velocity7 excimer laser delivers coherent, monochromatic short-pulse radiation through a hand-held device with a 20 × 20 mm circular spot size. It can emit a high-intensity laser beam (83,000 W/cm^2) by pulsed oscillation. This enables the delivery of higher fluence to deep skin lesions, resulting in the induction of apoptosis of tumour cells [9]. Furthermore, exposure of healthy skin to UV radiation may be avoided by targeted phototherapy using excimer laser [9]. In addition, we hypothesized that combination therapy with bexarotene and excimer laser treatment might have a synergistic effect, as combination therapy with bexarotene and PUVA tended to be more effective for classic MF at an early stage and led to a complete clinical response with fewer PUVA sessions using a lower PUVA dose compared to PUVA monotherapy [10]. Given the above, this combination therapy may be a useful therapeutic option for folliculotropic MF, although further research will be required to clarify the effectiveness of this therapy. ■

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COVID-19-associated livedo and purpura: clinical and histopathological findings

Cutaneous manifestations of coronavirus disease 2019 (COVID-19) have been classified as acral areas of erythema with vesicles or pustules (pseudo-chilblain), other vesicular eruptions, urticarial lesions, maculopapular eruptions, and livedo or necrosis [1, 2]. As there have been few reports of COVID-19-related cutaneous manifestations in Japan, it remains unclear whether this classification applies to Japanese patients. We report a case of cutaneous manifestations of severe COVID-19 infection in a Japanese patient, a 60-year-old woman with no significant medical history. She arrived at the referring hospital with a 10-day history of fever, cough, olfactory disturbance, and respiratory distress. A nasopharyngeal swab test for SARS-CoV-2 RNA amplification was positive. She was referred to our hospital, and remdesivir (Day 1: 200 mg/day; Days 2-5: 100 mg/day), ceftriaxone (2 g/day), and methylprednisolone (60 mg/day) were administered. Additionally, continuous hemodiafiltration and endotoxin adsorption therapy were performed. However, her condition worsened, and extracorporeal membrane oxygenation was initiated on the nineth day post-admission. On the eleventh day, livedo racemosa on both knees and elbows and purpura on the fingertips were observed (*figure 1A, B*).

Knee skin biopsy revealed pauci-inflammatory vascular thrombosis with endothelial injury in the superficial dermis, and necrosis of keratinocytes and sweat gland cells (*figure 1C-H*). Finger skin biopsy revealed dilated blood vessels in the superficial dermis, and congested blood vessels with proliferation of vascular endothelial cells in the deeper dermis (*figure 1I-M*). Immunostaining revealed positive staining for C3d (Bioss Antibodies, BJS, CN), SARS-CoV-2 envelope and spike protein (Gene Tex Inc., CA, USA), as well as type I interferon-inducible myxovirus resistance protein A (MXA; Santa Cruz Biotechnology, CA, USA) on vascular endothelial cells (*figure 1N-Q*).

Laboratory tests revealed abnormalities in coagulation/fibrinolysis: 95,000 platelets/μL (normal: 158,000-348,000 platelets/μL), 22.3 μg/mL fibrinogen/fibrin degradation products (normal: ≤ 5.0 μg/mL), and 11.8 μg/mL D-dimer (normal: ≤ 1.0 μg/mL). In addition, monoclonal IgM and cryoglobulin were not detected. The eruptions gradually improved, disappearing on the 29th day post-admission.

COVID-19-related skin manifestations with livedo/necrosis have been reported as relatively rare (6%), occurring transiently, in elderly patients and severe cases [1, 3].

