Post-COVID-19 interstitial lung disease: A new treatment challenge in rheumatoid arthritis patients

Enfermedad pulmonar intersticial post-COVID 19: Un nuevo reto de tratamiento en pacientes con artritis reumatoide

Dear Editor:

The coronavirus disease 2019 (COVID-19) is the result of infection with the SARS-CoV-2 virus that is making us live one of the worst pandemics of the 21st century. It has affected the management of rheumatoid arthritis (RA), since these patients are treated with immunosuppressants such as disease-modifying drugs and biologics (bDMARDs). At the beginning of the pandemic, when a patient with RA required hospital admission for COVID-19, immunosuppression was suspended until improvement.[1] Over time, we have learned about SARS-CoV-2 infection, showing that use of bDMARDs is not associated with worse outcomes[2] except for rituximab and JAK inhibitors.[3]

However, the management is challenging. When a patient with RA without prior interstitial lung disease (ILD) is hospitalized with severe SARS-CoV-2 pneumonia passes the acute phase, and suffers a flare of RA, there is an understandable concern to reintroduce immunosuppression. In this phase, the patient is normally still on low-dose steroid treatment, but the bDMARDs that can be used for SARS-CoV-2 infection have been stopped (such as tocilizumab or bariticinib, also useful for RA). Therefore, the rheumatologist must decide to reintroduce the RA baseline treatment or to change it due to the new ILD secondary to the virus. We would like to share our experience.

We present the case of a 72-year-old woman with RA since 1997 treated with 25 mg of methotrexate (MTX) weekly and 125 mg of abatacept weekly, in remission. In 2018 she complained of a dry cough and was studied with CT scan (normal, Fig. 1A), and finally diagnosed with gastric reflux.

In March 2020, she was admitted to the intensive care unit for severe global bilateral SARS-CoV-2 pneumonia. MTX and abatacept were suspended, she was intubated and treated with corticosteroids, antivirals, and later tocilizumab. Her evolution was favorable, but on the 40th day of hospitalization, despite maintaining 0.5 mg/kg of prednisone, she presented a severe polyarticular RA flare. At that time, MTX and abatacept were reintroduced. She has been in remission to date.

In September 2020, one month after hospital discharge, she was still reporting stable dyspnea on moderate efforts, the CT scan was as shown in Fig. 1B (ground glass areas and thickening of interlobular septa in both lower lobes, patchy ground consolidation in all lobes, and honeycomb changes in the left upper lobe), and the functional tests were as follows: FEV1 2140 ml (104% of predicted value), FVC 2620 ml (99%), DLco (corrected for hemoglobin) 3030 mmol/kPa/min (49%). She was treated by pneumologists with a descending dose of 0.5 mg/kg of prednisone for a month. Six months later functional tests improved – FEV1 2240 ml (111%), FVC 2740 ml (105%), DLco 3950 mmol/kPa/min (64%) – as well as the CT scan (Fig. 1C). To date, she has not reported dyspnea and her baseline saturation is 99%. She has maintained MTX and abatacept without any adverse event or RA flare. NSAIDs or other corticosteroids have not been needed.

There is another report of a RA patient maintaining 10 mg of MTX during the hospitalization period, and her condition remained stable.[4] MTX does not have an increased risk of infections [5]and is not associated with an increased risk of RA-ILD in RA.[6] We suggest, sustained on current published data,[7–9] that reintroducing baseline treatment when RA patients surpass the critic phase of COVID-19 disease does not worsen the evolution of ILD secondary to SARS-CoV-2, as it appears to be independent. However, given that the bDMARD in our case is abatacept, which has a

