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Case Report

Corticosteroids induced avascular necrosis of hip, a “long COVID-19” complication: Case report

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\textbf{ABSTRACT}

\textbf{Introduction and importance:} Since it first surfaced, the new Coronavirus has multiplied and mutated into different forms, leading to a significant impact on people’s lives. COVID-19’s long-term impact is not completely known; it can only be hypothesized based on the prior outbreak of severe acute respiratory syndrome (SARS). Avascular necrosis (AVN) is one of these consequences, which if left untreated can lead to catastrophic events and bone collapse. It’s important to remember that individuals who have recovered from COVID-19 infection are still at risk of developing AVN. The pathological findings in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection are very similar to those seen in severe acute respiratory syndrome coronavirus (SARS-CoV) infection.

\textbf{Case presentation:} We present cases of 27 and 69-year-old men with no comorbidities admitted with complaints of bilateral hip pain post covid treatment with corticosteroids and antivirals. The diagnosis was established based on history, physical examination, and magnetic resonance imaging (MRI).

\textbf{Clinical discussion:} The use of corticosteroids in the treatment of SARS-CoV-2 infection has saved many lives, and it is still advised for moderate to severe cases on a short-term basis. The long-term use of corticosteroids is associated with numerous side effects. One of the most prevalent side effects of steroids is avascular necrosis of the femoral head, which is aggravated by the disease process.

\textbf{Conclusion:} Early detection of Avascular necrosis is very crucial in its management due to its high progression rate. Low therapeutic doses of corticosteroids with minimal effective duration remain the key to halting its occurrence.

\textbf{1. Introduction}

The zoonotic virus responsible for the current global health catastrophe, Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), is ringing its hazardous bells on its post-disease condition [1]. The treatment and prevention of acute disease have overwhelmed health organizations and governments. Meanwhile, evidence is accumulating that surviving the acute illness is not the end of the story, and many COVID-19 survivors continue to suffer from symptoms and disability. Fatigue, dyspnoea, brain fog, chest pain, joint or muscle pain, palpitations, anosmia and dysgeusia, hair loss, cognitive symptoms memory and concentration deficiencies), and psychosocial distress are the most common persistent symptoms [2].

Long COVID is a term coined by renowned research institutes to characterize a variety of persistent symptoms that might present long after the acute SARS-CoV-2 infection. Long COVID also damages multiple organs including, but not limited to, the respiratory, musculoskeletal, neurological, cardiovascular, and gastrointestinal systems [3]. Among India’s second wave of COVID-19, complications such as mucormycosis, new-onset diabetes, blood clots, and chronic fatigue became increasingly common in recovered coronavirus patients. Now, osteonecrosis has been added to the list [1].

Many drugs that may be potentially effective against COVID-19 have been used since the beginning of the pandemic, including Antivirals, Angiotensin receptor blockers, Chloroquine phosphate, and Corticosteroids. However, the efficacy of Chloroquine and Angiotensin receptor blockers was not well established. Although Corticosteroids are life-saving in the treatment of COVID-19, they are also a significant

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predicator of Avascular necrosis (AVN). Based on this hypothesis, there could be a rebound in the frequency of AVN cases due to the widespread use of life-saving corticosteroids [4].

Early diagnosis plays a major role in arresting osteonecrosis’ progression to critical states requiring replacement surgery. 92%–97% of the patients don’t require any surgical management if diagnosed in stage I or II classifications of AVN hip according to Ficat-Arlet [5].

Here, we report two cases of critical AVN which progressed from stage II to stage IV, thus requiring hip replacement following COVID-19 management. This case report was reported in line with the SCARE guidelines [6].

2. Case presentation

2.1. Case 1

A 69-year-old male patient with no comorbidities was admitted to the hospital with a complaint of pain in the bilateral hip regions. Previously, he was diagnosed with COVID-19 in April 2021 and was managed with Oseltamivir, Doxycycline, and Methylprednisolone at home. Methylprednisolone was administered for 17 days, tapering from 16 mg twice daily for 7 days followed by 8 mg twice daily for 5 days to 4 mg twice daily for another 5 days. The total dose of methylprednisolone received by the patient was 344 mg, equivalent to 430 mg of prednisolone. On the 15th day of steroid treatment, the patient developed pain over the left leg which was radiating to the lower side. Later, the patient’s pain severity increased, for which he was diagnosed with bilateral avascular necrosis of the hip in an outside hospital in November 2021. According to the Ficat classification [5], his AVN is classified as stage II on the left and stage I on the right in December 2021. He was then posted for left hip core decompression and conservative management on the right side. He was admitted into the emergency room in February 2022 after complaining of increased hip ache in both the left and right hips (left > right). An attempt made to reclassify the Ficat classification of AVN showed that the disease progressed to stage III to IV on the left side and stage II on the right side of the hip. Considering the critical state of the disease, he was surgically managed with total hip replacement surgery and hip core decompression on the left and right hip respectively (Fig. 1).

