Retiform purpura as a dermatological sign of coronavirus disease 2019 (COVID-19) coagulopathy

Dear editor,

Since December 2019, coronavirus disease 2019 (COVID-19) has spread worldwide to become a pandemic. Multiple skin manifestations related to the infection have been described progressively. Recalcati1 asserted that 20.4% of infected patients developed cutaneous manifestations, and Galván-Casas et al.2 have recently proposed five clinical patterns (pseudo-chilblain, vesicular, urticarial, maculopapular and livedo/necrosis). We report a case of COVID-19 with retiform purpura and its histopathological correlation.

A 79-year-old woman presented to the Emergency Department with a 7-day history of high temperature (up to 39°C), asthenia, cough, shortness of breath and livedoid skin lesions on her legs. Physical examination showed painful retiform purpuric-violaceous patches of 15 cm with some haemorrhagic blisters and crusts on both legs (Fig. 1) suggestive of retiform purpura. Two punch biopsies were performed. Conventional histology showed multiple thrombi occluding most small-sized vessels of the superficial and mid-dermis (Fig. 2a). Direct immunofluorescence showed the deposition of IgM, C3 and fibrinogen within superficial-to-deep dermal blood vessel walls (Fig. 2b). In addition, C9 deposition was also revealed on the vessel walls by immunohistochemistry (Fig. 2c). Blood tests showed elevation of acute phase reactants, leukopenia and D-Dimer of >10 000 ng/ml (reference value, <500). RT-PCR from a nasopharyngeal swab specimen confirmed a SARS-CoV-2 infection. The patient was hospitalized and treated with hydroxychloroquine (200 mg bid), azithromycin (250 mg/day), lopinavir-ritonavir (200 mg/50 mg bid) and low-molecular-weight heparin. After some days, given the lack of clinical improvement and the need for oxygen therapy a chest CT was performed, showing a segmental pulmonary thromboembolism in the right lower lobe. Anticoagulation was changed to fondaparinux due to progressive thrombocytopenia. Anti-platelet factor IV, antiphospholipid antibodies, lupus anticoagulant, crioglobulinemia and serum and urine immunofixation were all negative. Three weeks after hospital discharge, the patient continues with anticoagulation treatment and her cutaneous lesions are slowly recovering.

COVID-19 can be associated with coagulopathy which indicates a worse prognosis.3 The activation of both alternative and lectin-based complement pathways plays a key role in this pro-coagulant state and microvascular injury,4 but the exact pathophysiology is still unclear. Skin manifestations of COVID-19 coagulopathy can vary from transient unilateral livedo reticularis in mild cases5 to disseminated intravascular coagulation with true-ischemic lesions in critically ill patients.6 Purpura, Raynaud’s phenomenon, chilblain-like and erythema multiforme-like lesions in young asymptomatic patients have also been observed with this infection, although the connection with coagulopathy is unknown.7,8 Our patient presented with retiform purpura as a cutaneous manifestation of COVID-19 coagulopathy. Galván-Casas et al.2 linked the livedoid/necrotic lesions to older patients and severe disease (10% mortality) but no biopsies were performed. In the present case, histology showed thrombi in small cutaneous vessels, with complement pathway activation as demonstrated by C3 and C9 deposition. Heparin was changed to fondaparinux after suspecting heparin-induced thrombocytopenia, but Fan et al.9 described mild thrombocytopenia (100–150 × 10^9/L) in 20% of COVID-19 patients.

Our case highlights the concomitant presentation of cutaneous microthrombi presenting as retiform purpura and macrothrombi presenting as pulmonary thromboembolism in the setting of COVID-19 coagulopathy. To our knowledge, there have been no histologically proven cases describing this phenomenon. We hope that in the coming months, pathophysiology of skin manifestations secondary to coagulation alterations will be better understood. From now on, we will have to include...
COVID-19 infection in the differential diagnosis of retiform purpura.10

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Conflict of interest
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References
1 Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. J Eur Acad Dermatol Venereol 2020; 34: e212–e213. https://doi.org/10.1111/jdv.16387
2 Galván Casas C, Català A, Carretero Hernández G et al. Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases. Br J Dermatol 2020. https://doi.org/10.1111/bjd.19163. [Epub ahead of print].
3 Xiong M, Liang X, Wei Y-D. Changes in blood coagulation in patients with severe coronavirus disease 2019 (COVID-19): a meta-analysis. Br J Haematol 2020. https://doi.org/10.1111/bjh.16725. [Epub ahead of print].
4 Magro C, Mulvey JJ, Berlin D et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: a report of five cases. Transl Res 2020; 220: 1–13. https://doi.org/10.1016/j.trsl.2020.04.007
5 Manalo IF, Smith MK, Cheeley J, Jacobs R. A dermatologic manifestation of COVID-19: transient livedo reticularis. J Am Acad Dermatol 2020. https://doi.org/10.1016/j.jaad.2020.04.018. [Epub ahead of print].
6 Zhang Y, Cao W, Xiao M et al. Clinical and coagulation characteristics of 7 patients with critical COVID-19 pneumonia and acro-ischemia. Zhonghua Xue Ye Xue Za Zhi 2020; 41: E006.
7 Bouaziz J, Duong T, Jachiet M et al. Vascular skin symptoms in COVID-19: a french observational study. J Eur Acad Dermatol Venereol 2020. https://doi.org/10.1111/jdv.16544. [Epub ahead of print].
8 Fernandez-Nieto D, Jimenez-Cauhe J, Suarez-Valle A et al. Characterization of acute acro-ischemic lesions in non-hospitalized patients: a case series of 132 patients during the COVID-19 outbreak. J Am Acad Dermatol 2020; 83: e61–e63. https://doi.org/10.1016/j.jaad.2020.04.093
8 Fan BE, Chong VCL, Chan SSW et al. Hematologic parameters in patients with COVID-19 infection. Am J Hematol 2020; 95: e131–e134. https://doi.org/10.1002/ajh.25774
9 Llamas-Velasco M, Alegria V, Santos-Briz Á et al. Occlusive nonvasculitic vasculopathy. Am J Dermatopathol 2017; 39: 637–662.

Retroauricular dermatitis with vehement use of ear loop face masks during COVID-19 pandemic

To the Editor
The coronavirus disease 2019 (COVID-19) pandemic forged the exponential use of masks of various kinds, not just by health workers but also by general population as a personal protective equipment (PPE). Although contact dermatitis due to PPE is well reported, mask induced dermatitis is a relatively unexplored phenomenon. In this article, we report a preliminary data of patients experiencing retroauricular dermatitis due to ear loop face masks.

From 1st April to 30th April, we came across 14 patients including both healthcare workers and general population who...