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Rheumatoid Arthritis and Post-Covid Syndrome

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Abstract

As the SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) pandemic enters its third year, physicians are increasingly confronted with a new pathology, Post-COVID Syndrome (PCS). One of the common manifestations of PCS is a musculoskeletal symptom complex, manifested by myalgia, arthralgia, and arthritis. Today, there is no universally accepted term, definition, classification, diagnostic criteria, or consensus on the duration of PCS. In the literature there are enough descriptions of cases of the occurrence of rheumatoid arthritis (RA) after SARS-CoV-2. The question arises: is this a coincidence or could COVID-19 (coronavirus disease 2019) be a trigger factor for RA? From the perspective already expressed in medical circles, COVID-19 can unmask previously undiagnosed RA or cause disease de novo. In addition, the onset of arthritis can be a manifestation of PCS and can be transient. The trigger role of a SARS-CoV-2 infection in the occurrence of RA seems likely. The emergence of arthritis in the post-COVID period may pose problems in the differential diagnosis of joint damage.

Keywords: SARS-CoV-2; COVID-19; Post-COVID syndrome; Rheumatoid arthritis

1 Introduction

The third year of the COVID-19 pandemic (Coronavirus disease 2019) related to infection with the SARS-CoV-2 virus (Severe Acute Respiratory Syndrome Coronavirus 2) is underway and doctors are increasingly faced with a new pathology confronted, which is defined as "post-Covid-syndrome" (PCS). There are many names for PCS in the literature, the most common being the term "Long COVID-19". This term was first proposed by Elisa Perego, a doctor from Italy (who recovered from COVID-19 herself), to describe the symptoms that appear after a full (or partial) recovery from an acute infection. However, despite the patients suffering from PCS and articles devoted to this problem, at present there is no generally accepted definition, classification, diagnostic criteria, consensus on the duration and general principles for the treatment of PCS has not been developed. According to the definition of the expert panel of the World Health Organization [7], people who have had a probable or definite infection with SARS-CoV-2 according to their medical history can be referred to as a "post-COVID condition". However, this article does not define the duration of PCS.

Using the example of rheumatoid arthritis (RA) as one of the common "reference" immunoinflammatory rheumatic diseases (IERE), I would like to discuss the possible time frame of PCS and the differential diagnosis in the development of arthritis in the post-COVID period in this article.

The course of COVID-19 can be divided into several stages:

- Acute COVID-19: Signs and symptoms of COVID-19 lasting up to 4 weeks.
- Persistent symptomatic COVID-19: Signs and symptoms lasting 4 to 12 weeks.

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- PCS: Signs and symptoms that occur during or after a typical COVID-19 infection, persist for more than 12 weeks and cannot be explained by an alternative diagnosis.
- Prolonged COVID: This term is often used to describe signs and symptoms that persist or develop after an acute COVID-19. It includes both ongoing symptomatic COVID-19 (4 to 12 weeks) and post- COVID syndrome (12 weeks or longer).

The clinical manifestations of PCS are diverse and include more than 100 clinical symptoms [6]. PCS is more common in patients with severe SARS-CoV-2 infection but can also occur in patients with mild SARS-CoV-2 infection. The most common groups of symptoms are the following: generalized; Respiratory tract; Cardiovascular; neurological; Gastrointestinal; musculoskeletal system; psychological / psychiatric; dermatological. Musculoskeletal manifestations—arthralgia, arthritis, myalgia—are among the most common symptoms not only of PCS [9] but also of many other viral infections. These symptoms occur in 50–90% of patients in the acute phase of COVID-19 [10–12].

They can be associated with damage to muscle tissue and joints caused by immune complex inflammation, systemic microcirculatory disorders and tissue hypoxia. Myalgia or arthralgia usually resolves on its own and requires no treatment, and the presence of arthritis, particularly intractable (oligoarthritis or polyarthritis), can pose serious problems in the differential diagnosis. In this context, I would like to elaborate on the emergence of arthritis after SARS-CoV-2, including the outbreak of RA. There are more than 30 publications describing the occurrence of reactive arthritis (ReA) after COVID-19 [13-23], which is more correctly defined as viral or postviral arthritis from a rheumatological point of view. S. Parisi et al. [18] observed a 58-year-old patient who developed ankle arthritis 25 days after the onset of symptoms of COVID-19. The etiological role of SARS-CoV-2 was confirmed by the absence of laboratory signs of other rheumatic diseases, including an increase in the level of rheumatoid factor (RF), antibodies to cyclic citrullinated peptide (CCP), antinuclear factor (ANF), HLA-B27. Later M. Gasparotto et al. [19] presented the observation of postcovid arthritis and 6 other cases of the development of this pathology, described in the publications of other authors. A systematic review [24] analyzes about 100 cases of newly occurring rheumatic and musculoskeletal diseases in connection with a SARS-CoV-2 infection. This is consistent with data on the possible trigger role of respiratory and other viruses in the development of this pathology [25- 26]. We also propose that SARS-CoV-2 infection (or vaccination against SARS-CoV-2) may be a trigger for joint damage, including exacerbation of RA or induction of development of RA [27-36]. In an observational case described in the *Lancet* in 2021, a patient in whom an increase in CCP and RF titers was not observed shortly before COVID-19 disease [28], nor was damage to the small joints of the hand characteristic of RA. One month after a documented infection with SARS-CoV-2, the patient developed a typical RA clinical picture with severe morning stiffness, symmetrical polyarthritis of the wrists and elevated levels of C-reactive protein (CRP), RF. Later, during the month, a significant increase in CCP concentration was noted. Despite the high initial activity of the disease, against the background of treatment with methotrexate and methylprednisolone in small doses, a rapid decrease in activity was noted (DAS28-CRP = 2.2). Also in the literature there are observational data from several more cases of RA debut (CCP positive) after COVID-19, but the patients were not studied before the development of COVID-19. Therefore, the presence of “subclinical” RA in the period prior to SARS-CoV-2 infection in these patients cannot be ruled out.

The combination of arthritis in the post-COVID period with the detection of autoantibodies, especially CCP, poses serious differential diagnostic problems. It is known that the frequency of detection of various autoantibodies against the background of SARS-CoV-2 infection is 20-50% [37- 39]. Elevated CCP levels can persist long after recovery [37]. There are significant problems in the differential diagnosis of IERE in elderly patients during the COVID-19 pandemic. There is evidence of the development of polymyalgia rheumatica (with or without giant cell arteritis) and other IEREs against the background of infection with the SARS-CoV-2 virus and, in particular, vaccination against this infection [39-46].

2 Conclusion

Therefore, the development of arthritis in the post-COVID period can lead to serious problems in the differential diagnosis. The initiating role of SARS-CoV-2 infection in the development of RA and possibly other IEREs is highly likely and represents a serious medical concern. Post-COVID-19 arthritis lasting less than a year can be identified as a manifestation of the PCS are viewed. For rheumatologists, uniform, clear definitions must be created as quickly as possible, possibly through the interim recommendations for PCS within the framework of EULAR.

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