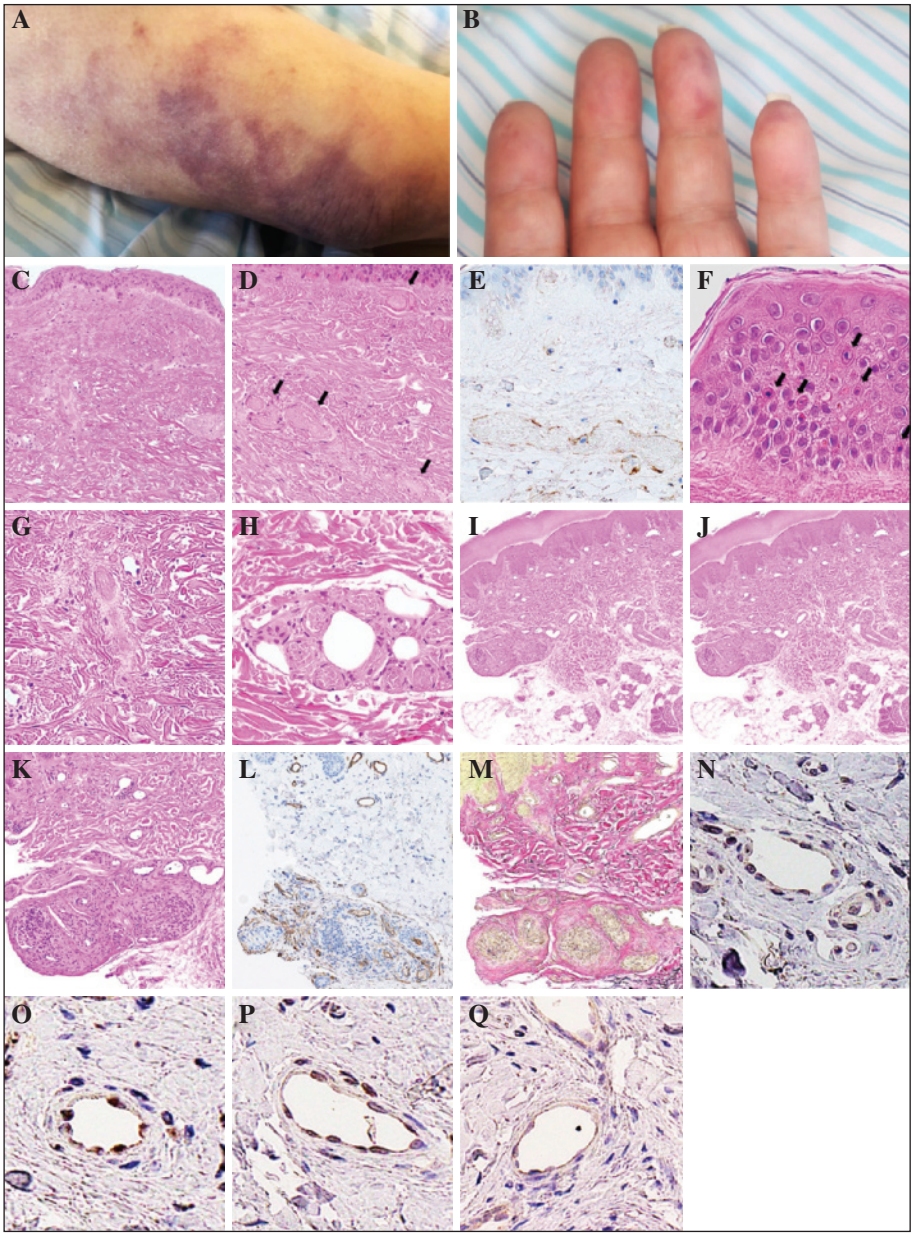

Figure 1. **A**) Clinical features of livedo on the right knee. **B**) Clinical features of purpura on the fingertips of the left hand. **C**) Biopsy specimen taken from livedo on the right knee (H&E; x40). **D**) Pauci-inflammatory vascular thrombosis with endothelial injury (black arrow) in the superficial dermis (H&E; x100). **E**) Vascular endothelial cells in the superficial dermis, immunoreactive to CD34 (x100). (**F**) Necrosis of keratinocytes (black arrow) (H&E; x400). **G**, **H**) Necrotic changes in sweat gland cells (H&E; x400). **I**) Biopsy specimen taken from purpura on the finger (H&E; x40). **J**) Dilated blood vessels in the superficial dermis (H&E; x100). **K**) Proliferation of vascular endothelial cells in deeper dermis (H&E; x100). **L**) Vascular endothelial cells immunoreactive to CD34 (x100). **M**) Blood vessels have no elastic membrane based on Elastica-van Gieson staining (x100). **N**) C3d deposition on vascular endothelial cells in the superficial dermis (x400). **O**) MXA, an established marker of type I interferon signalling, is observed on blood vessels in the dermis (x400). **P**) SARS-CoV-2 envelope protein and **Q**) spike protein on blood vessels in the dermis (x400).

