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LETTER TO THE EDITOR

ACE inhibitor-related angioedema in a COVID-19 patient—a plausible contribution of the viral infection?

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To the Editor,

The COVID-19 outbreak has resulted in a global public health crisis. In these challenging times, we are fighting against the disease with "multiple faces". COVID-19 is primarily an acute respiratory disease caused by a novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), with major implications that go far beyond the lungs [1]. The infection can result in an excessive systemic inflammation, hypercoagulable state, endothelial dysfunction, and increased vascular permeability. The latter along with extravasation of intravascular fluid plays a pivotal role in the development of angioedema [2].

We would like to share a case of a COVID-19 patient who developed ACE inhibitor-related angioedema. We posit that the viral infection was a contributing factor in the development of this potentially life-threatening condition.

A 53-year-old male patient was admitted due to myocardial infarction 1 week after being diagnosed with COVID-19 by PCR. Before admission, he had been stable and self-isolated at home. On presentation, the patient was stable with ongoing chest pain. Urgent coronary angiography revealed multivessel coronary thrombosis (with an underlying coronary lesion only in the left anterior descending artery) which is a rare phenomenon in patients without cardiovascular risk factors [3]. Following the procedure, the patient was transferred to a COVID-19-dedicated ward and guideline-based medical therapies were initiated, i.e., aspirin, ticagrerol, rosuvastatin, bisoprolol, and ramipril (2.5 mg once daily). One day after discharge and 5 days after ramipril initiation, the patient was readmitted due to tongue swelling thought to be associated with ACE inhibitor-induced angioedema. He did not have any rush or pruritus, and denied having shortness of breath, nausea, or fever. Furthermore, no allergies or angioedema was documented in the patient's and his family history. He was switched from ramipril to telmisartan and treated with appropriate medications (glucocorticosteroid, famotidine, diphenhydramine). Ultimately, the patient was discharged from the ward in a good clinical condition.

Endothelial dysfunction and increased vascular permeability are well-documented pathological features of COVID-19 [1]. As these phenomena may result in extravasation of intravascular fluid, an increased risk of angioedema in the abovementioned group of patients seems to be pathophysiologically justified. However, angioedema in the presented patient still raises many questions. Prior to the hospital admission, the patient had been apparently healthy with no pre-existing conditions or medications taken, including ACE inhibitors. Given the above, the angioedema could be exclusively related to the initiation of ramipril therapy. On the other hand, it is known that ACE-2 receptor is essential for COVID-19 invasion. Binding the virus to the receptor leads to downregulation of ACE-2 which is one of the enzymes responsible for bradykinin breakdown [1, 4, 5]. Therefore, in the presented case, both ramipril and COVID-19 infection could have contributed to the angioedema by increasing levels of bradykinin. In the available literature, there is a case of a COVID-19 patient who presented with 12 h of lip and facial swelling [4]. Importantly, he had been treated with lisinopril for 10 years prior to his admission. Considering the fact that late-onset angioedema on ACE inhibitors is rarely observed, the cited case report supports the notion on the role of COVID-19 as a contributing factor to angioedema. Tongue swelling in a patient taking benazepril for 4 months, unknowingly with COVID-19, has been also recently reported [5].

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The presented case report suggests that COVID-19 infection may increase the risk of developing angioedema in patients on ACE-I which should be taken into account by healthcare professionals when planning a guideline-based treatment [4, 5]. Considering the fact that ACE inhibitors are one of the most widely used medications for hypertension and heart failure, clinicians should bear in mind the potentially increased risk of angioedema in the context of COVID-19.

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