CASE REPORT

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Bilateral Avascular Necrosis of the Femoral Head After COVID-19 Infection: A Case Report

COVID-19 Enfeksiyonu Sonrası Femur Başının Bilateral Avasküler Nekrozu: Bir Olgu Sunumu

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ABSTRACT

Aim: Avascular necrosis of the femoral head is a condition characterized by limited range of motion, pain, and gait disturbance resulting from insufficient blood flow. We aim to evaluate the relationship between COVID-19 and avascular necrosis.

Case: Herein, we present a 63-year-old male patient who developed avascular necrosis of the bilateral femoral head after COVID-19.

Conclusion: COVID-19 infection alone and corticosteroids given to treat it can increase the incidence of avascular necrosis of the femoral head. MRI of the hip is highly specific in detecting early stagea vascular necrosis of the femoral head and can reduce patient's disability and need for surgery.

Keywords: COVID-19, Avascular necrosis, Femoral head, Osteonecrosis, Case report

ÖZ

Amaç: Femur başının avaskuler nekrozu, yetersiz kan akımı neticesinde gelişen, eklem hareket açıklığında kısıtlanma, ağrı ve yürüme bozukluğu ile karakterize bir tablodur. COVID-19 ve avasküler nekroz arasındaki ilişkiyi değerlendirmeyi amaçlıyoruz.

Olgu: Burada, COVID-19 sonrası her iki taraf femur başında avaskuler nekroz gelişen 63 yaşında bir erkek hastayı sunuyoruz.

Sonuç: Tek başına COVID-19 enfeksiyonu veya tedavi etmek için verilen kortikosteroidler, femur başı avasküler nekroz insidansını artırabilir. Kalça MRG, erken evre femur başı avasküler nekrozunu saptamada oldukça spesifiktir ve hastanın sakatlığını ve ameliyat ihtiyacını azaltabilir.

Anahtar Sözcükler: COVID-19, Avasküler nekroz, Femur başı, Osteonekroz, Vaka raporu

INTRODUCTION

People infected with COVID-19 experience various symptoms, such as fever, fatigue, musclepain, söre throat, headache, diarrhea, dry cough, and shortness of breath. Systemic hyperinflammation caused by the virüs leads to various serious complications, such as acute respiratory distress syndrome, acute renal failure, thrombotic events, acute myocardial infarction, cardiomyopathy, cardiac arrhythmias, cerebrovascular disease, and sepsis (1). In addition to the above complications, in the case report series of Agarwala et al., it was stated that avascular necrosis (AVN) of the femoral head developed in three patients, who received corticosteroids in the treatment of COVID-19 (2). AVN of the femoral head is a disease characterized by bone marrow necrosis and loss of osteocytes as a result of insufficient blood supply to the bone tissue.

During the healing of the bone tissue, while the necrotic trabeculae are cleared by increased osteoclastic activity, the trabecular bone weakens. Later, subchondral collapse develops because of the fracture of the weakened bone tissue under the weight of the body. Hip pain, limited range of motion and gait disturbance occur (3).

It is estimated that between 20,000 and 30,000 diagnosis of AVN are made each year in the United States and between 5% and 12% of total hip arthroplasties are performed concerning this diagnosis (4). By presenting this case, we wanted to draw attention to the relationship between COVID-19 and AVN and the importance of early diagnosis.

CASE REPORT

A 63-year-old male patient was admitted to our outpatient clinic with complaints of pain and limitation of motion in the left hip for 4 months and in the right hip for 2 months. The patient had gait disturbance due to pain. Previously, the patient, who applied to a local hospital with the complaint of hip pain for 2 weeks, was evaluated by X-ray, and was told that he had osteoarthritis at that visit and pain medication was prescribed. He did not go to the control examination, although his complaints did not go away afterwards. On our physical examination, it was determined that the existing pain was aggravated by hip joint flexion or rotation. Limited range of motion was detected due to pain in both hips, more prominently in the left hip. There was no pain during the movements of other joints except the hip, and the range of motion was within normal limits. The patient's muscle strength was normal. Deep tendon reflexes were normoactive. The patient did not have any specific risk factors that could cause AVN of the femoral head, such as alcohol intake, smoking, sickle cell disease, trauma, steroid usage, or systemic lupus erythematosus. However, the patient was diagnosed with COVID-19 via SARS-CoV-2 PCR test 5 months before the onset of left hip pain. The patient had mild to moderate COVID-19 infection at that time and did not use corticosteroid therapy. AP Pelvis X-ray taken 9 months after COVID-19 diagnosis showed increased bilateral femoral head sclerosis and left-sided collapse (Figure 1). While the patient had stage II (early in Ficat-Arlet stage) AVN in the right femoral head, there were signs of an advanced stage AVN in the left femoral head on hip MRI (Figure 2,3). The routine laboratory blood tests were unremarkable (Table 1). Bed rest and mobilization with a walker were recommended to the patient. Weekly oral 70 mg alendronate therapy was prescribed. The patient whose complaints did not regress at the 3rd month of the treatment was consulted to the orthopedic surgeon and operation was planned for the left hip.

