Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

and parietal infiltration by mononuclear cells and neutrophils, followed by accelerated pyroptosis and thrombosis. This pathology can further evolve through activated B lymphocytes that generate plasma cells, in turn leading to a deposition of polyclonal immune complexes and complement fractions in vessels walls.

This immunocomplex-mediated peri/pan-arteritis, evident on histology with neutrophil infiltration and accumulation of fibrinoid materials, seems to be a more severe leukocytoclastic vasculitis (Fig, *A*).[4] The associated inflammatory state causes an increased release of cytokines, typically interleukin-6, and, at the same time, recruitment of platelets to perform, in agreement with their myeloid lineage, a covercytosis against the virions. Moreover, platelets strictly adhere to damaged endothelia and surround the fibrin aggregates. Newly manufactured antiphospholipid antibodies, as in a secondary antiphospholipid-like syndrome, favor, together with the basic COVID-19 procoagulative state, local thromboses, that acquire the particular feature of immunothrombosis.

In medium and large arteries, this pathology involves the external VV as well, while the internal VV, because of their small caliber, thinner walls, and lower blood inflow, disappear as a direct result of the antecedent endothelial damage (Fig, *B*).[5] As shown,[6] the subsequent hypoxia in arterial walls produces hypoxia-inducible factor 1a, in turn releasing other substances, such as matrix metalloproteinases, macrophages, monocytes, and chemoattractant proteins, specific for secondary degenerative-inflammatory lesions. In addition to endothelin-1 and angiotensin II type 1, vasoconstrictors are active on the VV as well.[6] This process worsens the local preinflammatory or inflammatory conditions, already promoted by preexisting endothelial dysfunction, increases the degradation of collagen and elastic fibers, and greatly decreases the population of smooth muscle bundles in the media layer. In the VV, we have to consider, as an additional functional factor hampering blood inflow, their radial or circumferential external compression by inelastic atherosclerotic vessels, mainly when stressed by arterial hypertension. This cascade of pathological events directly explains the pathogenesis of penetrating endothelial ulcers that connect with the entire group of acute aortopathies associated with COVID-19, including mural thrombosis, intramural hematoma, and dissection (Fig). In contrast, the acute or subacute development of an aneurysm, which is in this case inflammatory, hypothesized to be caused by the decreased elasticity and increased fragility of the aortic walls, has not yet been reported.[7] This unified anatomo-clinical notion of acute aortopathies, including different pathologies with reciprocal connections, fits well with the wide spectrum of COVID-19 features and prompts research on this disease complications, which may be otherwise overlooked.

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Reply

We thank Dr Roncati for reading and commenting[1] on our case reporting an acute aortic intramural hematoma (IMH) in a SARS-CoV-2 positive patient.[2] The author[1] suggests a combination of different pathophysiologic mechanisms of aortic injury in these patients, which is undoubtedly an interesting aspect to consider in the ever-growing association between SARS-CoV-2 infection and vascular disease.[3] In the clinical setting, SARS-CoV-2 is associated with hypercoagulability leading to peripheral arterial and venous thrombosis, but some aortic phenomena have been described as well.[3,4]

Historically, acute aortic syndromes and mostly IMHs have been associated with vasa vasorum degeneration and/or rupture.[5] Roncati et al suggest a SARS-CoV-2-related vasa vasorum "endotheliitis" driven by the innate and adaptive immune systems and also involving platelet activation. This immunothrombosis ultimately

leads to medial degeneration, the pillar of acute aortic syndrome pathogenesis. We believe that a pre-existing state of damaged vasa vasorum due to hypertension and advanced age have laid the foundation for the inflammatory degeneration that led to the IMH in our patient.

Aortic inflammation in relation to SARS-CoV-2 has to be further investigated from a histology, pathophysiology and clinical perspective. Even though it is difficult to demonstrate a direct link between aortic disease and SARS-CoV-2 infection, some studies suggest a potential association. However, it seems reasonable to assume that an endothelial inflammatory mechanism might incite acute aortic syndromes such as the one seen on our patient.

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