



# Similarities between COVID-19 and anti-MDA5 syndrome: what can we learn for better care?

To the Editor:

The coronavirus disease 2019 (COVID-19) pandemic has struck worldwide, leading to more than 7 million cases by June 2020, with a ~5.5% mortality rate, mainly due to acute respiratory distress syndrome (ARDS) [1].

Current conventional treatment is mainly based on support therapy and there is an urgent need for effective, specific treatments.

As yet, no direct-acting antiviral drugs have demonstrated efficacy in the disease. In contrast, increasing evidence indicates an immune-mediated pathophysiology that is paving the way for the evaluation of immunomodulation strategies [2]. In support of this view, we would like to highlight the striking similarities between COVID-19 and a rare autoimmune disease: the anti-MDA5 syndrome.

The hallmark of this disease is the presence of auto-antibodies targeting MDA5, an intracellular sensor of viral RNA (including coronavirus) that triggers the innate immune response [3]. The syndrome is characterised by systemic signs resembling COVID-19, and ARDS is the main cause of death (figure 1a) [4, 5]. In addition, chest computed tomography findings [6], as well as blood cytokine profiles [7, 8] are very similar in the two conditions (figure 1b and c), further supporting common pathophysiological mechanisms. So far, there is no evidence that patients with COVID-19 have anti-MDA5 autoantibodies but, while other diseases causing ARDS feature “cytokine storm”, few show such similarities with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

Beyond these similarities, anti-MDA5 syndrome responds to glucocorticoids and immunomodulatory drugs, among which tofacitinib (a JAK inhibitor) [9, 10] and a combination of tacrolimus and

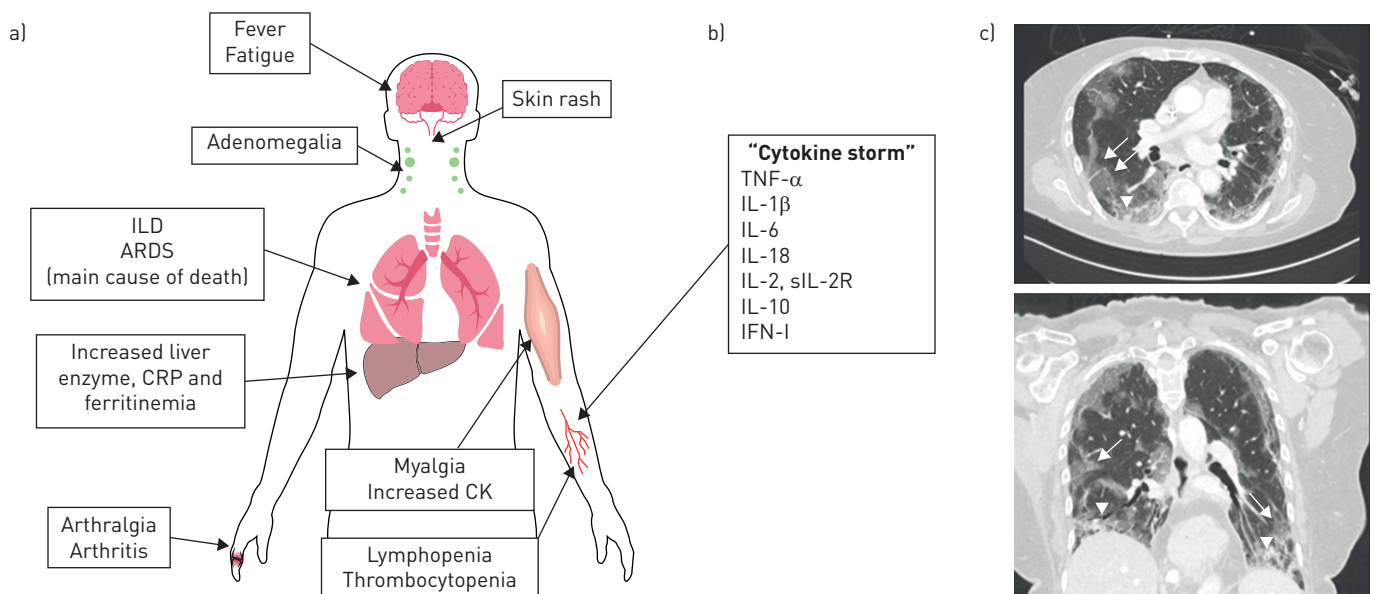


FIGURE 1 a) Clinical and biological features of anti-MDA5 syndrome. b) Cytokines whose levels are increased in anti-MDA5 syndrome patients' serum. c) High-resolution computed tomography of an anti-MDA5 syndrome patient, showing bilateral peripheral subpleural ground-glass opacities prevailing in the lower lobes (arrows), with limited consolidation (arrowheads). ILD: interstitial lung disease; ARDS: acute respiratory distress syndrome; CRP: C-reactive protein; CK: creatine kinase; TNF- $\alpha$ : tumour necrosis factor- $\alpha$ ; IL: interleukin; s-IL-2R: soluble IL-2 receptor; IFN-I: interferon type I.

cyclophosphamide [11] have recently been shown to improve survival *versus* conventional strategies. Likewise, even though an immunological reaction is necessary to eliminate SARS-CoV-2 infection and corticosteroids are not currently recommended by the World Health Organization [12], in severe COVID-19 patients, dexamethasone has been reported to improve survival [13] and ruxolitinib (another JAK inhibitor) results in a greater chest tomography improvement and faster clinical improvement with no death compared with standard of care [14]. Moreover, tacrolimus has been shown to inhibit SARS-CoV replication [15].

These data support further evaluation of employing such an immunomodulatory strategy in COVID-19.



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**Similarities between COVID-19 and anti-MDA5 syndrome support further evaluation of employing an immunomodulatory strategy in COVID-19** <https://bit.ly/3dN6lJ8>

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