

AMPATHCHAT

Dr Shaun Naicker, Anatomical Pathologist

Cutaneous manifestations of COVID-19

Introduction

SARS-CoV2, the cause of COVID-19, was identified in Wuhan, Hubei, China, in December 2019. Its unremitting worldwide spread led to the World Health Organisation (WHO) declaring a worldwide pandemic in early March 2020.

Currently, more than 23 million people have been infected worldwide with more than half a million cases reported in South Africa alone. More than 13 000 South Africans have succumbed to the virus and its related complications.

Multi-organ dysfunction, progressive respiratory failure and generalised coagulopathy are associated with high mortality (Magro et al., 2020). Cutaneous manifestations are well known to occur in the setting of a viral illness.

The sudden onset of a skin rash can raise suspicion of the possibility of COVID-19 infection, especially in patients with fever and cough who show urticarial skin lesions, chilblains, targetoid lesions (erythema multiforme-like), exanthema, maculohaemorrhagic rash or chicken pox-like lesions (Gianotti et al., 2020).

Background

- 20.4% of COVID-19 patients (18/88) in the Italian cohort developed cutaneous abnormalities.
- 1.8% (2/1 099) showed cutaneous manifestations in a Chinese cohort (Young et al., 2020).
- 8.8% of COVID-19 patients listed skin rash as a symptom (from 336 000 across the UK that participated via the COVID app) from a study conducted in King's College.
- 20% (375) of COVID-19 patients in an Italian ward had cutaneous lesions (Casas Galvan et al., 2020).
- Skin manifestations of COVID-19 are therefore significant and timely, and the accurate identification of these cutaneous manifestations will play a role in early diagnosis and management.

Classification (Elmas et al., 2020)

1. **Urticarial lesions:** A total of 19% of 375 patients (Casas Galvan et al., 2020). These are mostly distributed on the trunk or dispersed and do not appear to be related to disease severity. They may occur in the prodromal stage of infection as an initial sign of COVID-19 infection, and may be related to circulating immune complexes created by the virus inducing urticarial reactions or urticarial vasculitis.
2. **Maculopapular lesions:** These can be caused by drugs, bacterial and viral infections (eg. infectious mononucleosis, measles, hepatitis, HIV and herpes). Casas Galvan et al. (2020) reported that 47% of 375 patients with COVID-19 had a maculopapular eruption. Some showed perifollicular distribution and scaling while others were similar to pityriasis rosea or were erythema multiforme-like.
3. **Papulovesicular eruptions:** Many primary cutaneous diseases, drug eruptions, bacterial and viral infections (eg. chicken pox) may present with vesiculobullous and papulovesicular eruptions. Maizena et al. (2020) identified varicella-like eruptions in 12 of 22 patients with COVID-19. Casas Galvan et al. (2020) described small monomorphic vesicles located on the trunk in 9% of 375 patients with COVID-19. These vesicular eruptions were unlike polymorphic vesicles of chicken pox.
4. **Purpuric eruptions:** Infection-related purpuric eruptions may occur due to vascular invasion of the infectious agents or DIC caused by toxic vascular effects of the infection. These eruptions are associated with high rates of morbidity and mortality.
5. **Livedo reticularis:** This takes the form of cutaneous findings consisting of a mottled reticulated vascular pattern that appears as a lace-like purplish discoloration. It can be associated with progressive ischaemia with or without any evidence of systemic diseases. Casas Galvan et al. (2020) reported that 6% of 375 patients with COVID-19 demonstrated livedo-reticularis-like lesions. These lesions might be associated with microthrombosis (Manalo et al., 2020), and may be unilateral.

6. **Thrombotic Ischaemic lesions:** These lesions may occur due to direct vascular invasion of the infectious agent, vascular occlusion or DIC. Casas Galvan et al. (2020) identified pseudo chilblain-like lesions (asymmetrical erythema and oedema with vesicles or pustules) in 19% of 375 patients with COVID-19. Mazotta et al. (2020) reported erythematous purple-coloured macular lesions on the toes of a 13-year-old boy with COVID-19 ("COVID toes"). These lesions may be caused by acro-ischaemia due to endothelial damage and microthrombi induced by the virus.
7. **Vasculitis:** Leukocytoclastic vasculitis is an inflammation of the small blood vessels in the skin. They appear as red spots on the feet, ankles and lower legs and may spread up to the thighs and trunk. They may be caused by a viral infection like COVID-19 or medication.