2.2. Case 2

A 27-year-old male patient with no comorbidities was admitted to the emergency department with pain on both sides of the hip (left > right) for 2 months. He had a history of COVID as of December 2021. Considering the severity and oxygen requirement, he was admitted to a hospital where oxygen supplementation, antivirals, and steroids were used in the management of the disease. A dose of 80 mg of intravenous methylprednisolone was administered for 7 days, followed by oral methylprednisolone for 2 weeks. The total dose of methylprednisolone administered to the patient was 560 mg and 272 mg through the intravenous and oral routes respectively. Therefore, the total dose consumed was 832 mg, which is equivalent to 1040 mg of prednisolone. This insidious pain was first experienced in February 2022 and gradually progressed to avascular necrosis of the hip, which was finally detected in April 2022. Right hip decompression and left hip replacement were chosen as a part of management as the stage of hip necrosis was stage II on the right and stage IV on the left at the time of diagnosis (Fig. 2).

3. Clinical discussion

AVN of the Hip, also called osteonecrosis of the femur head, affects young generations predominantly and is known to have a large number of etiological factors. The long-standing history of association between corticosteroids and risk for AVN describes no specific dosage and duration pattern of corticosteroid therapy needed to elicit the effect of avascular necrosis in the hip region [7]. According to a meta-analysis conducted in the year 2015 by Mont et al., a cumulative dose of 2000 mg prednisone or other steroids of its equivalent was required to develop AVN [8]. More than 18 days of administration of methylprednisolone (>2000mg) showed a prevalence of 9.9% in the development of osteonecrosis, according to a cohort study by Chan et al. [9] However, a minimum dose of 290 mg and a maximum dose of 3300 mg can cause necrosis in various populations [10]. The actual pathogenesis behind steroid-induced avascular necrosis is not well established, but the mechanisms hypothesized include viral invasion related to the release of inflammatory cytokines, hypercoagulable condition, bone marrow stem cell abnormality, hypoxia, fat hypertrophy, vascular endothelial dysfunction [11].

In our cases, the patients received a cumulative dose of 430 mg and 1040 mg of prednisolone for a duration of 17 and 21 days respectively. Usually, it takes 6–8 months for the development of osteonecrosis after corticosteroid treatment. However, a series reported on post-COVID AVN necrosis by Agarwala et al., showed that 46–67 days with a mean of 58 days can cause osteonecrosis [5]. Likewise, our patients developed the first symptom during the 15–30 days of steroid therapy. The sensitivity to develop AVN is high even with a low cumulative dose of corticosteroids as there is the involvement of viral inflammatory response and hypoxia over the femoral head. High profile vigilance should be implemented in patients suffering from hip joint pain especially if they are receiving steroids for a longer duration and are at high risk of developing osteonecrosis. Early detection is the primary goal to retard progression in AVN which is possible through MRI. Conservative...
management with bisphosphonates and core decompression surgically are indicated in the early stages whereas for end-stage disease surgical management with joint replacement surgery is reserved. Supplemental therapy with vitamin D and calcium in addition to bisphosphonates is beneficial [12].

4. Conclusion

Despite steroids being one of the life-saving medications in COVID-19 management, they should be used with high vigilance. To preserve clinical efficacy and reduce the risk of unwanted effects, employing the smallest effective doses and shortening the duration of steroids is crucial. Patients receiving steroids during COVID-19 management should be educated regarding its adverse effects and advised to monitor for the appearance of symptoms. Early detection is the key feature in halting the progression of avascular necrosis of the hip in long COVID-19 and initiating management of AVN according to the condition of the patient. With high vigilance, they should be used for reducing morbidity and improving an individual’s quality of life. The use of corticosteroids, the dose and duration of treatment, and methods for the prevention, early identification, and timely intervention of steroid-induced avascular necrosis are all essential topics that must be addressed in today’s global outbreak.

Ethical approval

The approval of the ethics committee was not necessary for the publication.

Author contributions

All authors provided clinical input to the case report and comment on the manuscript.

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Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Declaration of competing interest

The authors declare that there is no conflict of interest.

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Appendix A. Supplementary data

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