Correspondence

Nonuremic calciphylaxis in a COVID-19 patient

Dear Editor,

Nonuremic calcific arteriopathy (calciphylaxis) often presents with cutaneous lesions and may be due to a hypercoagulable state. Some studies have demonstrated that calcium deposition can occur in vascular beds without leading to visible manifestations.[1] Systemic hypercoagulable disorders have been found to be associated with COVID-19 infections with documented complications, such as venous thromboembolism.[2]

Calciphylaxis is diagnosed by skin biopsy, which classically shows calcium deposition, fibrointimal hyperplasia, and thrombosis in small arterioles of the affected organ.[1,3] Additionally, intimal proliferation, fat necrosis, and fibrosis can be visualized on biopsy. Risk factors for calciphylaxis include: female sex, obesity, diabetes mellitus, and Caucasian race.[3]

A 42-year-old Caucasian woman with a past medical history notable for hypertension and five previous miscarriages presented with an acute onset of severe pain along the bilateral flanks, hips, and lower abdomen. Her family history was remarkable for antiphospholipid antibody syndrome in her mother. She was diagnosed with COVID-19 28 days prior to admission, which was complicated by an acute submassive pulmonary embolism treated with unfractionated heparin subsequently transitioned to apixaban. On presentation, her examination demonstrated faint erythema with marked areas of linear cords induration along the bilateral flanks, abdomen, and proximal thighs with associated hyperalgesia (Fig. 1). Her admission blood work (including creatinine, creatine kinase, complete blood count) was normal, except for elevated inflammatory markers (CRP and ferritin). Magnetic resonance imaging revealed moderate subcutaneous edema of the hips and thighs but did not display any myonecrosis. An extensive rheumatologic and hematologic workup was performed, including beta-2 glycoprotein 1 antibody, cardiolipin antibody panel, antinuclear antibody, scleroderma antibody, anti-SS-A antibody, anti-SS-B antibody, anti-streptolysin O antibody, and myositis-specific antibody panel, and hexagonal phase phospholipid neutralization, dilute Russell's viper venom time, parathyroid hormone, calcium level, C3, C4, protein C and S activity, and SPEP were all within normal limits. Her pathology from an area of induration demonstrated calcium deposition in the small arterioles of the abdomen and fat necrosis diagnostic of calciphylaxis (Fig. 2). She was treated with sodium thiosulfate infusions with prompt symptomatic improvement.

COVID-19 is known to be associated with multiple extrapulmonary manifestations, commonly including pyrexia, diarrhea, anosmia, dysgeusia, and myalgias. There is an increased risk of venous and arterial complications related to COVID-19, including deep vein thrombosis, pulmonary embolism, ischemic stroke, myocardial infarction, and acute kidney injury. To date, calciphylaxis has been observed in two COVID-19 patients, one with end-stage renal disease and the other being treated with warfarin.[4,5] Our patient was nonuremic and did not receive warfarin.

We hypothesize that our patient had risk factors predisposing her to calciphylaxis in the context of her recent COVID-19 infection. Her past history of multiple prior miscarriages and strong family history of antiphospholipid antibody syndrome suggest that she may have an underlying hypercoagulable state that has yet to be defined. The associations of calciphylaxis with thrombophilia and thrombosis are well known.[6,7] COVID-19 presumably served as a precipitant for her prior thromboembolism and calciphylaxis. Her workup to date has been unrevealing though.

Sodium thiosulfate remains the first-line treatment for uremic calciphylaxis.[3] Based on our patient's response to sodium thiosulfate, we recommend that its use be considered as first-line therapy for COVID-19 patients with calciphylaxis.

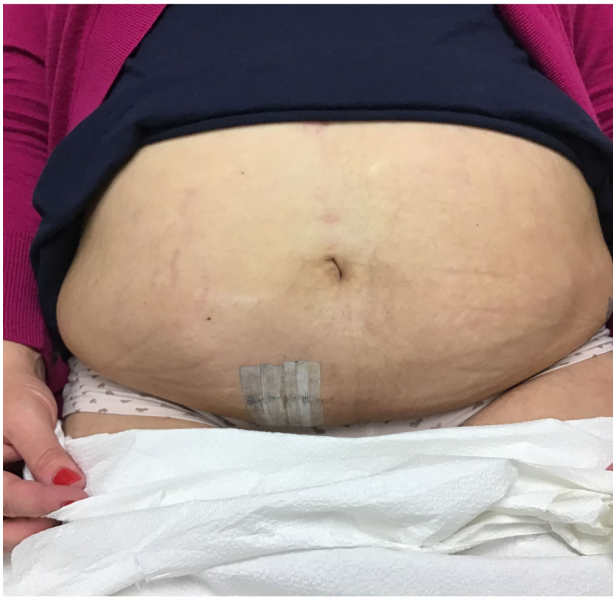

Figure 1 An edematous abdomen with areas of slight erythema is shown, which upon palpating, further revealed cords of firm induration

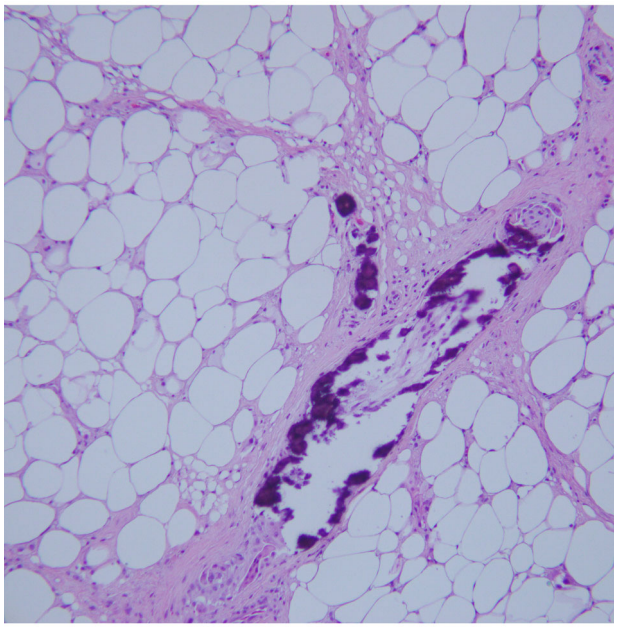

Figure 2 Histopathology shows calcium deposition within vessel lumens and areas of fat necrosis diagnostic of calciphylaxis (Hematoxylin and eosin, ×100)

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Conflict of interest: None.
Funding source: None.

doi: 10.1111/ijd.15661

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