COVID-19

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COVID-19: angiotensin II in development of lung immunothrombosis and vasculitis mimics

From a radiological perspective, there is strong evidence that the initial pathological process of COVID-19 lung disease dominantly affects the pulmonary vessels via systemic microvascular immunothrombosis, as is supported by pathological reports.[1] We read with considerable interest the recent Viewpoint by Dennis McGonagle and colleagues on COVID-19 vasculitis and vasculitis mimics.[2]

In this Viewpoint, the model presented describing so-called pulmonary intravascular coagulopathy proposes that one of the two broad types of systemic vasculitis described in patients with COVID-19 is mediated by microembolic material that escapes the capillary bed of the lungs and is distributed via systemic arteries to other parts of the body. Importantly, this mechanism assumes the presence of thrombosis within pulmonary vessels on the distal side of the capillary bed, beyond the embolic filtration network of the alveolar capillaries and, thus, the presence of thrombosis in the pulmonary venules of the lung periphery. The model is aligned with growing evidence of the pivotal involvement of pulmonary veins in severe COVID-19, as evidenced by the presence of pulmonary infarcts in the majority of patients at autopsy,[1] and the presence of thrombosis in pulmonary venules, not only in pulmonary arterioles.[3]

Our own understanding of the pathogenesis of immunothrombosis in COVID-19 lung disease is based on the model of viral interaction with the angiotensin-converting enzyme 2 (ACE2) receptor on the alveolar capillary endothelium, and the subsequent increase in circulating angiotensin II. In 2018, Senchenkova and colleagues described the direct and immediate pathophysiological effects of angiotensin II,[4] implicating angiotensin II as a pro-inflammatory and pro-thrombotic mediator. This model of the biophysiological effects of angiotensin II has been adopted by the expert group from the Netherlands that advised early prophylactic anticoagulation treatment of systemic microvascular thrombosis and inflammation in patients admitted to hospital with COVID-19, as they considered this to be the primary disease process in these patients.[5] This advice led to changes in the clinical regimen in the Netherlands, implemented from May, 2020, in which patients were given anticoagulation prophylaxis on presentation to hospital whenever COVID-19 was proven or clinically suspected.[5]

We propose that, after the initial interaction between the virus and the ACE2 receptor, increased circulating angiotensin II could form part of the complex trigger that leads to endotheliitis (capillaritis) and more extensive in-situ immunothrombosis. This simple concept would help explain some of the vasculocentric phenomena that are visible radiologically. We ask McGonagle and colleagues whether they have considered the direct role of angiotensin II as a potential contributor in the development of lung immunothrombosis and vasculitis mimics?

We declare no competing interests.

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