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Editorial

Can NLRP3 Inflammasome Be Related to Covid-19 Pathophysiology?

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The 2019 coronavirus disease pandemic (COVID-19), caused by the coronavirus 2 that causes acute respiratory syndrome (SARS-CoV-2), began in December 2019 in Wuhan, China, and spread rapidly to reach all countries around the globe [1], threatening global health and damaging the global economy. In Brazil, the number of cases has already exceeded 4 million and there have been more than 127 thousand deaths [2].

Individuals infected with SARS-CoV-2 may have clinical severity ranging from asymptomatic individuals to severe disease characterized by pneumonia requiring oxygen supplementation, and progression to acute respiratory distress syndrome with systemic inflammatory response syndrome, septic shock and multiple organ failure, coagulopathy and death [3]. The primary symptoms of COVID-19 include fever, dry cough and fatigue [4]. However, some patients diagnosed with COVID-19 did not show these typical symptoms at diagnosis; instead, they only exhibited neurological symptoms as early symptoms, for example, non-specific manifestations of headache, malaise and unsteady walking, cerebral hemorrhage and cerebral infarction, in addition to other neurological diseases [5]. Regarding the pathological mechanisms, a significant part of the symptoms of COVID-19 can be explained by the excessive production of cytokines that the virus induces, leading to the systemic inflammatory response syndrome [6,7], which can lead to inflammation of the blood-brain barrier and increased permeability, facilitating the passage of more inflammatory cytokines and chemokines to the brain, exacerbating neuroinflammation and neurological symptoms [8].

Among the pro-inflammatory cytokines produced during viral and bacterial infections is IL-1β (Larson and Dunn, 2001) [9], a cytokine synthesized in a proforma whose activation is mediated by the NLRP3 inflammasome, an important cause of activation of the innate immune system by recognizing pathogens, including viruses [10,11]. The inflammasome is a multiprotein cytosolic complex composed of the NLRP3 receptor, the ASC adapter protein and the effector protein, pro- caspase-1 [12]. The formation of the inflammasome facilitates the autocleavage and activation of caspase-1, which proteolytically cleaves the pro-IL-1β and pro-IL-18 cytokines in their active forms, favoring pro-inflammatory and anti-microbial responses [13,14]. Among the inflammasomes described so far, NLRP3 is considered unique due to its ability to detect both pathogen- associated (PAMPs) and injury-associated (DAMPs) molecular patterns [15-17]. The mechanisms of activation of the NLRP3 inflammasome already described are K^+ efflux induced by ATP, lysosomal rupture and production of reactive oxygen species [18]. Some studies already suggest a relationship between the activation of the NLRP3 inflammasome and the pathogenesis of viral infections.

Taking into account the duration of this pandemic, its worldwide impact, and the fact that there is no specific and effective treatment for COVID-19, knowing the pathophysiology of this disease becomes essential. Exploring the role of the NLRP3 inflammasome in systemic inflammation associated with COVID-19 will contribute to the development of pharmacological interventions that will improve the course and prognosis of this disease, mainly related to its neurological consequences. Consequently, a better quality of life for patients in the post-infection period will positively impact the resumption of the global economy.

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