	20	+ve	Diffuse, morbilliform rash	Trunk and extremities	None	Along with fever	Not done	-	Admitted to ICU
				M								
A.Mahe[6]	Colmar, France.	Case report	1	64	+ve	Similar to SDRIFE	Antecubital fossa; trunk&axillary folds	None	3 days after fever	Not done	5 days	Resolution after 18 days
				F								
Wei-jie Guan[7]	China.	Crosssectional	2 out of 1099		+ve	Unknown	Unknown	Unknown	Unknow	Not done	Unknown	Unknown
			-0.18%									
Manalo[8]	Georgia	Case report	2	67M	+ve	Livedo reticularis	Lower limb	None	7days after systemic	Not done	19 h	Resolution

				47F				10 days			
										20 min	
Zhang Y[9]	Wuhan, China.	Retrospective	7	59; 4M 3F	+ve	Acro-ischemia	Finger/ toe	None	12-23 days after onset	Not done	NR	Death:5 (71%)
Beuy Joob[10]	Thailand	Case report	1	NR	+ve	Petechial rash(dengue like)	Unknown	Unknown	Before systemic symptoms	Not done	NR	NR
Kolivras A[11]	Belgium	Case report	1	23 M	+ve	chilblains like	Toes & lateral feet	Pain	3 days after fever& cough	Similar to chilblain lupus erythematosus	NR	Unknown
B. Diaz-Guimaraens[12]	Madrid, Spain	Case report	1	48 M	+ve	symmetrical pre-flexural erythematous papules and petechiae	buttocks, popliteal fossae, proximal anterior thighs, & lower abdomen	Mild pruritus	3 days after fever	RBC extravasation, dermal papillary edema, & scattered dyskeratotic keratinocytes .	5 days	Resolution
D. Henry[13]	Orléans, France	Case report	1	27 F	+ve	erythematous plaques eruption	Face, hands &feet	Pruritus	48 hours before fever	Not done	NR	Improvement
A. Alramthan[14]	Qatar	Case report	2	27 F	+ve	Chilblains like lesion	Fingers	None	Remain asymptomatic	Not done	NR	Remained a symptomatic
				35 F								
Najarian[15]	Newjersy	Case report	1	58 M	+ve	Morbilliform rash	Sparring the face, hands& feet	Pruritus	3 days after cough	Not done	2 days	Improvement
Muskaam[16]	Milan	Case report	3	71F	+ve	Maculopapular resembling Grover disease	Trunk	Pruritus	Few days after antibiotics and antiviral discontinuation	Not done	NR	Recovered
				77F		Morbilliform, maculohemorrhagic	Trunk, legs		Along with fever &cough	Not done	NR	Improvement
				72F		Papulovesicular	Trunk, hips& submammary	Pruritus	4 days after onset	Not done	10 days	Recovery

Maculopapular rash

One of the most commonly reported COVID-19 related skin manifestations was maculopapular rash. It tends to appear in older patients along with or after systemic symptoms and associated with itching in more than half of the reported cases. However, Patients with maculopapular rash were reported to have a higher rate of pneumonia (61%) and hospital admission (63%) [3]. As noted above, maculopapular rash tend to affect older patients which could explain the higher rate of pneumonia and hospital admission. 60% of patients developed this type of rash simultaneously with other systemic symptoms which might lead to misdiagnosis as a common viral infection if the physician is not aware of such a presentation. Over half

of patients (57%) reported itching and a minority reported pain or burning sensation (2.2%, and 5.08% respectively).

Chilblains like lesions

Chilblains is an inflammatory skin condition that occurs after repeated cold exposure. However, several cases were recently reported in warm weather and were linked to COVID-19. Interestingly, 98.6% of those patients did not have a history of periniosis or Raynaud's syndrome. COVID-19 related chilblains predominantly affected young patients and tend to appear later in the course of illness. However, there has been a case report of two patients who have not developed any symptoms apart from chilblains and had a confirmatory RT-PCR due to their travel history [14].

