Transient osteoporosis of the hip: a novel vascular manifestation of COVID-19?

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Key message: Is bone marrow edema a manifestation of endothelial dysfunction induced by COVID-19?

Dear Editor

Here we describe the case of a patient developing transient osteoporosis of the hip in close temporal correlation with SARS-CoV2 infection.

A 61-year-old Caucasian man was referred to our rheumatology outpatient clinic in July 2022 with a 4-weeks history of acute-onset left hip pain. Three days before hip pain presentation, the patient reported low-grade fever, cough and sore throat. A reverse transcriptase-polymerase chain reaction from nasopharyngeal swab was positive for SARS-CoV2 infection. The patient was instructed to start a short course of ibuprofen and acetylcysteine, with rapid improvement of respiratory symptoms. Following a 10-day isolation period, a repeated SARS-CoV2 molecular test yielded negative result. Due to worsening hip pain, with severely limited range of motion, the patient was evaluated by his primary care physician. Ibuprofen and paracetamol were prescribed, leading to minor symptomatic relief but no functional improvement. Radiography of the left hip was unremarkable.

The patient was then referred to our rheumatology clinic for further evaluation. He had a BMI of 26.8 kg/m^2, conducted a sedentary lifestyle, was a moderate smoker and did not use alcohol or illicit drugs. No trauma was reported and the patient had no history of corticosteroid administration. Before the recent SARS-CoV2 infection, the patient already had COVID-19 pneumonia in August 2021 and received NVX-CoV2373 vaccine (Novavax) in March 2022.

On examination, a limp was present and the gait was antalgic. He had to use walking aid devices and reported dull pain in the left groin and hip area, worsened by weightbearing activities. Pain was scored 9.2 on a 10-point visual analogue scale (VAS). Pain was elicited by active mobilization of the left hip and range of motion (ROM) was limited to 85° in flexion and to 10° in internal and external rotation. There was no swelling or changes in skin color and temperature in the painful area. The patient denied any sensory symptom such as paresthesia, allodynia or hyperalgesia. The remainder of the musculoskeletal examination was normal.

Laboratory findings, including complete blood count, liver, kidney and thyroid function, serum and urinary levels of calcium and phosphate, alkaline phosphatase, parathyroid hormone, uric acid and acute phase reactants were within normal values, while 25-hydroxyvitamin D was slightly reduced at 16.4 ng/ml (reference range 20 – 100 ng/ml).

Magnetic resonance imaging (MRI) of the pelvis was performed. Coronal short tau inversion recovery (STIR) images showed hyperintense signal in the left femoral head and neck region (Figure 1) indicative of extensive bone marrow edema. No areas of avascular necrosis and no stress fractures were noted. There was no synovitis or significant joint effusion. A diagnosis of transient osteoporosis of the hip was established. Since the symptoms presented during SARS-CoV2 infection, a potential etiopathogenetic role of the virus was suspected.

Ischemia is a well-recognized cause of avascular necrosis and, in general, it can be the etiology of bone marrow edema syndromes (1). Ischemic and thromboembolic events are possible complications of COVID-19 (2, 3) and cases of avascular necrosis have been described after the infection (4). Indeed, the available evidence suggests a crucial role of altered endothelial function in the pathophysiology of COVID-19 (5). Endothelial cells express angiotensin-converting enzyme 2 (ACE2), which is the major entry receptor of SARS-CoV-2 (6). Through ACE2, SARS-CoV2 might mediate vascular endothelium dysfunction leading to the activation of a prothrombotic cascade (7). Besides the direct infection of the endothelium by SARS-CoV2, vascular injury could also result from cell toxicity induced by viral proteins or from pro-inflammatory cytokines (8).

In consideration of the severely restricted mobility but also of the possible ischemic etiology of the bone marrow edema, enoxaparin 4000 IU once daily by subcutaneous injection was recommended. Furthermore, the patient was treated with intravenous infusions of neridronate 100 mg every three days for a total of four times, ibuprofen 600 mg three times a day for 15 days, oral calcium carbonate 1000 mg and cholecalciferol 2000 IU per day for 30 days. A rehabilitation program and pulsed electromagnetic field therapy were also initiated.

At the one-month follow-up visit, the VAS pain score decreased to 1.7 on a 10-point VAS and the patient was able to walk in full weight bearing without any device.

