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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Could Sars-coronavirus-2 trigger autoimmune and/or autoinflammatory mechanisms in genetically predisposed subjects?

Dear Editor,

We have read with interest the recent article by Favalli et al. published in Autoimmunity Reviews [1]. We agree with the Authors that Corona Virus Disease 2019 (COVID-19) pandemic is unquestionably conditioning therapeutic strategies of autoimmune disorders, such as rheumatoid arthritis (RA). Indeed, RA patients show increased infectious risk because of impairment of immune system and immunosuppressive related-therapy. The Authors also suggest that the increasing knowledge about the pathophysiology of Sars-coronavirus-2 (SARS-CoV-2) infection is leading to consider cs-, b- and tsDMARDs as potential therapeutic strategies for COVID-19 [1].

This point is of valuable interest for Rheumatologist and Immunologists cause among the most important mechanisms underlying COVID-19, it has been reported cytokine release storm leading to interstitial pulmonary inflammation, extensive lung damage and acute respiratory distress syndrome [2,3].

In particular, in a recent study by Qin C, et al.in which among 452 patients with COVID-19, most of them had increase of several inflammatory cytokines such as tumor necrosis factor (TNF)-α, interleukin (IL)-1and IL-6 [3].

Further, higher serum levels of pro-inflammatory cytokines (i.e. TNF-α, IL-1 and IL-6) were found in patients with severe COVID-19 as compared to the non-severe ones [3]. Additionally, in severe cases, a reduction of CD4+ and CD8+ T cells and a decrease of regulatory T cells has been found, likely due to high expression of proinflammatory cytokines in COVID-19 patients [3].

However, so far, it remains unclear why SARS-CoV-2 may lead to variable cytokine modulation and different phenotypes of patients, maybe linked to both viral characteristics and host susceptibility.

Reviewing different clinical studies on COVID-19 cohorts, we noticed that radiological aspects of lung involvement in patients with COVID-19 are mainly represented by ground-glass opacities (GGO) (86%) or mixed GGO and consolidation (64%) and vascular enlargement in the lesion (71%) [2,4]. These resemble findings characterizing pneumonia of autoimmune diseases (i.e. RA, systemic sclerosis and eosinophilic granulomatosis with polyangiitis), and autoinflammatory diseases (i.e. systemic juvenile idiopathic arthritis, SJIA) [5].

During autoinflammatory and autoimmune syndromes, it has been hypothesized that triggering factors, such as viruses, drive the activation of an aberrant innate and acquired immune response, with increased synthesis of cytokines, mainly TNF-α, IL-6 and IL-1β, IL-17, IL-18, in genetically predisposed individuals [6]. In particular, following an environmental stimulus, transcriptional and post transcriptional mechanisms are not able to control cytokines synthesis and release, leading to their dysregulation and overproduction with overresponse of innate and adaptive mechanisms [6,7]. Remarkably, in SJIA patients, the pulmonary involvement triggers a hyper-inflammatory reaction and occurrence of secondary haemophagocytic lymphohistiocytosis (sHLH), since the up-regulation of IFN-signature, IL-1β and IL-6 may be observed [5,8].

Of note, Mehta et al. suggested that COVID-19 severity is associated with a cytokine storm syndrome resembling sHLH [9]. Also for sHLH, it is hypothesized that environmental factors may trigger or exacerbate an aberrant innate and acquired immune response, with massive synthesis of cytokines in genetically susceptible subjects [10].

Not surprisingly, as well as in course of infectious diseases, sHLH has been described in patients with autoimmune and autoinflammatory syndromes, following a triggering stimulus [10].

As highlighted by Favalli et al., at present, different antirheumatic strategies are currently included in the treatment protocol for the management of COVID-19 infection. In particular, anti-cytokine therapy, by the use of the IL-6 humanized monoclonal antibody, tocilizumab, successfully used for autoimmune and autoinflammatory diseases, is under investigation for COVID-19 patients with severe pneumonia [11].

A growing body of evidence showed that genetic host characteristics, such as IL-6 polymorphisms, may contribute to virus susceptibility, in specific populations and ethnicities [12], thus, in our opinion, the shared pathogenetic mechanisms and clinical-radiological aspects between hyper-inflammatory diseases and COVID-19 may suggest that SARS-CoV-2 could act as a triggering factor for the development of a rapid autoimmune and/or autoinflammatory dysregulation, leading to severe interstitial pneumonia, in genetic predisposed individuals.

Further studies are advocated to clarify our hypothesis. These could be useful not only for considering new therapeutic strategies but also for better addressing genetic susceptibility studies (i.e. on interleukins polymorphisms and Human Leucocyte Antigen) of COVID-19 patients for pneumonia risk stratification.

Declaration of Competing Interest

The authors declared that there are no conflicts of interests.

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