Axial and peripheral spondyloarthritis triggered by sars-cov-2 infection: a report of two cases

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SUMMARY

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection can show musculoskeletal symptoms such as peripheral arthritis. In rare cases, peripheral arthritis can develop after the resolution of SARS-CoV-2. We present two cases of spondyloarthritis induced by SARS-CoV-2; one case with axial and peripheral spondyloarthritis and the other with peripheral spondyloarthritis. Both cases refer to Lebanese patients who were HLA-B27 positive.

These two cases highlight the possible predisposition of HLA-B27 positive patients to the development of spondyloarthritis symptoms triggered by SARS-CoV-2.

Key words: *Spondyloarthritis; COVID-19; HLA-B27.*

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INTRODUCTION

Although the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has not been reported to involve skeletal muscles, joint, or bones, arthralgia and myalgia can occur in up to 15% of the cases (1). Arthralgia, the feeling of joint pains without inflammation, can be the initial presentation of Coronavirus 2019 disease (COVID-19) (2, 3). The cascade of inflammatory mediators can lead to systemic symptoms, including musculoskeletal manifestations such as inflammatory arthritis (4, 5).

The term *spondyloarthritis* refers to a group of chronic inflammatory disorders (6). These usually present with chronic low back pain, peripheral arthritis, enthesitis, dactylitis, or association with psoriasis (7). Extra-articular manifestations include uveitis, iritis, and conjunctivitis (7). Moll and colleagues (8) described five subtypes of spondyloarthritis: (1) ankylosing spondylitis, (2) psoriatic arthritis, (3) reactive arthritis, (4) enteropathic arthritis, and (5) undifferentiated spondyloarthritis.

Human leukocyte antigen (HLA)-B27 is considered a major genetic risk factor (6). Herein, we present two cases of HLA-B27 positive axial and peripheral spondyloarthritis with onset of symptoms after the resolution of COVID-19.

CASE REPORTS

Case #1

A 25-year-old Lebanese man presented to the rheumatology clinic with severe pain, swelling, and redness of his left ankle and right elbow, which he had for a few days. The pain was associated with severe low back pain and early morning stiffness.

The patient usually resides in the Democratic Republic of Congo. Soon after he arrived in Beirut, he developed a febrile illness associated with severe continuous cough and change of smell. He had a positive real-time reverse transcription polymerase chain reaction (rT-PCR) for SARS-CoV-2 test. His fever and cough subsided after two weeks. He was retested for COVID-19 and was negative. The back pain and joint symptoms developed 19 days after the

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Figure 1 - Swelling and redness of the left ankle (left) and swelling of the right elbow (right).

onset of the Coronavirus infection. The patient denied any past history of back pain, psoriasis, uveitis, inflammatory bowel disease, dysuria, mouth ulcers, or genital or intestinal infections. He was not a smoker. He had taken naproxen 500 mg twice a day for 2 weeks with little benefit.

On physical examination, the patient was not febrile. The left ankle and the right elbow were both swollen with overlying erythema (Figure 1). The range of motion of both joints was slightly reduced due to pain and swelling. The examination of the spine indicated that the patient could not reverse his normal lumbar lordosis and had tenderness over both sacroiliac joints.

His C-reactive protein (CRP) was raised at 207 mg/L, but his full blood count, serum uric acid, liver function, and renal function tests were normal. His anti-nuclear antibody (ANA), cyclic citrullinated peptide (CCP) antibodies, and rheumatoid factor (RF) were negative. The HLA-B27 was positive. X-rays of the left ankle and right elbow did not reveal any abnormality. Magnetic resonance imaging (MRI) scan of the sacroiliac joints showed bilateral sacroiliitis with evidence of subchondral sclerosis, oedema, and erosions (Figure 2).

A diagnosis of axial and peripheral spondyloarthritis (SpA) post SARS-CoV-2 infection was made, and then 40mg prednisolone and sulphasalazine 500 mg twice a day were started. The patient started to improve slowly. A month later, the back pain eased, the ankle and elbow swelling subsided and CRP dropped to normal levels.

