

Letter to the Editor (Case report)

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Reactive arthritis after SARS-CoV-2 infection

Key message

- ReA should be considered in patients with acute arthritis after SARS-CoV-2 infection.

DEAR EDITOR, ReA, a subtype of SpA, is a sterile inflammatory arthritis, predominantly involving the lower extremities. It usually occurs 1–3 weeks after a remote mucosal infection (gastrointestinal or genitourinary). It is also known as Reiter's syndrome in the presence of the classical triad: urethritis in men and cervicitis in women, ocular inflammation (conjunctivitis or uveitis) and arthritis of large joints. *Chlamydia trachomatis*, *Campylobacter*, *Salmonella*, *Shigella* and *Yersinia* are a few of the common bacterial infections that can cause ReA [1]. A few other bacteria and viruses have also been associated with the pathogenesis of ReA. The novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as a cause of ReA has been reported previously in six cases [2–7]. Here, we report a case of ReA after SARS-CoV-2 infection. Written informed consent was obtained from the patient.

A 27-year-old female was hospitalized after 2 days of fever and body aches. On evaluation, SARS-CoV-2 RT-PCR from a nasopharyngeal swab was positive, and CT imaging of the chest showed bilateral peripheral ground glass opacities COVID-19 Reporting and Data System (CO-RADS-4). Other laboratory parameters during hospitalization showed leucopenia ($3200/\text{mm}^3$), elevated CRP (114 mg/l) and D-dimer (three times upper normal limit), and normal levels of lactate dehydrogenase, ferritin and IL-6. She was diagnosed with coronavirus disease 2019 (COVID-19) pneumonia and received 1 mg/kg CS in the form of oral methylprednisolone and favipiravir. Oxygen saturation was well maintained on room air throughout the disease course. Fever subsided on day 3 of hospitalization, and she was discharged on day 8 with tapering doses of CS. Two weeks after testing positive for SARS-CoV-2 infection, while on 0.25 mg/kg of CS, she developed acute onset arthritis in both lower extremities and relatively mild arthritis in the small joints of the right hand. She did not have any history of recent diarrhoea, cervicitis or uveitis.

On examination, bilateral knee, ankle and midfoot joints were extremely tender and swollen. Mild tenderness was also noted in the small joints of the right hand (wrist, MCP and PIP joints). The rest of the physical examination was normal. RT-PCR for SARS-CoV-2 was negative. RF was positive in low titres. ACPA, ANA and

HLA-B27 were negative. A probable diagnosis of ReA secondary to SARS-CoV-2 infection was made. She received NSAID and additionally required oral opioid analgesic to manage the pain. CS was gradually tapered and stopped over next 3 weeks. At 4-week follow-up, the arthritis had improved significantly, allowing withdrawal of opioid analgesic and tapering of NSAID.

Although ReA causes asymmetric oligoarthritis in the lower extremities, a mild form of upper limb arthritis can also occur, as seen in our patient [6]. In contrast to this, Danssaert *et al.* [5] reported arthritis of unilateral hand joints without involvement of lower extremities. Liew *et al.* [4] described a patient with acute right knee arthritis manifesting 3 days after fever and simultaneously being positive for SARS-CoV-2 infection. Schenker *et al.* [6] and De Stefano *et al.* [7] described cases of ReA associated with cutaneous vasculitis and psoriatic skin lesions, respectively. The patient reported by Ono *et al.* [2] had severe respiratory distress requiring mechanical ventilation, whereas respiratory involvement was milder in the other five patients [3–7], including our patient. All these cases are summarized in Table 1.

Other manifestations of ReA include inflammatory back pain, dactylitis, enthesitis, tendinitis and bursitis. There are no specific laboratory tests for ReA, and diagnosis relies on the typical clinical presentation with detection of the triggering infection [8]. Arthritis persists for >6 months in 30–50% of patients [1]. The most effective treatment for ReA is NSAID. IA glucocorticoid can be used for mono- or oligoarticular disease. In chronic cases, SSZ can be effective when started within 3 months of disease onset [8].

Our patient developed lower limb predominant inflammatory arthritis, 2 weeks after SARS-CoV-2 infection. The presence of RF in low titres was possibly attributable to an immune response to the recent infection. The classical clinical picture, a preceding infection, absence of other autoantibodies, absence of autoimmunity in the family and response to NSAID, supported the diagnosis of ReA.

This case, along with previously reported cases, suggest SARS-CoV-2 infection as an aetiology in the pathogenesis of ReA. More observations are required to strengthen this association.

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Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article.

TABLE 1 Reported cases of possible reactive arthritis after SARS-CoV-2 infection

Parameter	Ono <i>et al.</i> [2]	Saricaoglu <i>et al.</i> [3]	Liew <i>et al.</i> [4]	Danssaert <i>et al.</i> [5]	Schenker <i>et al.</i> [6]	De Stefano <i>et al.</i> [7]	Our case
Age, years	50	73	47	37	65	30	27
Sex	Male	Male	Male	Female	Female	NA	Female
Onset of ReA after SARS-CoV-2 infection, days	22	14	Simultaneous	12	>10	20	14
Musculoskeletal manifestations	Ankles, right Achillis enthesitis	Hands, feet	Knee	Hand	Knees, ankles, wrists	Right elbow	Knees, ankles, feet, hand
Other manifestations	–	–	Balanitis	–	Cutaneous vasculitis	Psoriatic skin lesions	–
RF	–	–	NA	–	–	–	+
ACPA	–	–	NA	NA	–	–	–
HLA-B27	–	NA	NA	NA	+	–	–
ANA	–	NA	NA	+	–	–	–
Arthrocentesis	No crystals, sterile	NA	No crystals, sterile	NA	NA	No crystals	Not done
Radiograph	Normal	Normal	Normal	NA	NA	NA	Not done
Treatment	NSAID, IA CS	NSAID	NSAID, IA CS	Opioid, gabapentin	CS	NSAID, topical CS for skin	NSAID, opioid

NA: not available.

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