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Exacerbation of livedoid vasculopathy after coronavirus disease 2019

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 typically presents with fever, fatigue, myalgia, headache, diarrhoea, cough and dyspnoea [1], and was declared a pandemic by the World Health Organization on 11th March, 2020. Cutaneous manifestation of COVID-19 was first described as a "rash" and was observed in 0.2% of 1,099 hospitalized patients in China [2]. The reason why there were so few reports of cutaneous symptoms may be because cutaneous lesions were not generally included in the COVID-19 clinical spectrum. Recalcati was the first to analyse cutaneous manifestations that were identified in about 20% of COVID-19 patients [3]. Despite the increasing incidence of cutaneous manifestations of SARS-CoV-2 infection, effects of COVID-19 on patients with underlying cutaneous diseases are rarely reported. Here, we describe the exacerbation of livedoid vasculopathy (LV) by SARS-CoV-2 infection.

A 68-year-old man visited our clinic due to worsening lower leg pain after three days of asymptomatic SARS-CoV-2 infection. In 2009, he was diagnosed with LV after physical examination and histopathological analysis (*figure 1A, B*). He had been taking clopidogrel bisulphate for 10 years with no associated adverse effects.

Physical examination revealed bilateral brownish erythematous livedoid skin changes on the lower limbs and painful palpable erythema with crusting on the ankles. One month after the COVID-19 outbreak, he experienced skin ulceration. Treatment with rest and topical treatment improved the ulcer after three months (*figure 1C*).

The cutaneous manifestations of COVID-19 are classified into six main clinical patterns: (1) urticarial rash; (2) confluent erythematous/maculopapular/morbilliform rash; (3) papulovesicular exanthem; (4) chilblain-like acral pattern; (5) livedo reticularis/racemosa-like pattern; and (6) purpuric "vasculitic" pattern [4]. Although the exact pathophysiology of these symptoms is unknown, hyperactive immune response, complement activation, microvascular injury, vasculitis, vascular thrombosis and neoangiogenesis are implicated [4]. Pulmonary and cutaneous thrombotic microvascular damage with deposition of complement protein and SARS-CoV-2 spike glycoprotein were reported in five patients with COVID-19 and severe respiratory failure [5]. The complement component of SARS-CoV-2-specific spike glycoprotein was present in both the lungs and skin. COVID-19 may induce thrombotic microvascular injury syndrome via activation of alternative and lectin complement pathways [5], thereby resulting in cutaneous manifestations such as LV. Furthermore, high levels of von Willebrand factor (vWF) are common in COVID-19 patients, possibly due to endothelial damage. An explanation for this could be that SARS-CoV-2 enters cells via the transmembrane protein angiotensin-converting enzyme (ACE) 2 [6]. ACE2 is expressed on the surface of alveolar epithelial cells, as well as arterial and venous endothelial cells [7]. The entry of the virus could contribute to inflammation and damage of endothelial cells causing release of prothrombotic mediators, primarily vWF from Weibel–Palade storage bodies, and exposing underlying collagen to which vWF binds [6].

LV is a condition of thrombotic vasculopathy, which manifests as recurrent reticulated purpura of the legs associated with erythematous or purpuric papules. The reticulated purpura develops into small ulcers and eventually heals to form atrophie blanche [8]. Histopathologically, LV is thrombosis in the blood vessels of the dermal vascular endothelium [9, 10]. Inactivation of antithrombotic function in the dermal vascular endothelium is the most likely aetiology of LV. As previously described, livedo reticularis is a cutaneous manifestation of COVID-19. We speculate that the eruption was exacerbated by SARS-CoV-2 infection due to the overlap in aetiology.

