Clinical case

Reactive arthritis after COVID-19 infection

Keisuke Ono,1 Mitsumasa Kishimoto,1 Teppei Shimasaki,2 Hiroko Uchida,1 Daisuke Kurai,2 Gautam A Deshpande,3 Yoshinori Komagata,1 Shinya Kaname1

ABSTRACT

Reactive arthritis (ReA) is typically preceded by sexually transmitted disease or gastrointestinal infection. An association has also been reported with bacterial and viral respiratory infections. Herein, we report the first case of ReA after the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. This male patient is in his 50s who was admitted with COVID-19 pneumonia. On the second day of admission, SARS-CoV-2 PCR was positive from nasopharyngeal swab specimen. Despite starting standard dose of favipiravir, his respiratory condition deteriorated during hospitalisation. On the fourth hospital day, he developed acute respiratory distress syndrome and was intubated. On day 11, he was successfully extubated, subsequently completing a 14-day course of favipiravir. On day 21, 1 day after starting physical therapy, he developed acute bilateral arthritis in his ankles, with mild enthesitis in his right Achilles tendon, without rash, conjunctivitis, or preceding diarrhoea or urethritis. Arthrocentesis of his left ankle revealed mild inflammatory fluid without monosodium urate or calcium pyrophosphate crystals. Culture of synovial fluid was negative. Plain X-rays of his ankles and feet showed no erosive changes or enthesophytes. Tests for syphilis, HIV, anti-streptolysin O (ASO), Mycoplasma, Chlamydia pneumoniae, antinuclear antibody, rheumatoid factor, anticyclic citrullinated peptide antibody and Human Leukocyte Antigen-B27 (HLA-B27) were negative. Gonococcal and Chlamydia trachomatis urine PCR were also negative. He was diagnosed with ReA. Nonsteroidal Anti-Inflammatory Drug (NSAID)s and intra-articular corticosteroid injection resulted in moderate improvement.

INTRODUCTION

Reactive arthritis (ReA) is a known entity, typically causing asymmetric monoarthritis or oligoarthritis involving lower limbs (ankles and knees), and usually occurring 1–3 weeks after sexually transmitted or gastrointestinal infection.1 Although less described in the literature, respiratory bacterial infections such as Chlamydia psittaci, Chlamydia pneumoniae, Staphylococcus aureus and Streptococcus pneumoniae or viral infections have been associated with some cases of ReA. Herein, we report the first case of ReA after SARS-CoV-2 infection.

CASE REPORT

This male patient is in his 50s who was admitted for COVID-19 pneumonia. He had a medical history of steatohepatitis. He was in his usual state of health until 5 days prior to admission when he developed fever with chills and severe fatigue. He was referred to our hospital from a neighbouring clinic for unremitting symptoms. At admission, he was mildly hypoxic (SpO2 of 93% in room air) and laboratory tests showed white blood cell (WBC) of 3.6×103/μL, platelet of 12.3×104/μL, serum creatinine of 1.85 mg/dL, lactic dehydrogenase (LDH) of 39 8IU/L and C-reactive protein (CRP) of 8.31 mg/dL (table 1). Chest CT scan revealed bilateral ground-glass opacities, and on August 8, 2022 by guest. Protected by copyright. http://rmdopen.bmj.com/ RMD Open: first published as 10.1136/rmdopen-2020-001350 on 6 August 2020. Downloaded from http://rmdopen.bmj.com/ on August 8, 2022 by guest. Protected by copyright.
14-day course of favipiravir with clinical resolution of pneumonia. On day 21, 1 day after starting physical therapy, he developed acute bilateral arthritis in his ankles, with mild enthesitis in his right Achilles tendon. He had no rash, conjunctivitis, or preceding diarrhoea or urethritis. Arthrocentesis of his left ankle revealed mild inflammatory fluid without monosodium urate (MSU) and calcium pyrophosphate crystals. Culture of synovial fluid was also negative. Plain X-rays of his ankles and feet showed no erosive changes or enthesophytes. Tests for syphilis, HIV, ASO, Mycoplasma, Chlamydia pneumoniae, antinuclear antibody, rheumatoid factor, anticyclic citrullinated peptide antibody and HLA-B27 were negative (table 2). Gonococcal and Chlamydia trachomatis urine PCR were also negative. He was diagnosed with ‘ReA’; NSAIDs and intra-articular corticosteroid injection resulted in moderate improvement.

**DISCUSSION**

SARS-CoV-2 is now known to cause a host of extrapulmonary complications, including cardiovascular, neurologic and dermatologic sequelae, many occurring or lasting for weeks after infection. We report the first case of ‘ReA’ after SARS-CoV-2 infection.

No diagnostic or classification criteria have been established for ReA, but the American College of Rheumatology has issued general guidelines, and in 1999, the 4th International Workshop on ReA discussed the term ‘reactive arthritis’, proposing its use only for a clinical picture and microbes associated with HLA-B27 and spondyloarthritis. Consequently, the definition of ReA is now based on a diagnostic criterion (table 3) that largely focuses on enteral or urethral infections. However, we previously reported a case of clinical ReA after HIV infection; a syndrome consistent with ReA has also been reported with dengue and chikungunya virus, parvovirus B19, rubella and measles vaccines. In our case, the arthritis occurred precisely 3 weeks after the infectious episode; without a competing source of identifiable extra-articular infection, and synovial fluid cultures negative for bacteria, we are strongly led to a diagnosis of clinical ReA.

ReA tends to occur most often in men between ages 20 and 50. A 30–50% of patients with ReA carry HLA-B27. Although patients without HLA-B27 can develop ReA, as is in our case, some degree of genetic susceptibility is considered necessary, since ReA occurs in only 7–15% of infected population-level subjects. The association of...
positivity may be a poor prognostic factor, as a previous study has shown that the presence of HLA-B27 in ReA has been linked to more severe disease, higher frequencies of sacroiliitis and extra-articular manifestations, and an increased likelihood of persistent arthropathy.\textsuperscript{10}

A limitation of our study is that viral arthritis is also a known entity and we are unable to completely exclude an acute viral arthritis, though this typically occurs during the acute fever episode,\textsuperscript{11} and the pattern described here was notably different. Additionally, bacterial coinfections are reported in severe COVID-19 patients\textsuperscript{12} and ReA due to an occult bacterial respiratory coinfection is possible. However, sputum and blood cultures prior to initiation of empirical antibiotics failed to identify a competing bacterial cause, and the clinical course was not consistent with occult infection. Finally, our patient developed mild hyperuricemia, a known side effect of favipiravir,\textsuperscript{13} and raising the possibility of a crystal arthropathy as a cause of symptoms. Careful synovial fluid analysis did not identify MSU crystals, which ruled out gouty arthritis.

To conclude, we report the first case of ‘ReA’ after SARS-CoV-2 infection. Our findings offer an opportunity to improve both early diagnosis and treatment of ‘ReA’ during the COVID-19 pandemic. A ‘definite’ diagnosis of ReA is based on the fulfilment of both major criteria and a relevant minor criterion, while a ‘probable’ diagnosis is characterised by both major criteria but no relevant minor criterion or one major criterion and one or more of the minor criteria. The identification of the trigger infection is also required.

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ORCID iD Keisuke Ono http://orcid.org/0000-0002-2651-1509

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