

Case report | Prikaz bolesnika

Rheumatoid Arthritis Following SARS-CoV-2 Infection: a Case Report

Reumatoidni artritis nakon SARS-CoV-2 infekcije: prikaz bolesnika

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Keywords:

Rheumatoid Arthritis
SARS-CoV-2
Anti-Citrullinated Protein Antibodies
Rheumatoid Factor

Ključne riječi:

reumatoidni artritis
SARS-CoV-2
protutijela na cikličke citrulinske proteine
reumatoidni faktor

Primljeno: 07-01-2022

Received: 07-01-2022

Prihvaćeno: 09-03-2022

Accepted: 09-03-2022

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Abstract

We present a case report of a new-onset seropositive rheumatoid arthritis in a 60-year-old patient, occurring six weeks after SARS-CoV-2 infection. The patient had pain and swelling of several joints with positive rheumatoid factor and anti-citrullinated protein antibodies.

Sažetak

U ovom smo prikazu slučaja prezentirali pacijenta s novonastalim seropozitivnim reumatoidnim artritisom. Pacijent je bio hospitaliziran zbog pneumonije uzrokovane SARS-CoV-2 infekcijom, a šest tjedana kasnije pojavile su se otekline i bolovi u zglobovima, uz pozitivan reumatoidni faktor i protutijela protiv cikličkih citruliniranih proteina.

Introduction

SARS-CoV-2 infection can cause multiple organ damage, affecting the respiratory, cardiovascular, neurologic, and musculoskeletal systems^[1]. The infection can result with severe inflammation and it has been suggested to induce several autoimmune diseases^[2,3]. Researches on whether it can induce rheumatoid arthritis are conflicting. In the current literature, there are few published case reports about rheumatoid arthritis occurring after SARS-CoV-2 infection^[2]. The autoantibodies in patients with COVID-19 have been described^[5]. Patients after SARS-CoV-2 infection sometimes have positive antinuclear antibodies (ANA) or elevated rheumatoid factor (RF) without any rheumatic symptoms. In this case report, the pa-

tient had the onset of significant rheumatic symptoms which have affected his functioning and activities in daily life. The patient had positive both anti-citrullinated protein (ACCP) and RF.

COVID-19, caused by SARS-CoV-2, has been associated with inflammation and autoimmune phenomena^[2]. Many studies have reported autoantibodies in patients with COVID-19, especially anti-cardiolipin, anti- β 2-glycoprotein I, and antinuclear antibodies^[2,5]. Positive ACCP antibodies with new-onset or flaring of rheumatoid arthritis symptoms after SARS-CoV-2 infection have also been reported^[6]. Autoantibodies can precede the development of clinical manifestations, sometimes for years. For example, a research by Klemenson et al. performed on a large cohort identified

that ACPA-IgG is elevated earlier pre-RA diagnosis than the other autoantibody isotypes. The median time of first positivity of the autoantibodies of ACPA-IgG was 1.9 years pre-RA, and RF-IgA 1.7 years^[7].

Case report

We present a 60-year-old man with severe joint pain and swelling which occurred six weeks after a SARS-CoV-2 infection. The patient was hospitalized for observation for a period of two days due to a mild COVID-19 pneumonia. The patient did not require supplemental oxygen therapy. The disease was manifested with fever, cough, diarrhea, dizziness, headache, and fatigue.

The patient had a positive medical history of asthma, was taking inhalation corticosteroids regularly, and had a nephrectomy ten years earlier due to a benign tumor. Due to complications of severe SARS-CoV-2 infection, his two brothers died during the pandemic. The patient was treated with peroral corticosteroid therapy for seven days.

In an outpatient post-COVID-19 clinic, six months after the infection, the patient reported severe joint pain, swelling, and morning stiffness, which particularly affected wrists, elbows, and shoulder joints bilaterally. Those symptoms occurred six weeks after the infection.

In the meantime, he was examined by a physiatrist on one occasion, and NSAID was recommended for suspected long COVID associated arthralgias.

The patient complained about pain in both knees and feet and experienced difficulties while rising from a sitting position. The clinical examination revealed swelling of proximal interphalangeal (PIP) joints on both hands, painful wrists, knees, shoulders, and feet. The strength of his left handgrip was reduced. The patient also reported a transitory sensation of tingling in the extremities. He was only taking NSAID as needed to reduce joint pain. The patient was afebrile, and his physical examination was otherwise unremarkable. His family history was negative for rheumatic diseases.

He had no respiratory symptoms. The chest X-ray was normal as well as the lung function tests (spirometry, lung diffusing capacity for CO, and arterial blood gas analysis). Laboratory tests revealed elevated rheumatoid factor value (RF) 49.6 IU/mL [normal values (N)<14 IU/ml], and ACCPA 34.1 U/mL [normal values (N) <17 IU/ml], CRP 14,9 mg/L [normal values (N): <8], erythrocyte sedimentation rate (ESR) 9 mm/hr [normal values (N):3-23 mm/h], IgA 1.71 g/L [normal values (N):0,7-4 g/L], IgG 15.80 g/L [normal values (N): 7-16 g/L], IgM 0.58 g/L, [normal values (N):0,4-2,3 g/L], C3 1.22 g/L [normal values (N):0,9-1,8 g/L], and C4 0.34 g/L [normal values (N):0,1-0,4 g/L] (Table 1). Blood cell count showed no cytopenia. Liver tests and renal function were unremarkable. According to 2010 ACR/EULAR criteria for rheumatoid arthritis, the patient had a score of 8 points (≥ 6 definite RA)^[8].