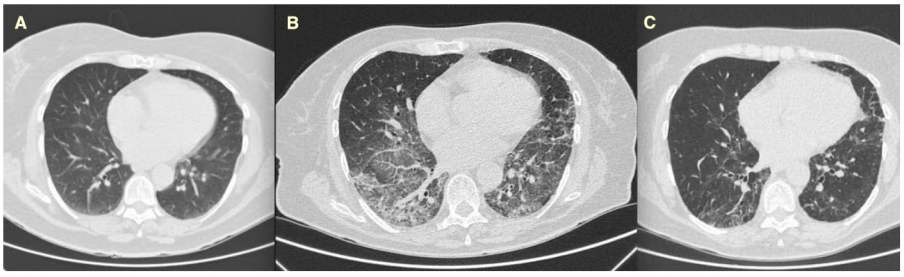

Fig. 1. Evolution of the CT scan of the patient.

good ILD profile in patients with RA, it would be of great interest to collect more data with all DMARDs and bDMARDs in these patients.

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Long COVID-19 and myalgic encephalomyelitis/chronic fatigue syndrome: Similarities and differences of two peas in a pod

COVID-19 persistente y encefalomielitis miálgica/síndrome de fatiga crónica: similitudes y diferencias

Dear Editor,

Coronavirus disease 2019 (COVID-19) is a highly contagious respiratory disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Prolonged recovery of COVID-19 symptoms, so-called Long COVID-19, has been described even in patients who have mild symptoms and did not required hospitalisation. Various studies showed that at least one out of ten COVID-19 symptomatic patients develop Long COVID-19.[1]

Although there is an absence of a evidence-based clinical practice guidelines neither a clear aetiopatogenesis, a clinical case definition of post-COVID-19 condition was proposed across the International Severe Respiratory and Emerging Infection Consortium (ISARIC) and the World Health Organization (WHO). Long COVID-19 occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis.[2]

Patients may present with a multifaced and marked variability of non-specific symptoms that might be fluctuate or relapse over time. Common symptoms include fatigue, pain, dispnoea, sleep disturbances, physical sequelae, psychological distress, and cognitive impairment but also others which generaly have an impact on quality of life. Symptoms may be persist from the initial illness or new onset, following initial recovery from an acute COVID-19 epsiode.[2] These clinical manifestations can lead to symptoms commonly presented in patients with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS).

ME/CFS is a long-term complicated, heterogeneous, multisystemic and disabling disorder, that was first proposed in 1988 by Holmes et al. to redefine the chronic mononucleosis syndrome as a post-viral fatigue syndrome (PVFS). It is diagnosed according to the 1994 Fukuda criteria, the Canadian consensus document published in 2003 or, more recently, the international consensus criteria of 2011; that offers a review on its physiopathology, symptoms and treatment.[3]

It is characterised by prolonged generalised and abnormal fatigue after exercise and non-remitting significantly with rest, recurrent headache and problems of concentration and memory, which are of recent appearance and that have lasted for at least 6 months. It is accompanied by such other symptoms as tender lymph nodes, musculoskeletal pain, sleep disruption and psychiatric problems.[4]

Although the cause is unclear, research into the aetiopatogenesis is ongoing. Female sex, type A personality, and family aggregation are established as a predisposing factors. Infectious agents (human herpesvirus family), toxicity exposure, and psychological and social experience are associated as a precipitating and trigger factors. Other conditions such as advanced age, delay in diagnosis, severe initial involvement, comorbidity, and adaptive disorder are those that maintain the illness once it has become established. Accumulating data indicates a relationship between redox imbalance, mitochondrial dysfunction and oxidative stress pathways in patients with ME/CFS. These abnormalities were also found in patients with Long COVID-19 and suggests that the two disorders may share common pathophysiological features.

However, any potential relationship between ME/CFS and Long COVID-19 is complicated, due to the great heterogeneity of both in its clinical expression and the lack of sensitive screening and standardised instruments to order its different symptoms or agreement regarding the diagnostic criteria. Based on the hypothesis that post-COVID-19 patients can develop a PVFS that is very strikingly similar to ME/CFS, we suggest subagrouping patients with Long COVID-19 into two clinical clustering phenotypes (Table 1).