A biopsy was done in a young patient who developed a violaceous, painful plaques on the toes and lateral aspect of the feet (Figure 1), which was preceded by a 3 days history of low grade fever and a 1 day history of cough. The patient had no history of Raynaud's syndrome, periniosis or acrocyanosis. Coagulation study and D- dimer were within normal limit and COVID-19 was confirmed using RT-PCR. The biopsy showed "superficial and deep lichenoid, perivascular, and perieccrine infiltrate of lymphocytes, with occasional plasma cells. There was vacuolar alteration along the basal layer of the epidermis, with scattered singly necrotic (apoptotic) keratinocytes, which were occasionally present in the superficial layers of the epidermis (Figure 2). The basement membrane zone was smudged, and there was papillary dermal fibrin confined near the ulcer edge. There was no pallor (edema) of the papillary dermis. The infiltrate was dense and lichenoid in the papillary and superficial reticular dermis, and the deeper dermis had a tightly cuffed perivascular and perieccrine distribution (Figure 3). Some nuclear debris was present, but no neutrophils were identified. The venules surrounded by the lymphoplasmacytic infiltrate had plump endothelial cells. No intraluminal fibrin thrombi were identified, and no fibrin was identified within venule walls. Direct immunofluorescence result was negative". The author hypothesized that this presentation is due to the microangiopathic changes induced by the early IFN-I response, this early INF-I response muted viral replication which could explain the chilblains association with a milder course of illness and it's higher incidence in younger patients as older patients tend to have a rather inadequate or late INF-I response [11].

Figure 1: Violaceous infiltrated plaques that appeared abruptly on an erythematous background, With features typical of chilblains [11].

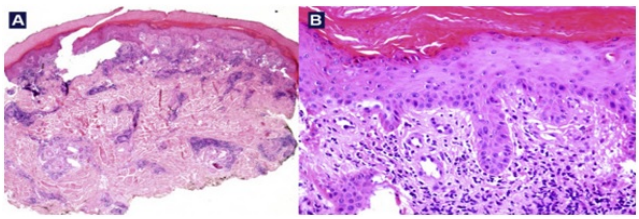

Figure 2: Coronavirus disease 2019–induced chilblains. A, Histopathologic findings simulating chilblain lupus with an absence of significant papillary dermal edema. There is a superficial and deep lymphoplasmacytic infiltrate. B, Vacuolar interface dermatitis with singly necrotic (apoptotic) keratinocytes and smudging of the basement membrane zone. Some of the necrotic keratinocytes are in the superficial layers of the epidermis. (Hematoxylin-eosin stain) [11].

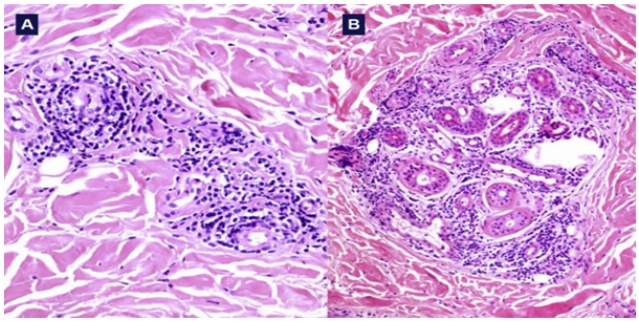

Figure 3: Coronavirus disease 2019 – induced chilblains. A, A predominantly lymphocytic infiltrate with occasional plasma cells, which is tightly cuffing vessels whose walls and lumina are devoid of fibrin deposition and thrombi. B, A perieccrine accentuation to the infiltrate. (Hematoxylin-eosin stain) [11].

Urticaria

Viral infection is a common cause of urticaria; it is not surprising for a COVID-19 infection to present as urticaria. In addition, it is probably difficult to ascertain whether it is a manifestation of the illness itself or the administered medications given the fact that they usually appear with or after systemic symptoms rather than as a presenting feature. Itching was a common associated symptom and was reported by 88.15% of the affected patients.

Varicella like lesions

In Italy, 22 patients with confirmed COVID-19 by nasopharyngeal swab developed papulovesicular rash, which mainly involved the trunk, in addition to limb involvement in 4 cases. The rash was diffuse in 6 cases, 8 patients reported itching which was generally mild, 2 patients reported pain and 2 reported burning sensation. The median duration between systemic and skin manifestations was 3 days and the median duration of this skin manifestation was 8 days. Biopsy was done in 7 patients which was consistent with viral infection [4] (Figure 4). Unlike true varicella, Lesions generally appear 3 days after systemic symptoms and disappear upon 8 days without scarring. Resolution was reported in 10 cases. Of note, death rate was reported to be 13.6%; this high death rate might be due to the fact that the observed patients' median age is 60 years.