We describe the first case of LV exacerbated by SARS-CoV-2 infection. COVID-19 can induce peripheral vasoconstriction in patients with LV, resulting in vaso-occlusive lesions and skin ulcers. This study highlights the importance of considering the possibility of LV exacerbation in patients with COVID-19, even in asymptomatic cases. ■

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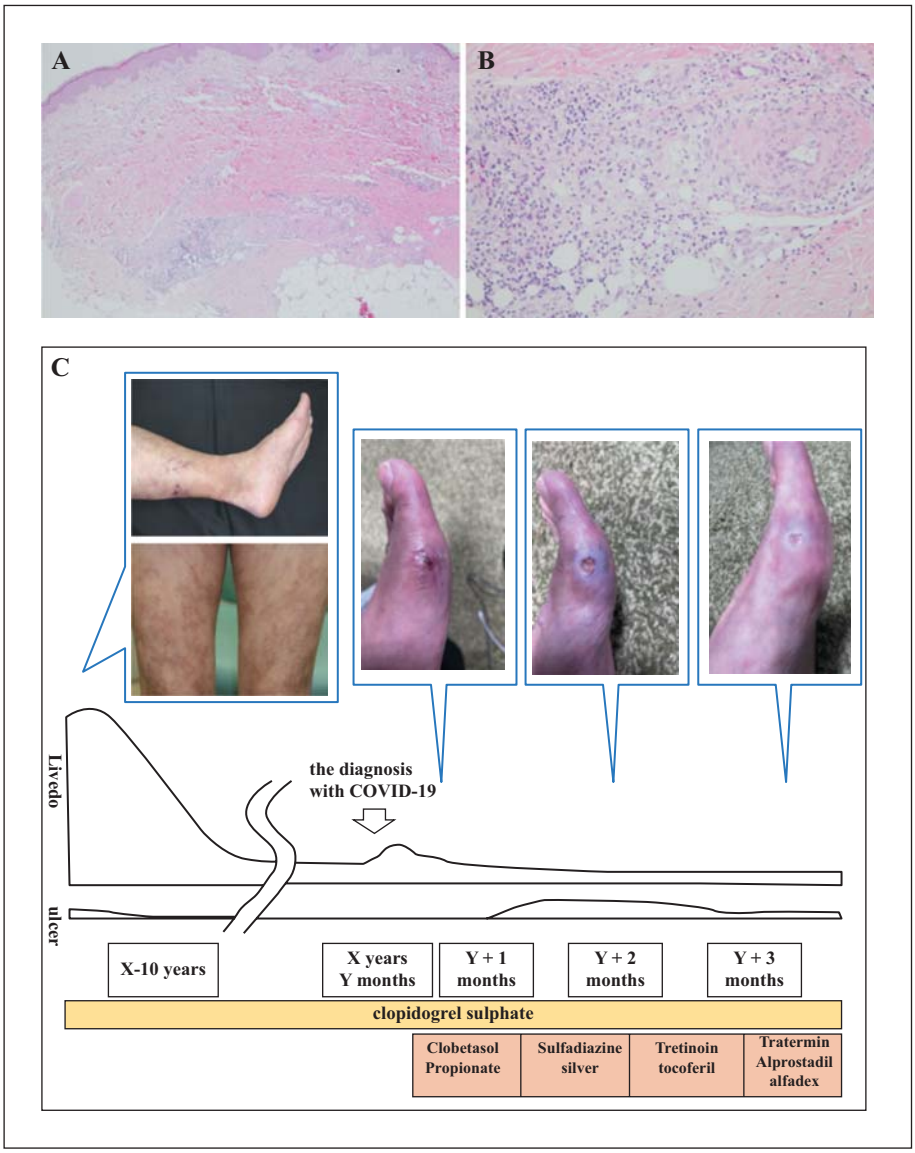

Figure 1. **A**, **B**) Histopathological examination of the skin biopsy specimen shows thickening of the blood vessel near the adipose tissue in the deep dermis with mild fibrinoid degeneration (haematoxylin and eosin; (**A**)×40 and (**B**)×200). **C**) Clinical course of the patient. He initially presented with bilateral brownish erythematous livedoid skin changes on the lower legs and painful palpable erythema with crusting on the ankles. One month after the diagnosis of COVID-19, a palpable nodule around the left toe with crusting was observed. Two months later, an ulcer formed after the removal of the crust. Three months later, the ulcer improved after treatment with topical steroid.

