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Reply to: “Reply: A dermatologic manifestation of COVID-19: Transient livedo reticularis”



To the Editor: We appreciate the additional information from Dr Christina Thomas¹ on our report² of transient livedo reticularis occurring in patients with COVID-19. Dr Thomas astutely notes that disseminated intravascular coagulation and macrothromboses appear to be more prominent in severely ill COVID-19 populations and that other potential factors, such as inflammatory cytokines or the viral mechanism of binding to angiotensin-converting enzyme 2, may play a role in microthrombi formation in less severe disease.

Our overall knowledge of the emerging COVID-19 infection and grasp of its mechanism causing coagulopathy in nonsevere cases is constantly evolving. Several mechanisms have been proposed, but in the largest analysis of cases published to date of 1099 patients with laboratory-confirmed COVID-19 in China, a D-dimer ≥ 0.5 mg/L was noted in 46.4% of nonsevere cases and in 59.6% of severe cases.³ Moreover, the International Society of Thrombosis and Haemostasis has issued recommendations of measuring D-dimer, prothrombin time, and platelet count in all patients with COVID-19, acknowledging that guidelines may change as our knowledge evolves.⁴ Interestingly, antiphospholipid antibodies (specifically anticardiolipin IgA and anti- β_2 -glycoprotein I, IgA, and IgG) have also been reported in severe COVID-19 infection.⁵

As cited in our original paper with findings of 62 publications indexed on PubMed when “COVID” and “thrombosis” are concurrently searched at the time of this writing, patients with COVID-19 have certainly been shown to exhibit a thrombophilic state.² In addition, transient livedo reticularis can mimic erythema ab igne, but neither of our patients had histories placing them at risk for erythema ab igne. We originally proposed that the 2 patients who exhibited transient livedo reticularis perhaps had low-grade disseminated intravascular coagulation. Although it is still a possibility, we propose expanding that hypothesis to them having had a low-grade thrombophilic or hyperviscosity state, with possible etiologies including the formation of intravascular thrombosis, cold agglutinins, lupus anticoagulant, cryofibrinogens, or cryoglobulins. The concurrent

hematuria in patient 1 could be explained by renal microinfarctions or intravascular hemolysis.

We continue to support our original statement that at this time, while the etiology for a hypercoagulable state is unknown, complete blood count, coagulation studies, fibrin degradation products, urinalysis, and tissue histopathology in patients with livedo reticularis related to COVID-19 may further clarify the pathomechanisms of this vasculopathy.

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REFERENCES

1. Thomas C. Reply to: “A dermatologic manifestation of COVID-19: transient livedo reticularis.” *J Am Acad Dermatol.* 2020;83(2):e155-e156.
2. Manalo I, Smith M, Cheeley J, Jacobs R. A dermatologic manifestation of COVID-19: transient livedo reticularis. *J Am Acad Dermatol.* 2020;83(2):700.
3. Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med.* 2020;382(18):1708-1720.
4. Thachil J, Tang N, Gando S, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. *J Thromb Haemost.* 2020;18(5):1023-1026.
5. Zhang Y, Xiao M, Zhang S, et al. Coagulopathy and antiphospholipid antibodies in patients with Covid-19. *N Engl J Med.* 2020;382(17):e38.

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