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EDITORIAL COMMENT – OPEN ACCESS

Anti-IL-1 Therapy in Management of Patients with Behçet's Disease During the COVID-19 Pandemic

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Coronavirus disease 2019 (COVID-19) emerged in late 2019 and became a global challenge. Patients with rheumatic diseases are one of the groups that is especially vulnerable to viral infection due to the immunosuppressive medications they use. However, accrued data regarding the pathophysiology of COVID-19 led to an inspiration that antirheumatic drugs may be useful in the management of this new disease (1). Interleukin 1 (IL-1) is a pro-inflammatory cytokine and a mediator of local and systemic inflammation. IL-1 blockade has proven effective in several rheumatic diseases, including autoinflammatory syndromes (2). The novel coronavirus may induce aberrant macrophage activation and cytokine storm syndrome, resulting in coagulopathy and multi-organ involvement in some patients (3). Several drugs, including corticosteroids, IL-1 blockade, Janus kinase inhibitors, and the anti-IL-6 receptor tocilizumab, are currently under evaluation in several clinical trials for use in the management of macrophage activation syndrome associated with COVID-19 (4–8). For example, anakinra, an IL-1 inhibitor, was administered subcutaneously to patients with COVID-19-associated pneumonia at 100 mg twice daily for 72 hours and 100 mg/day for the following 7 days or 300 mg for 5 days, tapered to 200 mg daily for the next 2 days, and 100 mg for another day, both of which yielded benefits of reducing the need for invasive mechanical ventilation and mortality (4).

Behçet's disease (BD) is a type of vasculitis that may affect vessels of variable size and is characterized by recurrent oral aphthae, genital ulcers, skin lesions, uveitis, arthritis, central nervous system involvement, and gastrointestinal lesions (9). BD requires a therapy tailored to organ and system involvement. The management strategy may include synthetic disease-modifying anti-rheumatic drugs (DMARDs), such as colchicine, azathioprine, cyclosporine-A, and corticosteroids, and biologic DMARDs, such as tumor necrosis factor-alpha inhibitors (TNFi) and IL-1 blockers (10). Some studies suggest that IL-1 might represent a good therapeutic target for patients with mucocutaneous manifestations and refractory eye involvement (11).

General recommendations for patients with BD during the COVID-19 pandemic include nonspecific precautions, such as maintaining social distance and good hygiene measures, and awareness of how to get medical attention in case of emergency (12). The Behçet's Centres of Excellence in the United Kingdom recommend the Pfizer/BioNTech and the Oxford/AstraZeneca COVID-19 vaccines for Behçet's patients unless a significant flare is present (13). BD may increase the risk for COVID-19 infection, and some characteristics, including internal organ involvement, comorbidities, and/or use of immunosuppressive agents, may necessitate further formal shielding (12). Since data on the course of COVID-19 in BD are as yet insufficient, current considerations are based on first principles and lack strong scientific evidence. In patients without COVID-19, these principles are to reduce the use of immunosuppressive drugs together with postponing biologic agents in high-risk scenarios. In cases of BD patients who have contracted COVID-19, local corticosteroids and colchicine may be continued, whereas it recommended that DMARDs like azathioprine, cyclosporin, methotrexate, and apremilast be discontinued. The decision to continue or suspend biologic DMARD use, including TNFi or IL-1 receptor inhibitors, depends on whether it is in use for a severe, organ-threating condition. A specialist should be contacted in the event that continuation of immunosuppressive therapy might be required based upon individualized assessment. More evidence is required to firmly establish the potential favorable effects of these agents in the prevention or treatment of some complications of COVID-19, including cytokine storm (12). Based on the proven efficacy of IL-1 inhibitors in macrophage activation syndrome, we believe that cautious use of these agents may be continued throughout a COVID-19 infection in selected cases with serious organ involvement.

However, given the delicate immune balance in these patients, scientific contributions regarding real-life experience are of great importance. There are limited data of the outcome of patients with BD since the COVID-19 outbreak. A case series from Turkey presented data of 10 BD patients who were on colchicine (5 patients), aza-

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thioprine (3 patients), TNFi (3 patients), and oral corticosteroids (2 patients); none were on an IL-1 blocker. Since the frequency of pneumonia was high (60%) and thrombosis emerged in 1 patient, the authors concluded that close monitoring of BD patients is warranted (14). This novel infection remains a mystery to rheumatologists, who are rather familiar with infectious diseases mimicking or triggering rheumatic conditions. Upcoming reports from ongoing registries of COVID-19 and inflammatory diseases are required to further elucidate these issues.

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