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Scarring after chemical tattoo removal: a retrospective study

The prevalence of tattoos has greatly increased. In Europe, 15% to 25% of the 25-34-year-aged population has tattoos [1]. A recent study showed that 14.4% of participants regret a current tattoo [2]. Thus, the tattoo removal market is constantly flourishing. Laser removal by a Q-switched laser is the gold standard [3].

Chemical tattoo removal is an old procedure, reported in 1888. The process involves performing punctuations through the tattooed skin prior to application of a corrosive solution. A scab subsequently forms containing the dissolved pigments, which then falls off, taking away the colour. Many commercial products based on this concept have been and are widely available through the internet. Most use lactic acid as an active compound (Tattoo2away®, Dermapen®, Kataderm®, Skinial®). However, manufacturers do not provide the exact composition. These products are injected into the dermis using microneedles (Tattoo2away®, Dermapen®, and Rejuvi®) or applied on the skin after scratching the skin surface with a micropigmentation device (Skinial®). Chemical tattoo removal is popular because it is readily available in tattoo shops or aesthetic centres and deemed to be faster, cheaper and safer than lasers. However, the side effects are rarely reported.

We performed a retrospective study from 2019 to 2020. A standardized case report form was sent to the members of the French Society of Lasers in Dermatology. All participants had strong expertise in the management of tattoos by lasers. The inclusion criterion was a history of scarring, defined as permanent abnormal skin texture and/or colour, following chemical tattoo removal. The results are summarized in *supplementary table 1*.

All patients were women. The average age was 35 years. Tattoo removal was often performed in aesthetic centres (*n*=9), almost exclusively with products containing lactic acid (*n*=13) including Skinial® (*n*=7), Dermapen® (*n*=1) and an unspecified brand (*n*=5). Hypertrophic scars were the most frequent (n=7; 50%) (*figure 1A*), followed by atrophic

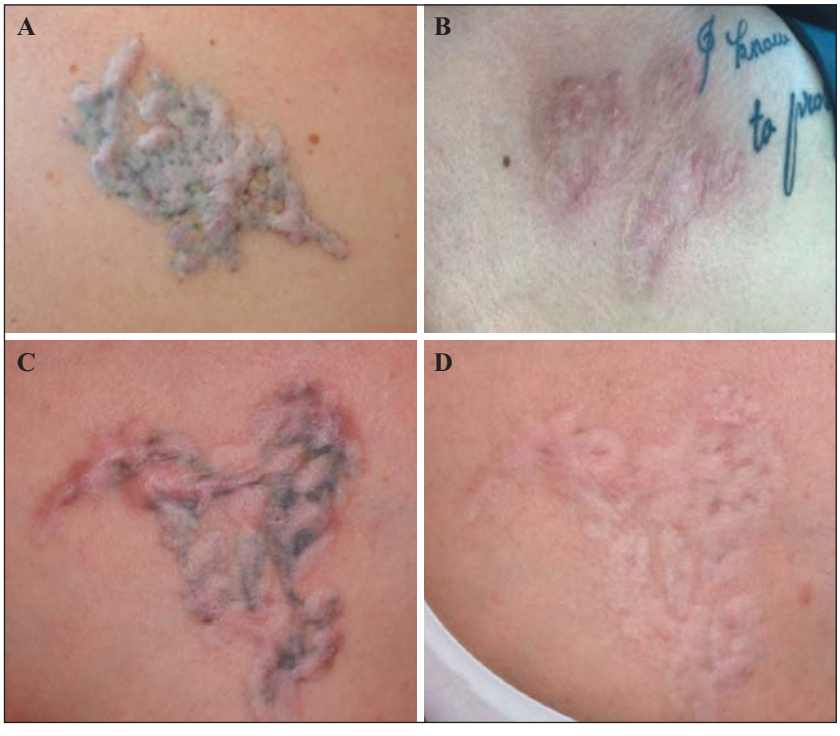

Figure 1. Scarring induced by chemical tattoo removal. **A**) Hypertrophic scar. **B**) Atrophic scar. **C**) Hypertrophic scar with remnants of pigment, before laser treatment. **D**) Same scar as in (**C**) after two sessions of fractional ablative laser and Q-switched 1064-nm laser.