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 coagulation, 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 India. 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 in 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; 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 in mild collapse of femoral heads and myositis of the hip muscle compartments.

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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 intake.

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

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. 2A: STIR image; Fig. 2B: T1-weighted image).
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. Corticosteroids have shown significant benefits in reducing mortality in patients with moderate to severe disease requiring respiratory support. It is well documented that prolonged use of corticosteroids can lead to osteonecrosis, most commonly involving the hip joints, followed by the knee. 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 osteonecrosis. However, cases have been reported even with cumulative doses as low as 760 mg. 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 treatment. However, rarely cases such as our patient have been reported with symptomatic osteonecrosis within 1 month of treatment with corticosteroids. 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. There is evidence of disseminated intravascular coagulation (DIC), vascular endothelial damage, and thrombotic microangiopathy in COVID-19. 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 LDH. 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 erythematosus or oncologic patients. 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 patients. 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 infection. In our patient, the ESR were significantly elevated, indicating the possibility of DIC and microangiopathy.
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.

References