DISCUSSION

There are traumatic and nontraumatic risk factors associated with the development of AVN. The main traumatic risk factors leading to the development of AVN are fractures,

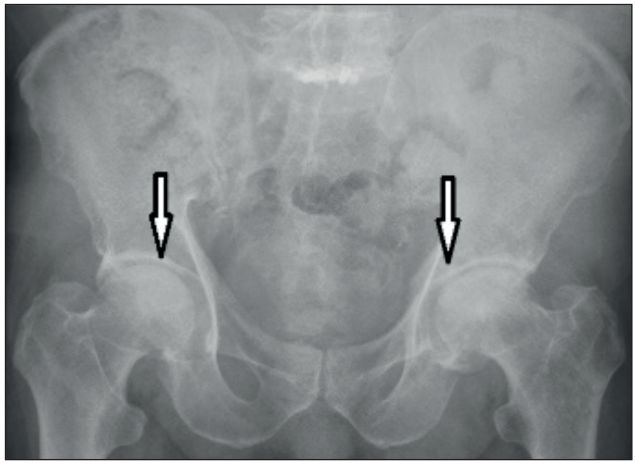

Figure 1: X-ray of the pelvis with bilateral hips in anteroposterior view.

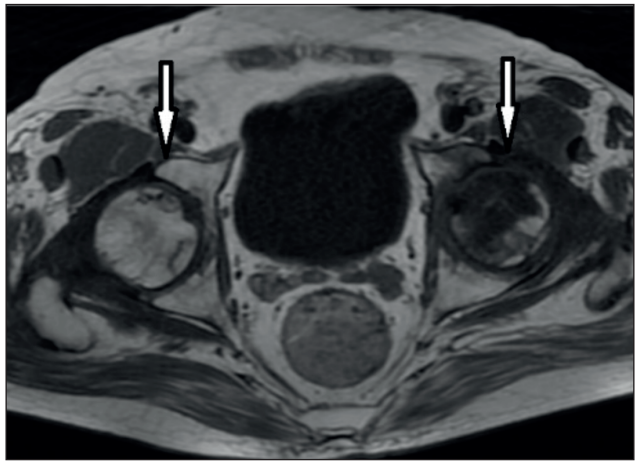

Figure 2: Axial T1-weighted MRI of bilateral femoral head.

Table 1: Laboratory values and clinical characteristics of the patient

Parameters	Results	Normal Ranges
HGB	14.2 g/dl	13.5-17.5 g/dl
Sedimentation Rate	16 mm/h	0-22 mm/h
CRP	3.3 mg/L	0-5 mg/L
RF	5 IU/ml	0-14 IU/ml
Uric Acid	5.1 mg/dl	2.6-7.6 mg/dl
TSH	1.72 mIU/L	0.24-4.2 mIU/L
Vitamin D3 (25-OH)	27.3 ng/mL	30> ng/mL
PTH	29.6 ng/L	15-65 ng/L
Creatinine	0.91 mg/dl	0.5-1.1 mg/dl
ALT	16 U/L	5-32 U/L
Fasting Blood Sugar	94 mg/dl	70-110 mg/dl
Total Cholesterol	176 mg/dl	125-200 mg/dl
LDL Cholesterol	114 mg/dl	60-130 mg/dl
HDL Cholesterol	30 mg/dl	35-70 mg/dl
Clinical characteristics	• Gait disturbance (Antalgic pattern) • Bilateral hip pain aggravated by motion • Limited range of motion in both hips, more prominently in the left hip. • Normal muscle strength • Normoactive deep tendon reflexes	

HGB: Hemoglobin, **CRP:** C-Reactive protein, **RF:** Rheumatoid factor, **TSH:** Thyroid-stimulating hormone, **PTH:** Parathyroid hormone, **ALT:** Alanine transaminase, **LDL:** Low-density lipoprotein, **HDL:** High-density lipoprotein, **mg:** milligrams, **dl:** deciliter, **U:** unit, **L:** liter, **ng:** nanograms, **ml:** milliliter, **gr:** grams, **mIU:** milli-international units, **mm:** millimeters, **h:** hour.

