

Osteonecrosis with Concomitant Bacterial Osteomyelitis of Both Hips and a Knee in a Post–COVID-19 Patient

A Case Report

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Abstract

Case: We report the case of a coronavirus disease 2019 (COVID-19)-recovered, 42-year-old man with osteonecrosis and concomitant acute bacterial osteomyelitis of both hips and his left knee. The patient underwent total hip replacement for both hips and arthroscopic decompression and synovectomy of the knee joint. On follow-up, he has complete and painless range of motion with resolving osteomyelitis and no signs of active infection.

Conclusion: Corticosteroid therapy and COVID-19-associated thrombotic microangiopathy might have caused osteonecrosis in our patient. However, concomitant osteomyelitis is extremely rare and might be overlooked because of elevated inflammatory markers after recovery from COVID-19 infection.

The recent outbreak of coronavirus disease 2019 (COVID-19) has become a global pandemic. The pathophysiology of the disease and the effects on the various organ systems of the body are still not completely understood. COVID-19 infection has been shown to cause thrombotic microangiopathy, and disseminated intravascular coagulation¹, which in addition to corticosteroids used in the treatment of moderate and severe cases, might contribute to the development of osteonecrosis. Multifocal osteomyelitis and septic arthritis are uncommon in adults without any predisposing factors and can affect the treatment plan of osteonecrosis in such patients. Early onset osteonecrosis with concomitant osteomyelitis has not been previously reported in COVID-19.

The patient whose case is reported by us consented for his information to be published.

Case Report

A 42-year-old male patient presented to us with complaints of bilateral hip pain. The patient had a history of severe COVID-19 infection with lower respiratory tract infection and cytokine storm in August 2020. He was admitted and treated as per prevalent COVID-19 management guidelines by Ministry of Health and Family Welfare, Government of India². Laboratory values of the patient were as follows: white blood cell count (WBC) = 10,500/cumm (normal 4,000-11,000/cumm);

D-dimer >10,000 ng/mL (normal <500 ng/mL); interleukin-6 = 320.2 pg/mL (normal 0-7 pg/mL); C-reactive protein (CRP) = 65.87 mg/L (normal <6 mg/L); and lactate dehydrogenase (LDH) = 314 U/L (normal 140-280 U/L). He developed sepsis with a total WBC count of 20,700 that was treated with broad-spectrum antibiotics (Co-amoxiclav 1200 mg intravenous (IV) eighth hourly, Faropenem 300 mg orally, and linezolid 600 mg orally). He was treated with methylprednisolone (40 mg IV twice a day for 12 days), remdesivir (200 mg IV on day 1 followed by 100 mg IV for 4 days), tocilizumab (400 mg IV single dose), heparin (5000 units subcutaneously 12 hourly), and clexane (0.6 subcutaneously once a day). He was discharged on methylprednisolone 8 mg twice a day for 5 days followed by once a day for 5 days. Immediately after discharge by the end of August 2020, the patient developed bilateral hip pain. He was evaluated by a rheumatologist and was treated with deflazacort (6 mg thrice a day for 10 days) on suspicion of seronegative arthritis. Magnetic resonance imaging (MRI) of both hips was advised because there was no relief of symptoms, which was suggestive of bilateral hip arthritis and synovitis with mild collapse of femoral heads and myositis of the hip muscle compartments.

On presentation to us in mid-September 2020, the patient was bedridden and in agony. His laboratory values were as follows: WBC = 12,400/cumm; platelet count = 163,000/cumm

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Keywords COVID-19; coronavirus; THA; total hip arthroplasty; *E. coli*; multifocal osteomyelitis; AVN; avascular necrosis; osteonecrosis; steroid-induced osteonecrosis; knee; hip; femoral head



Fig. 1
Preoperative radiograph of both hips showing arthritis of both hips (Ficat-Arlet stage IV).

(normal 150,000-450,000/cumm); prothrombin time = 11.4 sec (normal 10-14 sec); International Normalized Ratio = 1.15 (normal 0.8-1.1); activated Partial Thromboplastin Time = 26 sec (normal 21-35 sec); CRP = 7.0 mg/L; erythrocyte sedimentation rate (ESR) = 34 mm/hr (normal 0-22 mm/hr); D-dimer = 576 ng/mL; and procalcitonin <0.05 ng/mL (normal <0.1 ng/mL). Urine analysis was not suggestive of urinary tract infection. He did not have any respiratory symptoms, and high-resolution computed tomography of the chest did not show any active focus of infection. He had extremely painful and grossly restricted range of motion of both hips. Plain radiographs showed bilateral collapse of the femoral head with arthritic changes (Ficat-Arlet stage IV) (Figs. 1 and 2).

The patient underwent staged bilateral total hip replacement with thorough debridement and irrigation with an intervening period of 2 weeks. Intraoperative changes typical of osteonecrosis were seen with flattened femoral heads and loss of normal articular cartilage in the acetabulum, and no frankly purulent collection was found. Intraoperative samples collected from both hips (synovial fluid, synovial tissue, and swabs from the acetabulum and femoral canal) showed multidrug-resistant *Escherichia coli* on culture. The patient was postoperatively started on IV antimicrobials as per sensitivity report (tigecycline 50 mg IV 12 hourly) for 6 weeks. The postoperative period was uneventful. (Fig. 3).

