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.

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Bone biology and COVID-19 infection: Is ACE2 a potential influence factor?

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ABSTRACT

The outbreak of coronavirus disease 2019 (COVID-19) has posed a severe threat to global health management system since it has been detected in the human body. This pandemic was prompted by severe acute respiratory syndrome coronaviruses 2 (SARS-CoV-2) and rapidly developed into a public emergency with an alarming increase in cases and deaths. The increasing explorations to SARS-CoV-2 infection guide us to consider whether bone lesion is followed by this pathologic process. We especially focus on the underlying pathobiology that SARS-CoV-2 possibly mediated in bone remodeling and analyze the association of bone destruction with ACE2 in COVID-19 incidence, for preferable understanding the pathogenesis and providing necessary clinical management in orthopedics.

Introduction

Coronavirus are pathogens with high diverse RNA virus that cause respiratory and digestive system injury. An in-depth annotation of newly discovered COVID-19 has revealed a serious and extensive damage to human body system. Once starting up the onset of interstitial pneumonia in progression, it will clinically give rise to severe acute respiratory distress syndrome (ARDS) and ulteriorly deteriorated into multiple organ failure (MOF).

Similar to SARS-CoV, which makes incursion into body, SARS-CoV-2 spike protein combines to its functional receptor ACE2 and then be activated to release peptides for fusing membrane [1]. Thus, the expression of ACE2 is a pivotal entrance for the invasion of SARS-CoV-2 and ameliorates congenial conditions for virus republication. Angiotensin-converting enzyme 2 (ACE2) is a critical enzyme in the protective axis of renin angiotensin system (RAS) which regulates numerous systemic functions [2]. It is one kind of carboxypeptidase which abundantly expressed in the kidney, cardiovascular and gastrointestinal tract, especially a small amount in alveolar epithelial type II (ATII) cells, leading to increased lung damage in view of the increasement of pulmonary vascular permeability [3]. The deficiency of pulmonary ACE2 caused by SARS-CoV-2 infection brings about the low production of Ang-(1–7) and exacerbates hypertension and fibrosis post-viral infection.

Hypothesis

Considering that coronaviruses arouses pneumonia and upper respiratory tract infection through ACE2 receptors in ATII cells, we also require taking notice of ACE2-dependent effects on bone tissue. Is ACE2 a potential influence factor that regulate bone biology during COVID-19 infection?

Justification of the proposed hypothesis

Evidence has shown that ACE2 locally expresses in human bone marrow-derived stem/progenitor cells (BMSPCs) and manipulates cytokine-sensing to promote skeletal repair [4]. ACE2 promotes AngII degradation and synthetizes Ang1-7, which perform functions by way of Mas receptor. In previous study, literatures revealed osteoblasts and osteoclasts express ACE2/Mas and illustrated how the ACE2/Ang-(1–7)/Mas axis can affect bone metabolism. More specifically, the activation of ACE2/Ang-(1–7)/Mas axis restrains bone resorption and exhibits anti-inflammatory property [5]. In Abuohashish's work, he verified ACE-2/Ang1-7/Mas worked as a beneficial RAS axis in order to accelerate the osteo-protective effects on postmenopausal animals, suggesting ACE2 is essential in maintaining bone structure [6]. Once ACE2 was targeted by SARS-CoV-2, the block of ACE2 may give occasion to a decreased bone mass and joint inflammation. Similarly, Duan et al. found ACE2 deficiency worsened diabetes-induced bone marrow

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microenvironment, which was supported by the dysfunction of migratory and proliferation in BMSCs [7]. Nozato et al. found the loss of ACE2 in mice exhibit earlier muscle weakness and a smaller muscle fibre size, Ang-(1–7) can reverse muscle weakness and bone volume in a Mas-dependent manner. As a consequence, COVID-19 may lead to an earlier muscle disorder and anaphase bone loss via targeting ACE2 in bone marrow microenvironment.

Conclusions

Although we have not fully grasped the whole features of COVID-19 and its likely host immunological reactions, pathophysiological proof of this pathogen has attracted our attention to bone metabolism. Without doubt, the deterioration of underlying diseases caused by SARS-CoV-2 infection tends to aggravate bone-forming capacity. The deficiency of ACE2, which caused by the invasion of virus, may lead to a decreased bone matrix and early muscle disorder.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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