TABLE 1. LABORATORY TEST RESULTS SIX MONTHS AFTER THE SARS-CoV-2 INFECTION

TABLICA 1. LABORATORIJSKI NALAZI ŠEST MJESECI NAKON INFEKCIJE SARS-CoV-2

Laboratory tests	Value	Normal values
ESR	9 mm/h	3-23 mm/h
WBC (total)	11,5x10 ⁹ /L	3,4-9,7 x10 ⁹ /L
Neutrophils	9,60x10 ⁹ /L	2,06-6,49 x10 ⁹ /L
Platelets	264 x10 ⁹ /L	158-424 x10 ⁹ /L
Lymphocytes	1,12x10 ⁹ /L	1,19-3,35 x10 ⁹ /L
RF	49,6 IU/mL	<14 IU/ml
ACCP	34,1 IU/mL	7-17 IU/ml
CRP	14,9 mg/L	<5 mg/L
C3	1,22 g/L	0,9-1,8 g/L
C4	0,34 g/L	0,1-0,4 g/L
IgA	1,71 g/L	0,7-4 g/L
IgG	15,8 g/L	7-16 g/L
IgM	0,58 g/L	0,4-2,3 g/L

Laboratory tests	Value	Normal values
CK	75 U/L	<177 U/L
LDH	162 U/L	<241 U/L

ESR=erythrocyte sedimentation rate; WBC=white blood cells; RF= rheumatoid factor; ACCP= anti-cyclic citrullinated peptide; CRP=C- reactive protein; Ig=immunoglobulin; CK= creatine kinase; LDH= lactate dehydrogenase

The symptoms of pain and swelling have regressed approximately after 10 months. The patient had been taking only non-steroidal anti-inflammatory drugs as needed after that period. Further evaluation with ultrasound and other specific laboratory tests (such as HLA genotyping) have not been performed because the patient refused further recommended diagnostic evaluation and further treatment. The patient was recommended to have follow-ups with a rheumatologist in an outpatient clinic.

Discussion

We presented a case report of a patient with new-onset seropositive rheumatoid arthritis occurring six weeks after SARS-CoV-2 infection.

Concerning positive autoantibodies after SARS-CoV-2 infection, in the study by Derksen et al.^[2], ACCP was measured in 61 patients five weeks after the hospitalization and none of the patients tested positive for ACCP, except two participants who were previously diagnosed with ACCP positive rheumatoid arthritis.

Cytokine IL-6 is connected with severe respiratory damage in COVID-19 and is also a treatment target in patients with rheumatoid arthritis^[9]. IL-6 is a cytokine involved in both autoinflammatory events and septic conditions^[10].

A case report from Perrot et al. suggests that SARS-CoV-2 is involved in triggering RF and ACCP-positive rheumatoid arthritis, but the possibility that the onset of arthritis could have been coincidental cannot be ruled out^[6].

Further studies are necessary to understand the pathogenesis of COVID-19 and different clinical phenotypes. Arthralgias in patients with acute COVID-19 are present in 14.9% of cases^[11], however, data on rheumatic and inflammatory manifestations are still missing. Serological tests such as positive RF and antinuclear antibodies (ANA) can be useful to establish a diagnosis in a proper clinical setting, but the possibility that low-titer positivity of autoantibodies can be detected in viral arthritides must also be considered with caution^[12,13].

The positivity of autoantibodies in a healthy population should also be taken into account. ANA is pres-

ent in significant titers in the general population in up to 25% of cases, while in lower concentrations it is present in up to 40% of the population^[14]. RF was also detected in lower values in the general population, and in the elderly population in up to 20%^[15]. Respiratory viral infections have been associated with the cases of rheumatoid arthritis (especially in women) and could be a risk factor for the development of rheumatoid arthritis, even though this patient was male^[16].

The long-term consequences of the SARS-CoV-2 infection are still not sufficiently known. The following years will reveal its potentially long-lasting effects on musculoskeletal, respiratory, cardiovascular, and other organ systems. Diagnostic evaluation of patients with long COVID-19 symptoms is often necessary with a multidisciplinary approach (a collaboration of a pulmonologist, neurologist, cardiologist, rheumatologist, physical therapist, etc).

In conclusion, in patients with new-onset arthralgias, joint tenderness and swelling occurring after SARS-CoV-2 infection, rheumatoid arthritis should be considered a differential diagnosis, and further laboratory and diagnostic evaluation by a rheumatologist should be performed to rule out or confirm the diagnosis.

Conflict of Interest: The authors have no conflict of interest to declare.

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