

Vascular skin symptoms in COVID-19: a French observational study

Coronavirus 19 (COVID-19) was declared as a pandemic viral infection by the World Health Organization on 11 March 2020. Usual clinical manifestations of COVID-19 infection include fever, fatigue, myalgia, headache, diarrhoea, dry cough and dyspnoea that may lead to acute respiratory distress syndrome and death.¹ Skin symptoms of COVID-19 have been poorly described but may include erythematous rash, urticaria and chicken pox-like lesions.²⁻⁷ Angiotensin-converting enzyme 2 (ACE2) is a cellular receptor for COVID-19. This peculiar mode of entry of COVID-19 in human cells induces angiotensin II accumulation. Excess angiotensin II may contribute to acute lung injury and vessel dysfunction such as vasoconstriction, vascular permeability and abnormal myocardial remodelling.⁸ Vascular skin lesions

during COVID-19 infection have never been described to date. We performed a retrospective observational nationwide study of skin lesions encountered during COVID-19 epidemic in France from 18 March 2020 to 6 April 2020 in an ambulatory setting of French dermatologists (national union of French dermatologists and venereologists, *SNDV*) and in 2 hospitals (Saint Louis hospital, Paris, and René Dubos hospital, Pontoise, France). All 14 patients reported had formerly proved COVID-19 infection using PCR on samples collected using nasopharyngeal swabs. Skin symptoms started a few days after first COVID-19 general symptoms unless specified in the Figure legend. All patients gave their informed consent for publication of their clinical pictures. Inflammatory lesions were reported in 7 patients: exanthema ($n = 4$), chicken pox-like vesicles ($n = 2$) and cold urticaria ($n = 1$) as already reported.²⁻⁷ Vascular lesions were reported in 7 patients: violaceous macules with 'porcelain-like' appearance ($n = 1$, Fig. 1A), livedo ($n = 1$, Fig. 1B), non-necrotic purpura ($n = 1$, Fig. 1A), livedo ($n = 1$, Fig. 1B), non-necrotic purpura ($n = 1$, Fig. 1C), necrotic purpura ($n = 1$, Fig. 1D), chilblain



Figure 1 Clinical features of COVID-19 + patients with skin vascular symptoms a: violaceous macules with porcelain appearance in a patient in intensive care unit for respiratory distress. b: livedo of the trunk with chest pain and cough. c: violaceous macule and Raynaud's phenomenon 10 days after fever and cough. d: necrotic purpura in a patient treated with leflunomide and systemic steroids for rheumatoid arthritis. e: chilblain appearance and Raynaud's phenomenon in a patient with anosmia, fever and cough. f: chilblains in a patient with cough. g: eruptive cherry angioma 21 days after COVID-19 healing of clinical symptoms.

appearance with Raynaud's phenomenon ($n = 1$, Fig. 1E), chilblain ($n = 1$, Fig. 1F) and eruptive cherry angioma ($n = 1$, Fig. 1G). Forty other patients with chilblain lesions were reported by the SNDV, but their PCR for COVID-19 detection was either negative ($n = 6$) or not performed ($n = 34$). The pathophysiology of these lesions is unclear but may include immune dysregulation, vasculitis, vessel thrombosis or neoangiogenesis. Infected COVID-19 patients with severe respiratory distress have an increased risk of pulmonary embolism⁹ suggesting a hypercoagulable state of these patients. Seven patients with acro-ischæmia (toe cyanosis, skin bulla and gangrene) and frequent disseminated intravascular coagulation (4 patients) have been reported during COVID-19 epidemic in Wuhan (China).¹⁰ A well-described case of antiphospholipid syndrome has been recently published.¹¹ Chilblain- 'like lesions' in our study had clinical similarities with digital changes observed in type 1 interferonopathies such as Aicardi-Goutières syndrome and STING-associated vasculopathy with onset in infancy that includes skin and pulmonary manifestations. Importantly, French dermatologists belonging to the SNDV reported numerous chilblain lesions in persons in close contact with COVID-19 + patients without COVID-19 PCR confirmation and without general symptoms of COVID-19 infections which raises 3 hypotheses: these chilblain lesions may: i/ be due to another confounding factor than COVID-19, ii/ be due to a postviral immunological reaction in asymptomatic forms of COVID-19 and iii/ represent a skin presentation of COVID-19 infection in a subgroup of patients with peculiar immune anti-viral response. As isolated sudden onset anosmia was recently described as a symptom highly suggesting COVID-19 infection,¹² eruptive chilblain lesions during spring and containment may be a new symptom revealing a pauci-symptomatic COVID-19 infection. The inclusion of our patients was declarative which did not allow us to analyse the frequency of vascular skin lesions in COVID-19-affected patients. Nonetheless, clinicians should be aware of these skin symptoms to optimize COVID-19 detection and quarantine procedures. Prospective study with skin biopsies, serological and PCR analysis of COVID-19-suspected patients with vascular skin symptoms are warranted in order to understand the pathophysiology and the prognosis of such vascular skin lesions.

Conflict of interest

No conflict of interest.

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