In conclusion, we describe for the first time a case of transient osteoporosis of the hip presenting during SARS-CoV-2 infection in a patient with no other known risk factors, with the exception of smoking. Although a causative role of COVID-19 can't be definitively established, there is an unquestionable temporal correlation between the two events. We hypothesize that the bone marrow oedema of the femoral neck might have a vascular aetiology caused by the endothelial dysfunction induced by SARS-CoV2. In this context, the association of prophylactic dosage anticoagulation and bisphosphonate therapy can be useful in determining a favourable outcome, as observed in our patient.

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Ethics: Informed consent has been received

Figure 1: Magnetic resonance imaging of the hips.

Coronal short tau inversion recovery (STIR) image showing hyperintense signal of the left neck and intertrochanteric region with mild joint effusion. No areas of osteonecrosis or stress fractures are noted.

References

1. Patel S. Primary bone marrow oedema syndromes. Rheumatology. 2013;53(5):785-92.
2. Castro RA, Frishman WH. Thrombotic Complications of COVID-19 Infection: A Review. Cardiol Rev. 2021;29(1):43-7.
3. Galyfos G, Sianou A, Frountzas M, Vasilios K, Vouros D, Theodoropoulos C, et al. Acute limb ischemia among patients with COVID-19 infection. J Vasc Surg. 2022;75(1):326-42.
4. Sulewski A, Sieroń D, Szyluk K, Dąbrowski M, Kubaszewski Ł, Lukoszek D, et al. Avascular Necrosis Bone Complication after Active COVID-19 Infection: Preliminary Results. Medicina (Kaunas). 2021;57(12).
5. Ma Z, Yang KY, Huang Y, Lui KO. Endothelial contribution to COVID-19: an update on mechanisms and therapeutic implications. J Mol Cell Cardiol. 2022;164:69-82.
6. Beyerstedt S, Casaro EB, Rangel É B. COVID-19: angiotensin-converting enzyme 2 (ACE2) expression and tissue susceptibility to SARS-CoV-2 infection. Eur J Clin Microbiol Infect Dis. 2021;40(5):905-19.
7. Kumar A, Narayan RK, Kumari C, Faiq MA, Kulandhasamy M, Kant K, et al. SARS-CoV-2 cell entry receptor ACE2 mediated endothelial dysfunction leads to vascular thrombosis in COVID-19 patients. Med Hypotheses. 2020;145:110320.
8. Evans PC, Rainger GE, Mason JC, Guzik TJ, Osto E, Stamataki Z, et al. Endothelial dysfunction in COVID-19: a position paper of the ESC Working Group for Atherosclerosis and Vascular Biology, and the ESC Council of Basic Cardiovascular Science. Cardiovasc Res. 2020;116(14):2177-84.

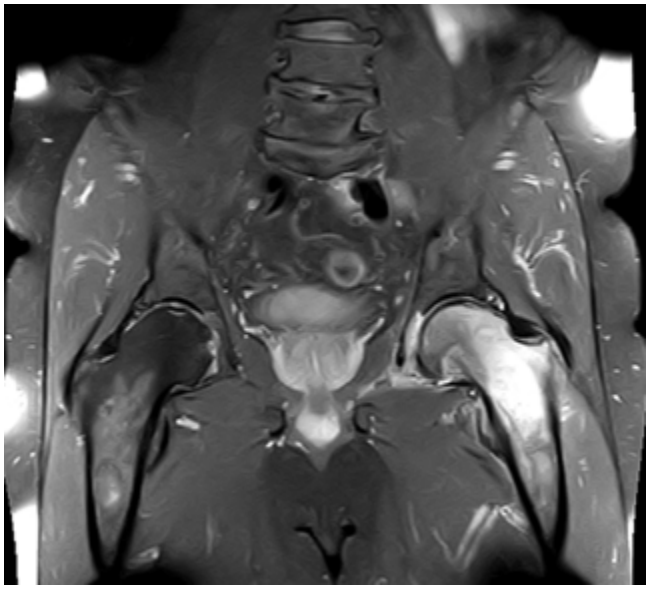

Figure 1: coronal short tau inversion recovery (STIR) image showing hyperintense signal of the left neck and intertrochanteric region with mild joint effusion. No areas of osteonecrosis or stress fractures are noted.

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