Drug reactions

It can be challenging to determine when the cause of cutaneous eruptions are medication-induced as opposed to truly being COVID-19 manifestations. Several of the drugs used to treat patients with COVID-19 are also known to cause cutaneous eruptions (Young et al, 2020).

Medication

1. **Chloroquine, hydroxychloroquine:** Urticaria, pruritus, acute generalised exanthematous pustulosis (AGEP), Stevens-Johnson-like syndrome (SJS), psoriasiform dermatitis, mucocutaneous dyspigmentation, alopecia, dry skin and bleaching of hair.
2. **Azithromycin:** Morbilliform drug eruption, angioedema, burning in eyes, generalised red or purple skin rashes, cutaneous leukocytoclastic vasculitis, Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), AGEP and SJS.
3. **Remdesivir:** Skin rashes, maculopapular rash, subcutaneous abscess, thrombophlebitis at location of drug infusion.
4. **Tocilizumab:** Papulopustular eruptions, psoriasiform dermatitis, pruritus, SJS.
5. **Lopinavir/Ritonavir and other antiretrovirals:** Maculopapular drug eruptions, exfoliative erythroderma, SJS or toxic epidermal necrolysis, injection site reactions, lichenoid drug eruption.
6. **Vaccines:** Urticaria, scleroderma, maculopapular rashes, injection site reactions.

Type of skin lesion	Time of appearance	Location	Associations
Urticarial * 19%	Early within a few days of or before symptoms.	Itchy lesions on trunk or limbs.	2% mortality. Can be presenting sign of COVID-19.
Maculopapular * 47%	Early within a few days of symptoms.	Itchy lesions on trunk or limbs, may be erythema multiforme-like.	Associated with more severe COVID-19 disease.
Papulovesicular * 9%	Early to mid infection.	Diffuse varicella-like or vesiculopapular eruptions. Small monomorphic vesicles located on the trunk. Itchy.	Duration of rash is approximately 10 days. Associated with intermediate severity.
Purpuric eruptions	Usually late in the infection.	Reddish brown skin lesions, especially on the limbs.	Associated with high rates of morbidity and mortality.
Livedo reticularis * 6%	Occurs late in evolution of the disease.	Lace-like purplish discolouration of trunk or limbs.	10% mortality. Associated with more severe disease. Associated with vascular damage and coagulopathy (thrombotic vasculopathy).
Thrombotic ischaemic lesions * 19%	Occurs late in evolution of the disease.	Acral areas of erythema-oedema with some vesicles or pustules (pseudo-chilblain) or perniosis-like. Affects hands and feet (COVID fingers and toes). Usually asymmetrical lesions, may be itchy and painful.	Associated with less severe disease. Usually affects younger cohort of patients. May last for approximately 12 days.

* Approximate figures (Casas Galvan et al., 2020)

References are available on request

COVID-19 CUTANEOUS MANIFESTATIONS

1. URTICARIA (HIVES)



Source: Gianotti et al., 2020

2. PAPULOVESICULAR CHICKEN-POX LIKE

Perifollicular and chicken pox appearance of crusted papular and vesicular lesions



Source: Gianotti et al., 2020

3. MACULOPAPULAR SKIN LESIONS



Papulomacular lesions coalescing into small plaques

erythema multiforme-like

Source: Gianotti et al., 2020

4. LIVEDOID SKIN LESIONS



Source: Gianotti et al., 2020

COVID-19 CUTANEOUS MANIFESTATIONS

5. THROMBOTIC ISCHAEMIC LESIONS "COVID TOES AND FINGERS"

Acral areas of erythema and oedema (pseudo-chilblain/ pernio-like)

Source: Gianotti et al., 2020



6. HAND SANITISER ASSOCIATED IRRITANT CONTACT DERMATITIS

Xerosis, erythema, lichenification, hyperkeratosis and chapping

Source: Thedoctorschannel.com
Pope, V., Ousley, L.
Consultant.
Published online: 30 April 2020

