Human Cell (2021) 34:1941–1942
https://doi.org/10.1007/s13577-021-00605-0

LETTER TO THE EDITOR

Neurological effects of elevated levels of angiotensin II in COVID-19 patients

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Received: 8 August 2021 / Accepted: 25 August 2021 / Published online: 27 August 2021

Keywords Angiotensin II · COVID-19 · SARS-CoV-2

Dear editor,

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused a great deal of damage to the world. Regarding the complications of this virus, although the pulmonary complications have received more attention, it can be very constructive to pay attention to its effects on the brain. Studies have been done on the effects of the SARS-CoV-2 on the central nervous system and it has been shown that this virus causes complications, such as seizure and cerebral hemorrhage [1]. About the probable mechanisms of these complications, increased entry of inflammatory cytokines into the brain as a result of the SARS-CoV-2 induced cytokine storm has been discussed. In this regard, angiotensin II (Ang II) can be a key factor in examining the association between the SARS-CoV-2 and the brain complications caused by it. After binding of the virus to its receptor, angiotensin-converting enzyme (ACE2), endocytosis of this receptor occurs with the virus [2]. Decreased levels of ACE2 at the cells surface increase Ang II levels, as reported in patients with COVID-19 [3]. Normally, Ang II cannot cross the blood–brain barrier (BBB), but in conditions, such as hypertension, increased levels of Ang II contribute to the BBB disruption [4]. It has been demonstrated that Ang II increases the BBB permeability through activation of the angiotensin II type 1 receptor (AT1R) [4]. Increased BBB permeability by Ang II can be a reason for the virus to enter the brain [5]. In addition, this condition can explain SARS-CoV-2-induced cerebral hemorrhage in COVID-19 patients, as the association between early BBB breakdown and hemorrhage has been reported in patients treated with thrombolytic drugs [6]. On the other hand, following the entry of the virus into the brain [5], it may cause endocytosis of ACE2 leading to an increase in the levels of cerebral Ang II, which by binding to its receptors on astrocytes can cause the expression of inflammatory cytokines [7]. On the other hand, elevated levels of Ang II may contribute to neuronal loss in different parts of the brain. It has been shown that Ang II causes dopaminergic neurons death and losartan, an AT1R antagonist, protects these neurons against apoptosis [8]. In addition, the association between Ang II and Alzheimer's disease is examined in different studies. For instance, it has been indicated that ACE2 is decreased in Alzheimer's disease leading to increase tau pathology [9]. In addition, Ang II has been shown to increase brain Aβ through modulation of amyloid precursor protein production and α-, β-, and γ-secretase activities in an animal model of Alzheimer's disease [10]. Overall, based on the available evidence, the effect of the SARS-CoV-2 on elevated Ang II levels should be given more attention and further studies in this field can be constructive.

Author contributions Not applicable.

Funding Not applicable.

Availability of data and materials Not applicable.

Declarations

Conflict of interest There is no conflict of interest to declare.

Ethics approval and consent to participate Not applicable.

Consent for publication Not applicable.

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