While it is not clear whether having varicella like lesions correlates with the disease severity, it appears to be an important clinical finding especially in regions where varicella viral infection is common as the clinical picture

could be mistaken leading to delay in diagnosis.

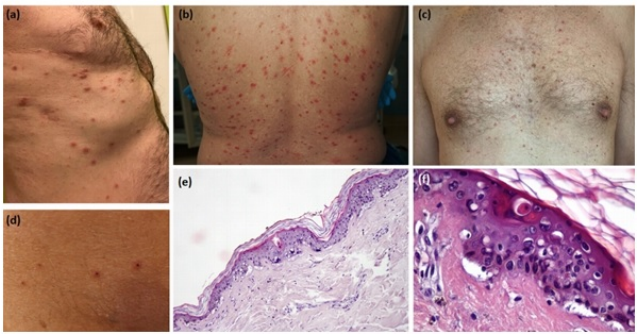

Figure 4: (a, b and c), predominance of papules is seen (d) mainly presenting with vesicles, exanthem resolution with crusts is evident; (e), Basket-wave hyperkeratosis, slightly atrophic epidermis, vacuolar degeneration of the basal layer with multinucleate, hyperchromatic keratinocytes and dyskeratotic cells. Note the absence of inflammatory infiltrate. Hematoxylin and eosin stain original magnification (f), Close-up with atrophic epidermis, vacuolar alteration with disorganized keratinocytes lacking orderly maturation, enlarged and multinucleate keratinocytes with dyskeratotic (apoptotic) cells. Hematoxylin and eosin stain, original magnification [4].

Livedo Reticularis and Acro-ischemia

Livedo/necrotic lesions were noted to affect older patient, associated with higher rate hospital admission and death [3].

It has been hypothesized that this rash could be the result of a transient, low grade DIC. This hypothesis could be further supported by the reported manifestations of 7 critical COVID-19 patients in the ICU/Wuhan who developed finger/toe cyanosis, skin bulla and dry gangrene. D- Dimer, fibrinogen and FDP were significantly high in most of them and 4 patients were diagnosed with DIC. LMWH was administered to 6 patients after which D- dimer and FDP was decreased with no change in the clinical picture [9].

Temporal relationship with systemic manifestations

Most cutaneous manifestations appeared after other systemic symptoms such as fever and cough; only 5.47% had those manifestations before developing other symptoms. Maculopapular rash was the most common type that might develop before any other symptom (30%) followed by pseudochilblain (26%). This could increase the rate of missing COVID-19 cases as maculopapular rash could be easily attributed to other common viral infections.

Correlation with the clinical outcome

There is insufficient data to give a firm conclusion whether certain skin manifestations might indicate a poor clinical outcome. However, acro-ischemia appears to be associated with a poor clinical outcome. In a retrospective study including 7 ICU admitted patients with acro-ischemia in Wuhan reported a case fatality rate of 71%; all the included patients had an elevated D-dimer, fibrinogen and FDP and 4 (75%) were diagnosed with DIC [9]. As Hypercoagulable state and DIC were linked to poor prognosis and a high death rate [17], it can be concluded that acro-ischemia is a manifestation of a severe infection. A similar outcome was noted in a prospective study in Spain which reported a hospital admission rate of 86% in patients with livedo/necrotic lesions and a case fatality rate of 10%. This is the highest death rate Compared to the clinical outcome of the rest of the patients included in the aforementioned study. Unfortunately, the coagulation status of those patients in unavailable.

Correlation with respiratory symptoms

Common symptoms of COVID-19, including fever, cough, and dyspnoea were found to be more commonly associated with a certain type of skin rash than others (Table 2). Fever was more commonly reported in patients with livedo/necrotic (86.6%) in addition to a higher rate of pneumonia (73.3%). Cough was less commonly reported by patients with chilblains (51.3%) compared to those who developed maculopapular rash (76.27%) and vesicular rash (73.6%). Overall, it appears that chilblains is more commonly associated with a milder clinical course while livedo/necrotic seems to develop in those with a more severe clinical condition as it is probably a manifestation of coagulopathy.

Table 2: Frequency of associated respiratory symptoms with a certain skin lesion type.

