Dear Editor,

We read with interest the published manuscript by Bekaryssova et al. [1] summarizing cases of post-COVID-19 reactive arthritis (ReA). In their manuscript, the authors started their review by discussing the definition of ReA and its progression over time. Then, they summarized cases of COVID-19 ReA and those of COVID-19 vaccination-induced arthritis. They described clinical features, therapeutic management of ReA, and outcomes of these patients.

Twenty-two cases of COVID-19 ReA were summarized [1]. Several studies showed that COVID-19 infection is not only responsible for ReA but also viral arthritis. Thus, it is necessary to specify whether articular manifestations are due to ReA or viral arthritis.

Viral arthritis is characterized by an early onset and is commonly associated with symptoms of disseminated viral infection. This diagnosis remains possible in cases of early onset of articular symptoms. In this review, two cases of early arthritis associated with signs of disseminated viral infection were considered ReA [2, 3]. Indeed, Houshmand et al. described the case of a 10-year-old boy who presented with a concomitant fever, urticaria, and arthritis. Urticarial lesions tended to appear simultaneously with systemic viral symptoms. They have been reported in 11 to 19% of patients with COVID-19 infections [4]. These findings support the diagnosis of viral arthritis rather than post-COVID-19 ReA in this patient. The post-COVID-19 ReA diagnosis can be established based on the occurrence of rheumatological manifestations with a delay between the onset of these manifestations and the confirmed diagnosis of COVID-19 and nasopharyngeal real-time polymerase chain reaction (RT-PCR) negativation at the time of articular signs onset [5]. It is important to emphasize that RT-PCR positivity can persist in patients who have already been in remission [6].

In this review, the authors did not specify the delay between the COVID-19 infection diagnosis and articular manifestations onset [1].

Besides, the authors did not describe the treatments received during the COVID-19 infection [1]. Indeed, articular manifestations can be triggered by several drugs prescribed during COVID-19 infection. Favipiravir may induce hyperuricemia and even acute gouty arthritis [7]. Likewise, interferon β1 treatment may be responsible for inflammatory rheumatic disease occurrence [8, 9].

There is no agreement on the ReA criteria. Therefore, we believe that ruling out differential diagnoses such as viral arthritis related to COVID-19, drug-induced arthritis, crystal-induced flares, or a recent onset of another inflammatory rheumatic disease is necessary before making the ReA diagnosis [10].

The authors included seven cases of ReA after COVID-19 vaccination with corona VAC, Sinovac, and SPUTNIK-V.

While some authors consider joint manifestations induced by anti-COVID vaccination a form of ReA, others consider it an autoimmune or inflammatory syndrome induced by adjuvants. Adjuvants are components added to subunit and inactivated vaccines to stimulate innate and adaptive immune responses. This stimulation increases the effectiveness of subunit and inactivated vaccines, but it can be responsible for autoimmune/inflammatory syndrome induced by adjuvant (ASIA) [11]. Diagnosis criteria have been suggested for ASIA. The first major criterion is exposure to external stimuli such as a vaccine, and the second is the appearance of typical clinical manifestations such as arthritis [11]. These manifestations typically occur 2 to 5 days after COVID-19 vaccination [12]. The detection of autoantibodies or anti-adjuvant antibodies is possible and considered a minor
diagnosis criterion [12]. It is not clear whether articular manifestations occurring after COVID-19 vaccination correspond to ReA or ASIA [11].

ReA post-COVID-19 infection or post-COVID-19-vaccination is a matter of concern that must support increased research into the pathophysiology of ReA.

**Declarations**

**Disclosures** None.

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