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.

Although we agree on the need to consider attentively the dosage of immunosuppressive drugs in patients with sarcoidosis to prevent deterioration from COVID-19, we would like to highlight some points.

First, most studies that evaluated the risk of infection were conducted mostly in rheumatoid arthritis, not sarcoidosis.[2] Immunomodulation differs significantly in sarcoidosis vs the other rheumatic disorders, and the macrophage/T-cell system alteration and granulomas formation represent key steps to trigger and maintain persistent inflammation. Immunosuppressive drugs, therefore, could interfere differently with the immune system.

Second, the specific effect of immunosuppression in the management of COVID-19 is still under study. Preliminary results from the RECOVERY trial have demonstrated that low dexamethasone doses significantly reduce the 28-day risk of death in patients with COVID-19 who are receiving invasive mechanical ventilation or oxygen.[3]

The interruption of the hyperinflammatory response has beneficial effects in the early phase of the disease; a rapid dose reduction of immunosuppressive agents such as glucocorticoids thus could worsen the COVID-19 progression. Considering also that an acute relapse of sarcoidosis could contribute to reduce the lung function, we suggest much caution in envisaging a drastic reduction of immunosuppressive therapy.

Third, specifically regarding tocilizumab, even if the compound has demonstrated some benefits in terms of oxygen status improvement in severe COVID-19 pneumonia, its effects on the global survival and in patients with sarcoidosis are unknown.[4]

Last, the recent observation that patients with autoimmune disorders who are treated with disease-modifying antirheumatic drugs are not at increased risk of severe COVID-19 does not exclude the fact that those patients who receive IL-6 or IL-12/IL-23 axis inhibitors might be protected against the severe forms of the disease.[5]

In this view, it could be useful to consider different treatment scenarios, based on the presence of COVID-19 coinfection, baseline treatment, and phase of both diseases. Ad hoc studies are needed urgently to investigate the interaction between the two disorders and how the immunosuppressive treatment could change their natural history.

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Response

To the Editor:

We would like to thank Tana et al for their interest in our commentary.[1] Their comments highlight the ongoing controversy surrounding the issue of management of patients with sarcoidosis during the coronavirus disease 2019 (COVID-19) pandemic. Large cohort studies addressing the issue of COVID-19 in patients with sarcoidosis are lacking. Thus, any guidance is based on expert opinion and extrapolation from other diseases. Obviously, such extrapolation is subject to errors, especially if these diseases are significantly different.

Although we agree with the assertion of Tana et al that immunomodulation differs in sarcoidosis vs other rheumatic diseases, it is unclear how great these differences are. More importantly, it is unclear if these differences have any relevance in terms of the risk and outcomes of infection from immunosuppression.

We also question the comments of Tana et al concerning the risks of corticosteroid therapy. It is true that dexamethasone has lowered the mortality rate of patients with severe COVID-19 infection who are receiving mechanical ventilation. However, it recently has also been shown that patients with rheumatic disease receiving ≥10 mg/d of prednisone had significantly higher rates of hospitalization from COVID-19 infection than those receiving <10 mg/d.[2] These seemingly conflicting data suggest that it is too simplistic to state that an immunosuppressive drug is helpful or harmful in the face of COVID-19 infection without considering the timing of administration. It may be that immunosuppression initially allows COVID-19 to gain a foothold in the body and replicate rapidly. However, immunosuppression may mollify a subsequent cytokine storm and/or the development of an overly aggressive adaptive immune response.

The main premise of our article was that our recommendations are in keeping with the standard management of sarcoidosis to minimize immunosuppression of non-life-threatening disease and to monitor carefully for exacerbations. Although we are extrapolating from other diseases, the evidence is robust that corticosteroids pose a great risk of infection that appears higher than other immunosuppressive agents.[3-5]

The game is continuing to change. We acknowledge that our understanding of COVID-19 infection in sarcoidosis is currently very limited. As we await more evidence-based recommendations, we should remain vigilant to the risk of concomitant infections in patients with sarcoidosis. Our decision-making should take into consideration the rapidly changing landscape of the available COVID-19 therapeutics.

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