Lesion type	Fever	Cough	Dyspnoea	Pneumonia
Chilblains	60.80%	51.30%	24.30%	13.50%
Vesicular rash	78.90%	73.60%	33%	17.50%
Urticaria	72.30%	63.15%	39.40%	50%
Maculopapular	79.60%	76.27%	57%	62.70%
Livedo/necrotic	86.60%	70%	50%	73.33%

Associated symptoms

Itching is the most common associated symptom which was reported in 88.1% of those with Urticaria and 56.1% of those with maculopapular rash. Pain was more common in patients with chilblains and was reported by 32.4% of cases (Table 3).

Table 3: Associated cutaneous symptoms.

Lesion type	Itching	Pain	Burning
Chilblains	28.30%	32.40%	10.81%
Vesicular rash	56.10%	5.20%	3.50%
Urticaria	88.10%	1.31%	1.31%
Maculopapular rash	57%	2.25%	5.08%
Livedo/necrotic	10%	3.33%	6.66%

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Conclusion

Being aware of what dermatological signs might be caused by COVID-19 could potentially prevent misdiagnosis. However, this is currently limited as further studies are needed to better understand how specific those changes are. Taking pictures, biopsy, and a detailed description of the skin rash, clinical condition, and outcome would definitely be of a great importance. In addition, evaluating the Coagulation profile of patients with livedo/necrotic is crucial as it could be a sign of coagulopathy.

References

1. Symptoms of COVID-19. WHO, 2020.
2. Recalcati S. Cutaneous manifestations in COVID-19: A first perspective. J Euro Acad Dermatol Vener. 34;2020:e212-e213.
3. Galvan Casas C, Catala A, Carretero Hernandez G, Rodriguez-Jimenez P, Fernandez Nieto D, Rodriguez-Villa Lario A, et al. Classification of the cutaneous manifestations of COVID - 19: a rapid prospective nationwide consensus study in Spain with 375 cases. Brit J Dermatol, 2020.
4. Angelo Valerio M, Genovese G, Fabbrocini G, Pigatto P, Monfrecola G, Maria Piraccini B, et al. Varicella-like exanthem as a specific COVID-19-associated skin manifestation: multicentre case series of 22 patients. J Am Acad Dermatol. 2020;0190-9622 (20):30657-30655.
5. Hunt M, Koziatek C. A case of COVID-19 pneumonia in a young male with full body rash as a presenting symptom. Clin Prac Cases Emerg Med. 2020:4;219-221.
6. Mahé A, Birckel E, Krieger S, Merklen C, Bottlaende L. A distinctive skin rash associated with Coronavirus Disease 2019. J Euro Acad Dermatol Venereol, 2020.
7. Guan W, Ni X, Hu Y, Liang WH, Ou C, He J. Clinical characteristics of coronavirus disease 2019 in China. New Eng J Med. 2020;328:1708-1720.
8. Manalo IF, Smith MK, Cheeley J, and Jacobs R. A dermatologic manifestation of COVID-19: Transient livedo reticularis. J Am Acad Dermatol, 2020.
9. Zhang Y, Cao W, Xiao M, Li YJ, Yang Y, Zhao J, et al. Clinical and coagulation characteristics of 7 patients with critical COVID-2019 pneumonia and acro-ischemia. Chinese J Haematol. 2020; 41:302-307.
10. Beuy J, Wiwanitkit V. COVID-19 can present with a rash and be mistaken for dengue. J Am Acad Dermatol. 2020;82:e177.
11. Athanassios K, Dehavay F, Delplace D, Thompson C, Van De Borne L, Richert B, et al. Coronavirus (COVID-19) infection–induced chilblains: A case report with histopathological findings. J Ame Acad Med. 2020;6:489-492.
12. Diaz-Guimaraens B, Dominguez-Santas M, Suarez-Valle A, Pindado-Ortega C, Selda-Enriquez G, Bea-Ardebol S, et al. Petechial skin rash associated with severe acute respiratory syndrome coronavirus 2 infection. JAMA Dermatol, 2020.
13. Henry D, Ackerman M, Sancelme E, Finon A, Esteve E. Urticarial eruption in COVID-19 infection. J Euro Acad Dermatol Venereol, 2020.
14. 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.
15. James ND. Morbilliform exanthem associated with COVID-19. J Am Acad Dermatol. 2020;6:493-494.
16. Sachdeva M, Gianotti R, Shah M, Lucia B, Tosi D, Veraldi S, et al. Cutaneous manifestations of COVID-19: Report of three cases and a review of literature. J Dermatol Sci, 2020.
17. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thrombosis Haemostasis. 2020;18: 786-787.

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