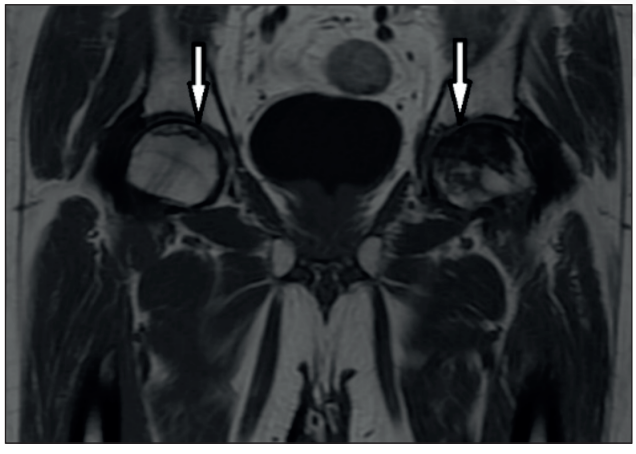

Figure 3: Coronal T1-weighted MRI of bilateral femoral heads.

dislocations, vascular trauma, and burns, while the main nontraumatic risk factors are hemoglobinopathies, such as thalassemia and sicklecell anemia, lipid emboli, systemic lupus erythematosus, alcohol consumption, smoking, corticosteroids, radiation and pregnancy (5). Corticosteroids, one of the most common AVN risk factors, play a life-saving role in the treatment of severe COVID-19 patients (6). Therefore, the number of patients diagnosed with AVN can increase due to the COVID-19 pandemic and the use of corticosteroids in severe COVID-19 cases worldwide.

Genetic and environmental interactions act together in the pathogenesis of AVN. The pathogenesis of steroid-associated AVN is not fully elucidated, but there are some putative mechanisms, such as intramedullary adipogenesis, fat embolism, vascular endothelial damage, microvascular thrombosis, decreased osteoblast differentiation, increased osteocyte death, and prolongation of osteoclast life span (7).

In the case report series of Agarwala et al., which they stated that AVN of the femoral head developed in three patients who received corticosteroids in the treatment of COVID-19, the average prednisone dose (750 mg) used in these three patients is lower than the average prednisone dose (2000 mg) that causes AVN in the literature. The mean duration from diagnosis of COVID-19 to onset of AVN symptoms was 58 days(2). Li et al. investigated 1406 patientswith COVID-19, they detected bilateral AVN of the femoral head in one patient who was treated with 1960 mg of methylprednisolone (8). Literature reports are showing that the mean time to AVN appearance after corticosteroid therapy is between 6 months and 1 year (5,9). Daltro et al., when they evaluated 23 patients who had AVN after COVID-19, they found that 66% of thepatients had moderate to severe COVID-19 infection and received corticosteroid therapy. The remaining 33% had a mild history of COVID-19 without corticosteroid use. Overall, in these 23 patients, they found the mean time between COVID-19 infection and onset of AVN to be 132.8 (between 64 and 180) days (10).

AVN that develops after steroid use in the treatment of COVID-19 seems to ocur earlier and with lower doses of steroids compared tot he AVN releated with the use of steroids for non-COVID-19 reasons. Moreover, AVN occurring in the post-COVID-19 period develops with or without the use of corticosteroids. This situation suggests that COVID-19 infection even may be a new risk factor associated with AVN. In the way of supporting this idea, in our case, AVN has developed without any steroid treatment. COVID-19 can affect bone tissue by various mechanisms.

The angiotensin-converting enzyme 2 (ACE2) receptor is found in many places in the body, including bone tissue. The COVID-19 virus invades cells through the ACE2 receptor (11). Awosanya et al., in their study on human ACE2-expressing transgenic mice infected with COVID-19, found a decrease in bone mass and an increase in TRAP+ osteoclasts 12–14 days after infection. Intercalarily, TNF-α, IL-1β, IL-6, IL-17, and CXCL10 cytokines, whose levels increase with the cytokine storm caused by COVID-19 in-

fection, can activate osteoclastogenesis (12). Moreover, endothelial dysfunction and hypercoagulability can be seen in patients with severe COVID-19 infection. Hypercoagulability can be further induced by prolonged bed rest and hypoxia (13).

Clinicians should be vigilant for the early diagnosis and treatment of AVN in post-COVID patients presenting with hip and groin pain, as COVID-19 infection alone and corticosteroid therapy given in its treatment may increase the cases of AVN. Physicians should keep in mind that early diagnosis and treatment of AVN reduce the patient's need for surgeryand the risk of disability. MRI of the hip is highly specific in detecting early stage AVN.

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None

Author Contributions

Alper Uysal identified the case, the authors have equal contribution in other parts.

Conflicts of Interest

The authors declare that they have no conflict of interest regarding the publication of this article.

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Ethical Approval and Consent

Ethical approval is not required at our institution to publish an anonymous case report. Written informed consent was taken from the patient.

Review Process

Extremely peer-reviewed and accepted.

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