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.

Surprisingly, very few studies are examining anti-TNF therapy as a potential treatment for COVID-19. The CATALYST randomised trial (ISRCTN40580903) is investigating the use of infliximab in patients admitted to hospital with clinical features of COVID-19. This trial is recruiting in the UK, where rates of hospital admission are now low and accrual rates are commensurately low. A pilot study in 17 patients is ongoing at Tufts Medical Center (Boston, MA, USA; NCT04425538) and another pre-hospital study is planned in the UK (ISRCTN33260034) to establish whether anti-TNF therapy can prevent progression to severe illness. These trials face considerable recruitment challenges because of the vast array of therapies under investigation.

There is great imperative to find effective treatments for COVID-19. The small effect size of the most promising agents so far means that we need to continue the search for agents with greater efficacy. The potential of anti-TNF therapy as a treatment for COVID-19 is supported by both biological plausibility and observational clinical data. Few current treatments under investigation have this level of supportive evidence. There is a long history of safe use of anti-TNF therapy in a diverse range of diseases, and supply is plentiful with many originator products available as well as many biosimilars. Anti-TNF therapy now has huge potential. We need to urgently investigate its value through prioritisation of clinical trial resources worldwide.

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Viral arthritis and COVID-19

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The current outbreak of COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is characterised by clinical signs and symptoms such as interstitial pneumonia, fatigue, and headache.[1] Arthralgia is one of the symptoms that occurs in patients with COVID-19, and is present in 14·9% of cases.[1] However, data on rheumatic and inflammatory manifestations (such as arthritis) are scarce.

Viral infections are a known cause of acute arthralgia and arthritis; monoarticular arthritides can occur after infection by various pathogens, including hepatitis B virus, hepatitis C virus, parvovirus, Epstein-Barr virus, HIV, alphavirus (eg, Chikungunya virus), and Zika virus.[2] Diagnosis of viral arthritis can be difficult to confirm, nonetheless it should be considered in all patients with sudden onset of polyarticular phlogosis; to date, approximately 1% of all cases of acute inflammatory arthritis have a viral origin.[3]

Ambient respiratory viral infections have been associated with an increased number of cases of rheumatoid

arthritis (especially in women and older patients), suggesting that respiratory viral infections might be an environmental risk factor for the development of rheumatoid arthritis.[4]

SARS-CoV-2 enters the cell via the angiotensin-converting enzyme-2 (ACE-2) and it is sensed by Toll-like receptor-7 (TLR7); bioinformatic analyses have shown that the SARS-CoV-2 genome contains a large number of fragments that are recognised by TLR7. In addition to its expression in immunological cells, TLR7 is expressed predominantly in the lung and bronchus, thus allowing SARS-CoV-2 to be highly recognised in the regions of its tropism. TLR7 activation leads to activation of c-Jun N-terminal kinase and nuclear factor-κB signaling, thus leading to the production of IL-6 and IL-12p40.[5] Therefore, it is conceivable that patients with COVID-19 might display symptoms and signs of inflammation, such as a viral arthritis.[6] Thus, from the point of view of a rheumatologist, evaluating the role of SARS-CoV-2 in inflammatory arthritis is essential for diagnosis.

Serological tests could be useful to establish a diagnosis, but the possibility that low-titre positivity for autoantibodies (such as rheumatoid factor [RF] or antinuclear antibody [ANA]) could be detected in viral arthritis must also be taken into account.[7]

A detailed analysis of epidemiological, clinical, and serological characteristics is required to help physicians diagnose viral arthritis; oligoarticular or polyarticular involvement (either symmetric or asymmetric), good response to NSAIDs, a clinical manifestation characterised by an early onset (within the first weeks of symptomatic infection) and a self-limiting presence are the elements that orientate toward a viral arthritis (appendix p 1).

See Online for appendix

We would like to share the case of a white woman, aged 58 years, who had a non-severe manifestation of COVID-19, and was treated with only paracetamol. The patient was tested for SARS-CoV-2 with qRT-PCR nasal swabs when admitted to hospital. 25 days after her prodrome of infection (arthralgia, fever, cough, nausea, diarrhoea, and dysgeusia), an ankle arthritis occurred; laboratory tests showed a slight increase in C-reactive protein (7·36 mg/L, normal range 0–5), relative lymphopenia (1·29 cells per 10^9/L, normal range 0·76–4·80; 12·5%, normal range 19–48), and normal liver and kidney function. ANA, antiextractable nuclear antigen, antidouble-strand DNA, RF, and anticyclic citrullinated peptide antibodies were negative. Additionally, testing for human leukocyte antigen-B27 was done to exclude predisposing factors, given it is strongly associated with spondyloarthropathies. On ultrasound, a synovial hypertrophy was detected in the tibiotarsal anterior and lateral recess with power Doppler signal score of 2 (according to OMERACT score). No signs of tenosynovitis emerged in the anterior and posterior compartments examined, but there was evidence of tendonitis of the Achilles tendon (appendix p 1). This manifestation showed a good response to NSAIDs (ibuprofen 600 mg twice a day). The nasopharyngeal swab was negative for SARS-CoV-2 30 days after the first symptoms. For confirmation, a second nasopharyngeal swab was taken 7 days after the last negative one. The initial symptoms of fever, cough, nausea, diarrhoea, and dysgeusia improved progressively until they resolved completely within 30 days. In particular, the fever (between 38°C and 39°C) and cough lasted about 10 days, the nausea and diarrhoea about 3–4 days, and dysgeusia about 20 days. The arthralgia resolved after ibuprofen, but the ultrasound examination remained stable after 30 days from pharmacological treatment, and synovitis (indicated by a power Doppler signal) was still present, even in the absence of pain. To date, the patient continues to be in rheumatological follow-up.

To our knowledge, this is the first case of arthritis in a COVID-19 patient in Europe; to date, cases of arthralgia have only been reported in China[1] and a single case of arthritis was reported in Thailand.[8]

Further studies are necessary to understand the pathogenesis of COVID-19 and its different clinical phenotypes, because it is important to recognise its correlation with arthritis by analysing the presence of both the virus and the antibodies in the synovial tissue; the incidence and evolution of inflammatory manifestations should be investigated as well.

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