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.

or sacral radicular arteries, when the Adamkiewicz artery originates abnormally high or is chronically occluded.[3] The variable intensity of sensorimotor deficits might be explained by the variable collateralization of the spinal arterial supply.[4] However, urgent revascularization is always required for both causes. The neurologic recovery will be better in the case of peripheral ischemia.

However, patients can also have spinal cord compression with no relationship to COVID-19 infection. The presence of COVID-19 infection can lead us astray, and we can miss the urgent diagnosis requiring medullar magnetic resonance imaging studies and surgical decompression.[5] Finally, the diagnosis might be acute myelopathy associated with COVID-19 infection[6]; however, this must remain a diagnosis of elimination, in particular, because no specific treatment is available. Thus, with or without COVID-19 infection, patient with acute paraplegia must very quickly undergo computed tomography and, if the findings are negative, medullar magnetic resonance imaging.

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COVID-19 thromboembolic complications: Deepening immunoinflammatory features

It was the end of 2019 when severe acute respiratory syndrome coronavirus-2, the respiratory pathogen capable of binding to human angiotensin-converting enzyme 2 receptors and responsible for coronavirus disease 2019 (COVID-19), was isolated in Wuhan, China; since then, COVID-19 has been affecting the worldwide population for its many clinicopathologic aspects, including vasculocoagulative ones.[1,2] The interesting study by Indes et al[1] correlates the high incidence of arterial thromboembolic events with COVID-19 severity, outlining, as key factors, an abnormal immune/inflammatory reaction, and a hypercoagulative state.[1] Deepening their pathophysiologic features helps to better understand this complication.

The lymphocytic endotheliitis, which is expressed early with endothelial cells damage, and a consequent accelerated pyroptosis can evolve toward a leukocytoclastic vasculitis, a frank acute necrotizing vasculitis owing to immune complexes and complement fraction depositions as well as activation in the vascular walls, characterized by the infiltration of neutrophils into the media and adventitial layers of small and medium arteries and the occurrence of fibrinoid necrosis.[3,4] This diffuse endothelial damage is followed by an increase in the circulating endothelial cells and a type III hypersensitive reaction.[4,5]

The severity of COVID-19 includes a progressively higher production of cytokines, inducing, among other complications, a hypercoagulative state. In particular, IL-6 correlates with an augmented megakaryocytopoiesis, proven by histologic study of bone marrow and lungs with a high number of denuded megakaryocytes.[6] This is followed by a greater release of circulating platelets, already active in the earlier stages of this disease in repairing damaged vascular endothelia, and, according to their myeloid origin, in performing covercytosis against virions.[6] In the meantime, from an immunologic perspective, a

secondary antiphospholipid immune syndrome may develop with the production of autoantibodies, such as lupus anticoagulant, anticardiolipin, and anti-β2-glycoprotein-I.[7] Their binding to the membrane phospholipids of platelets and vascular endothelia cells takes part in generating thrombi and inflammatory cells aggregates of different sizes. This abnormal immunothrombosis involves the microvessels and medium or large arteries, causing complete or mural thromboses, respectively.

Predisposing factors include endothelial dysfunction or local turbulent blood flow secondary to severe atherosclerosis, vascular prosthesis, or endografts.[7] Moreover, the histologic characteristics of COVID-19 are hyperimmune, rather than a common inflammatory pathology, and correlate, in larger arteries, with the absence of secondary intramural hematomas, dissections, and mainly inflammatory aneurysms, notwithstanding the thrombosis that affects in the big arteries the vasa vasorum.[7] We think that this cascade of pathologic events will be further elucidated when the impact of the host humoral response on COVID-19 course is better clarified.

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Reply

We would like to thank Roncati et al for their letter and comments related to our article. Approximately 1 year ago in the early stages of the coronavirus disease 2019 (COVID-19) pandemic, hospitals in New York City experienced some of the highest concentrations of cases in the United States. We cared for a great number of patients with arterial and/or venous thromboembolic complications related to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Among these were many patients with COVID-19 and acute arterial ischemia requiring emergent surgical treatment.

In addition to the greater mortality, we found these patients had a higher body mass index, higher average in-hospital D-dimer levels, and lower rates of antiplatelet usage. This constellation suggested that a generalized hyperinflammatory, hypercoagulable state, as nicely outlined in detail by Roncati et al in their letter to the editor, was primarily responsible. Finally, we found an unusual preponderance of large vessel thromboses, including those in the aortoiliac distribution. During the past year, the hypercoagulability seen in patients with COVID-19 has been increasingly elucidated and will continue to be further characterized. Although this has been an extremely difficult time for healthcare workers around the world, the opportunity for cross-specialty and global collaboration, as is illustrated by their letter to the editor and our article in the Journal, has been rewarding and hopefully will help expedite the characterization of these processes at a more detailed cellular and molecular level.

As we continue to treat patients with SARS-CoV-2 infection, we expect to encounter new and challenging obstacles such as the arterial and venous complications described. For example, we have seen in recent weeks the characterization of an even newer phenomenon, a condition known as SARS-CoV-2 vaccine–induced immune thrombotic thrombocytopenia. As was recently demonstrated in a *New England Journal* article, the mechanism of this hypercoagulable disorder related to COVID-19 vaccination is closely related to that which leads to heparin-induced thrombocytopenia.[1] This requires treatment with non–heparin anticoagulant agents. It is important to differentiate hypercoagulable complications such as these in patients with SAR-CoV-2 infection because the treatment implications could