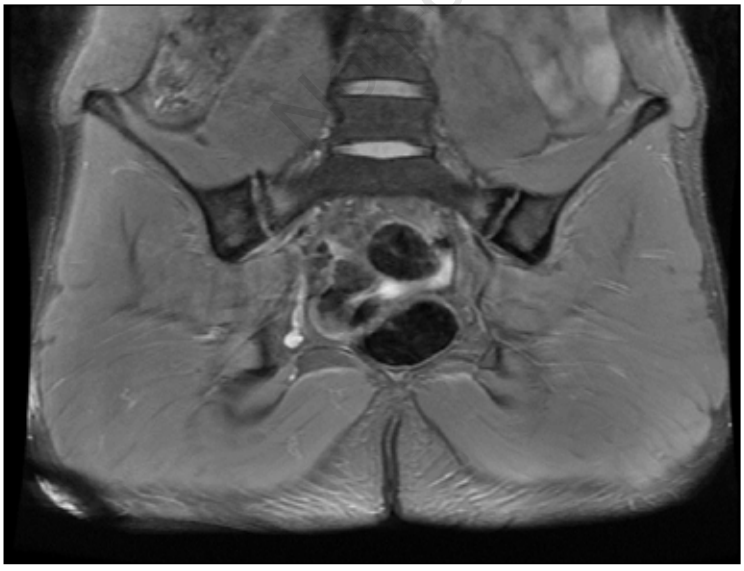

Figure 2 - Magnetic resonace imaging with fat saturation of the pelvis showing bilatera sacroiliitis with evidence of subchondral sclerosis, edema, and erosions.

Case #2

A 57-year-old Lebanese man was referred to our clinic with pain and swelling of the left wrist, which was worse in the morning, one month after recovery from SARS-CoV-2 infection. His COVID-19 symptoms consisted in 2 days of dry cough and fever reaching 38.7°C. After 12 days of an initial positive rT-PCR, his test became negative and his symptoms resolved.

The patient also complained of large joint migratory arthralgia. There was no past history of back pain, arthritis, uveitis, pso-

riasis, or inflammatory bowel disease. The patient denied to have had any dysuria, genital ulcers, or diarrhea.

On physical examination, the left wrist was tender and swollen with synovial thickening of the common extensor bursa and limitation of dorsiflexion and flexion. His spine was fully mobile.

His C-reactive protein was elevated at 28.9 mg/L, but his full blood count, uric acid, RF, anti-CPP, and extractable nuclear antigen antibodies (ENA) were normal. He was HLA-B27 positive.

An MRI of the left wrist showed extensive wrist joint synovitis with small bone erosions and joint effusion. There was a mild tenosynovitis of the flexor tendons. MRI of the sacroiliac joints showed no abnormality with no evidence of any bone marrow oedema.

Table I - Cases from literature with reactive arthritis after resolution of severe acute respiratory syndrome coronavirus 2 infection.