He developed pain in the left knee in January 2021. On examination, he was found to have synovial hypertrophy and effusion in the knee. Plain radiographs of the knee showed patchy osteopenic lesions involving the distal femur. An aspiration sample from the knee showed mild to moderate inflammatory infiltrate composed predominantly of neutrophils (total WBC count = 2,800 cells/cumm [normal <200 cells]; neutrophils = 90% [normal <25%]; and lymphocytes = 10%), and the bacterial culture showed no growth. MRI of the knee showed features suggestive of bony infarcts of the distal end of the femur and proximal tibia and osteomyelitis of the distal femur with extraosseous abscess (Figs. 4 and 5).

The patient underwent arthroscopic debridement, synovectomy, and drainage of the abscess. Samples collected at the time of surgery showed multidrug-resistant *Escherichia coli* on culture. The patient was started on oral alendronate (70 mg once a week for 3 months) and IV antimicrobials as per sensitivity report (tigecycline 50 mg IV 12 hourly) for 6 weeks.

He has been on regular follow-up with full painless range of motion of both hips and the left knee with no clinical signs of active infection at his last follow-up at 10 months. ESR and CRP have returned within normal range, and osteopenia and lytic lesions in the distal femur are resolving on serial radiographs. There has been no further involvement of other joints.

Discussion

Osteonecrosis is defined as the in situ death of a segment of bone because of interruption of blood supply of the bone segment. Although the pathophysiology is not entirely understood, common risk factors include trauma, alcohol, autoimmune diseases, hemoglobinopathies, and steroid intake³.



Fig. 2
Coronal magnetic resonance imaging of the pelvis with both hips showing signal changes in the femoral head and acetabulum, with femoral head collapse, synovitis, and myositis (Fig. 2-A: STIR image; Fig. 2-B: T1-weighted image).



Fig. 3

Fig. 3 Postoperative radiograph after bilateral hip replacement with debridement and irrigation. **Fig. 4** Radiograph of the left knee showing patchy osteopenic lesions (black arrows) in the distal femur.



Fig. 4

COVID-19 is a new disease caused by the severe acute respiratory syndrome coronavirus 2. Its pathogenesis and effects on the multiple organ systems of the human body are still a subject of ongoing research^{4,5}. Corticosteroids have shown significant benefits in reducing mortality in patients with moderate to severe disease requiring respiratory support⁶. It is well documented that prolonged use of corticosteroids can lead to osteonecrosis, most commonly involving the hip joints, followed by the knee⁷. There is no clear consensus regarding the dosage and duration of steroid intake that induces osteonecrosis. A cumulative dose of >2000 mg of methylprednisolone (or equivalents) has shown to be a significant risk factor for developing osteonecrosis⁸. However, cases have been reported even with cumulative doses as low as 760 mg⁹. Our patient had received a cumulative equivalent dose of 1176 mg of methylprednisolone.

A review of literature shows that symptomatic osteonecrosis of the femoral head usually develops 6 months to 1 year from the start of corticosteroid treatment. Nagasawa et al. described osteonecrosis because of steroid use as "very early" when symptoms developed within the first 3 months of treatment¹⁰. However, rarely cases such as our patient have been reported with symptomatic osteonecrosis within 1 month of treatment with corticosteroids¹¹. Our patient developed symptoms 25 days after diagnosis of COVID-19.

Multiple reports have described hypercoagulability and thrombotic events in critically ill COVID-19 patients and in patients with elevated D-dimer levels^{12,13}. There is evidence of disseminated intravascular coagulation (DIC), vascular endothelial damage, and thrombotic microangiopathy in COVID-19¹. Tiwari et al. have proposed that activation of extrinsic coagulation pathway, direct vascular endothelial injury, and activation of the complement system are possible mechanisms of thrombotic microangiopathy in COVID-19 infection as evidenced by presence of elevated D-dimer and LDH¹⁴. The pathogenesis and effects of thrombotic microangiopathy are an aspect of COVID-19 that is under investigation. In our patient, the D-dimer and LDH

were significantly elevated, indicating the possibility of DIC and microangiopathy.

Osteonecrosis with concomitant acute bacterial arthritis is uncommon and has been reported with patients with underlying conditions such as systemic lupus erythematosus¹⁵ or oncologic patients¹⁶. Septic arthritis caused by *E. coli* is relatively rare and more commonly seen in the elderly with comorbidities and young IV drug abusers. An underlying source of Gram-negative septic arthritis such as urinary tract infection (UTI) is found only in 50% of patients¹⁷. Our patient was young, with no comorbidities and no evidence of UTI or active pneumonia was found. Gameil et al. found that inflammatory markers such as ESR and CRP remain significantly raised even 3 months after recovery from COVID-19 infection¹⁸. In our patient, the ESR



Fig. 5

Coronal magnetic resonance imaging of the left knee with serpiginous areas suggestive of bony infarcts (white arrows). Extraosseous abscess (black arrowheads). **Fig. 5-A** T1-weighted gadolinium-enhanced image.

Fig. 5-B PDFS image.

and CRP were significantly raised which we had attributed to the post-COVID-19 alterations. Signs of osteomyelitis and septic arthritis such as fever and raised inflammatory markers (ESR and CRP) may be masked by similar features of COVID-19 infection.

We propose that in our patient, the corticosteroid therapy may be a contributing factor in the development of osteonecrosis of the joints. However, the microangiopathy and DIC associated with COVID-19, and secondary osteomyelitis seem to contribute to the very early onset of the osteonecrosis in this case.

To the best of our knowledge, a case of bilateral osteonecrosis of hips and the left knee with concomitant acute bacterial osteomyelitis in a recovered COVID-19 patient has not been reported previously. A high index of suspicion and early investigation of cases with musculoskeletal complaints in COVID-19 may be required as signs

of osteonecrosis, and osteomyelitis may be masked by the COVID-19 infection. ■

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