COVID-19 has been hypothesized to cause skin manifestations, predisposing patients to thrombotic disease affecting both venous and arterial circulation, due to excessive inflammation, platelet activation, endothelial dysfunction, and stasis [4]. Purpuric skin lesions have also shown pauci-inflammatory thrombogenic vasculopathy, with C4d and C5b-9 deposition. Additionally, co-localization of COVID-19 spike glycoproteins with C4d and C5b-9 in the cutaneous microvasculature has been reported [5]. Viral particles in cutaneous blood vessels could lead to lymphocytic vasculitis such as that observed in thrombophilic arteritis, induced by blood immune complexes activating cytokines, resulting in catastrophic microvascular lesions [6]. In accordance with this, complement deposition and

SARS-CoV-2 protein on vascular endothelial cells were observed (*figure 1N, P, Q*). The immune response to infection can lead to activation of Langerhans cells, resulting in vasodilation [6], consistent with finger purpura. We speculate that COVID-19-associated abnormal coagulation causes livedo, and that accumulation of microthrombus at these sites impairs skin circulation, resulting in necrosis of keratinocytes and sweat gland cells.

Our case showed positivity for C3d, SARS-CoV-2 envelope and spike protein, and MXA protein (*figure 1O*), and this is consistent with both COVID-19-induced thrombogenic vasculopathy and COVID-19-induced increased type I interferon (IFN) response [7]. Recently, biopsies from livedo/retiform purpura in severe COVID-19 patients were shown to exhibit pauci-inflammatory vascular thrombosis without any MXA, and blood vessels exhibited extensive complement deposition with SARS-CoV-2 protein [8]. Furthermore, it has reported that at least 3.5% of patients with life-threatening COVID-19 pneumonia had genetic defects at eight of the 13 candidate loci involved in Toll-like receptor 3- and interferon regulatory factor 7-dependent induction and amplification of type I IFNs [8]. Thus, cutaneous disease in patients with severe COVID-19 may be linked to a decreased type I IFN response. However, there are some studies reporting a high type I IFN response in severe COVID-19 [9, 10]. Therefore, it remains to be determined whether MXA expression correlates with disease severity.

Although the patient's general condition did not improve, the livedo and finger purpura finally disappeared after three weeks; cutaneous manifestations, therefore, did not correlate with COVID-19 disease activity. Such a correlation remains to be determined, and a large number of Japanese cases would be required to investigate this further. ■

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Linear porokeratosis with severe itch accompanied by lesional upregulation of interleukin 31, thymic stromal lymphopoietin, and periostin

Porokeratoses are heterogeneous keratotic disorders encompassing at least six subtypes: porokeratosis of Mibelli; punctate porokeratosis; porokeratosis palmaris et plantaris disseminata; disseminated superficial porokeratosis (DSP); disseminated superficial actinic porokeratosis; and linear porokeratosis (LP). Itch is a rare symptom in porokeratosis, but sometimes occurs in DSP once inflammation develops against DSP lesions; this condition is termed "eruptive pruritic papular porokeratosis" [1]. In addition, patients with hypertrophic lesions occasionally complain of itch [2]. We report a case of LP with hypertrophic lesions and severe itch that was accompanied by local upregulation of thymic stromal lymphopoietin (TSLP), periostin, and interleukin (IL)-31.

A 32-year-old Japanese man presented with a history of pruritic keratotic lesions on the left posterior upper limb since childhood. His medical history included well-controlled atopic dermatitis, but no contributory familial history was elicited. Physical examination revealed well-demarcated, irregularly shaped, hyperkeratotic white-reddish plaques with a raised peripheral ridge and slightly atrophic centre. These lesions were arranged along Blaschko's lines (*figure 1A, B*). Numerical Rating Scale (NRS) score for itch was 9 out of 10. Histological examination showed psoriasiform epidermal hyperplasia accompanied by vertical columns of tightly packed parakeratotic cells within a keratin-filled epidermal invagination, known as "cornoid lamella" (*figure 1C*). Perivascular lymphocytic infiltration in the upper dermis was also apparent, but neither eosinophils nor lichenoid tissue reaction was noted. LP was diagnosed. Administration of oral antihistamines, topical corticosteroid, and 10% salicylic acid for one month did not improve symptoms. Conversely, topical maxacalcitol, a vitamin D3 analogue (VDA), dramatically improved pruritus within two months (NRS score of 1) with ameliorated inflammation, redness, and excoriation (*figure 1D*).