Case	Time from COVID-19 resolution	Patient profile	Scenario	Treatment	Follow-up
Case 1 (12)	Eight days	73-year-old M Turkish DM HTN CAD	Swelling, redness, pain, and tenderness in the left first metatarsophalangeal, proximal and distal interphalangeal joints Uric acid normal RF, anti-CCP, and ENA negative Normal X rays	NSAID	Complete resolution
Case 2 (13)	Eight days	50s-year-old M Japanese	Acute bilateral arthritis in the ankles, with mild enthesitis in the right Achille's tendon Arthrocentesis HLA-B27 negative Normal X rays RF, anti-CCP, and ENA negative	NSAID Intra-articular corticosteroid injection	Moderate improvement
Case 3 (14)	Few days	37-year-old F CHF Asthma GERD Morbid obesity American	Acute onset of pain and swelling in the right hand Normal inflammatory markers MRI of the upper extremity showed inflammation around the extensor tendons Normal Lyme serology, ANA, RF, and uric acid level	Topical NSAID	Complete resolution
Case 4 (15)	Three days	57-year-old M HTN DL Japanese	Multiple joint pain in the left wrist, the right shoulder, and the bilateral knees CRP 4.8 mg/dL Negative RF, ANA, and ENA Synovial fluid negative for crystals polarized on microscopy	NR	NR
Case 5 (16)	Ten days	30s-year-old M Previously healthy Italian	Pain in the right elbow, with three itchy, clearly demarcated erythematous scaly patches on the extensor surface of both elbows and groin Negative ANA, ENA, RF, and anti-CCP Synovial fluid free from crystals on polarized microscopic examination Swollen right elbow on ultrasound Negative HLA-B27	NSAIDs Topical steroids	Improved pain and functional limitation
Current case	One month	57-year-old M HTN DL Lebanese	Acute-onset left wrist pain Morning stiffness Mildly elevated inflammatory markers RF, ANA, and ENA negative Positive HLA-B27 Non-significant MRI of wrist and sacroiliac joint	Short course of steroid NSAID	Complete resolution

COVID-19, coronavirus infection; M, male; F, female HTN, hypertension; DM, diabetes mellitus; CAD, coronary artery disease; DL, dyslipidemia; RF, rheumatoid factor; Anti-CCP, anti-cyclic citrullinated peptide; ENA, extractable nuclear antigen antibodies; NSAID, non-steroidal anti-inflammatory drug; HLA, human leukocyte antigen; CHF, congestive heart failure; GERD, gastroesophageal reflux disease; MRI, magnetic resonance imaging; NR, not reported.

The patient was fitted with a wrist splint and started on 30 mg of prednisolone daily with rapid improvement. Two weeks later, prednisolone was discontinued, and he was given naproxen 500 mg twice a day. The patient remained symptom free.

DISCUSSION AND CONCLUSIONS

Persistent peripheral arthritis has been reported in patients who are HLA-B27 positive post Parvovirus B19 infection (9). In the same report, a 35 year-old man had a severe relapse of his ankylosing spondylitis post Parvovirus B19 infection after being in remission for 15 years (9). It could well be that viral antigens persist in patients who are HLA-B27 positive causing the inflammation in the joints. The presence of erosions on MRI in our first case indicates that this is possibly an exacerbation of a previously asymptomatic disease. Nevertheless, chronic inflammatory arthritis can be triggered by SARS-CoV-2 infection (10, 11), thus indicating that viral antigens can trigger systemic autoimmunity.

To date, five other cases have reported the occurrence of peripheral spondyloarthritis in patients after their recovery from COVID-19 (12-16) (Table I). A patient from Turkey was reported to have developed reactive arthritis post SARS-CoV-2 infection. However, the HLA-B27 status of the patient was not known (12). In Turkey, HLA B-27 is positive in around 70 to 90% of patients with spondyloarthritis (17, 18), in line with the incidence reported by the worldwide association (19). Two patients from Japan were reported to develop signs of peripheral spondyloarthritis post COVID-19. The 50-year-old patient from Japan was HLA-B27 positive, but the status of the second Japanese patient was not mentioned. In Japan, HLA-B27 is found among 83% of patients with axial spondyloarthritis (20). The Italian patient, reported to have peripheral arthritis and psoriatic lesions after SARS-CoV-2, was HLA-B27 negative (16). Although there is no exact calculation of the HLA-B27 status in Italy, the prevalence of HLA-B27 among patients with psoriatic arthritis is estimated at 12% (21). In Lebanon, HLA-B27 was found positive among 13.85% and 26.32% of axial and peripheral spondyloarthritis patients, respectively (22).

In conclusion, SARS-CoV-2 can induce the clinical symptoms of reactive arthritis and axial spondyloarthritis after its resolution even in populations where HLA-B27 is less prevalent than the worldwide population. Any patient with recent recovery from COVID-19 presenting for new-onset arthritis might need to be investigated for spondyloarthritis for proper management.

Conflicts of interests

The authors declare no potential conflict of interests.

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