AJNR

Reply:

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AJNR Am J Neuroradiol 2021, 42 (2) E5
doi: https://doi.org/10.3174/ajnr.A6944
http://www.ajnr.org/content/42/2/E5

REPLY:

We thank Dr Miguel Quintas-Neves for his interest in our article[1] and for his useful comments. As mentioned in Dr Quintas-Neves's commentary, and in our article, mechanisms of injury related to hypoxic-ischemic injury and a hypercoagulable state were confidently ruled out in our patient on solid clinical and biologic grounds. On the other hand, the patient clearly presented with signs and markers of inflammation.

In that patient, multiple, diffuse cerebral lesions were present, mostly ischemic, some hemorrhagic, in a wide distribution that included the deep white matter of both hemispheres, the corpus callosum, the deep gray matter structures, and the middle cerebellar peduncles. Restricted diffusion was present in all of those lesions, some of which demonstrated a "patchy" pattern of contrast uptake.

Such patterns of diffuse punctate deep white matter/gray matter restricted diffusion with postcontrast "patchy/punctate" enhancement have been shown to be associated with active small vessel wall inflammatory changes in primary and secondary CNS angiitis and in some presentations of the reversible cerebral vasoconstriction syndrome and posterior reversible encephalopathy syndrome complex.[2,3] In those patients, hemorrhagic transformation has been speculated to possibly result from damage to the arterial wall in relation to a necrotizing pattern, allowing transmural passage of blood.[4]

Consequently and on the basis of the radiologic findings in that patient, we suspected and reported a vasculitis-like pattern. We further suggested that such a vasculitis-like picture may possibly be in relation to diffuse endotheliitis from the Severe Acute Respiratory Syndrome coronavirus 2 spike glycoprotein effect on the endothelial angiotensin-converting enzyme 2 (ACE-2) receptors. MRA demonstrated no evidence of large- or medium-sized vessel abnormalities. Although small, the potential risk of conventional cerebral angiography was not believed to be justified in that patient, considering the lack of substantial impact on the patient's management.

Indeed, both mechanisms suggested by Quintas-Neves, ie, direct viral affinity for endothelial ACE-2 receptors and cytokine storm–related endothelial injury, are plausible mechanisms that are entirely in line with our description. Indeed, too, such a pattern of endothelial inflammation leading to microvascular ischemia/thrombosis may conceivably affect randomly any part of the body.

We further believe it likely that other, unforeseen mechanisms may be present to explain CNS injuries in patients with coronavirus disease 2019. Hopefully, new research will educate us all on the various molecular mechanisms through which this new virus can cause harm, until an effective vaccine is found.

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http://dx.doi.org/10.3174/ajnr.A6944