International Journal of Orthopaedics Sciences

E-ISSN: 2395-1958
P-ISSN: 2706-6630
IJOS 2021; 7(4): 177-179

www.orthopaper.com
Received: 15-06-2021
Accepted: 20-07-2021

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Post COVID-19 osteoporosis and avascular necrosis of femoral head: A case report

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DOI: https://doi.org/10.22271/ortho.2021.v7.i4c.2881

Abstract
COVID pandemic has resulted in loss of many lives along with morbidity among young adults. The long term effect of COVID-19 is still unknown, one can only speculate from the previous epidemic of severe acute respiratory syndrome (SARS); still very little is known. The use of corticosteroid in COVID-19 infection has saved many lives and it is still recommended for severe types of disease, however its use has many adverse effects.
Avascular necrosis of the femoral head along with osteoporosis is one of the common adverse effects, where the disease process has again exacerbated its effect. One can only predict if these events will occur, so these patients should be followed up regularly and screened properly. Early detection and intervention should be the aim, so as to decrease morbidity and improve quality of living in those patients. Our case highlights an symptomatic AVN of femoral head and osteoporosis, which developed following treatment of COVID-19.

Keywords: COVID pandemic, avascular necrosis, corticosteroid

Introduction
Covid-19 was declared as pandemic by WHO from March 2020, since then 202,138,110 cases have been confirmed with total of 4,285,299 deaths [1]. The situation of pandemic is still unpredictable and specific treatment for Covid-19 is still not available [2]. Many treatment options like antiviral drug, anti-malarial drug, corticosteroids, immunomodulators and plasma therapy are been instituted, however the outcomes are debatable. The systematic review of clinical trials for the use corticosteroid in the treatment of Covid 19 patients has shown promising results and also recommends its use [3]. Patients who received corticosteroid before the need of high-flow oxygen therapy or mechanical ventilation showed greater improvements and decreased in-hospital death [4]. However, the use of corticosteroid has its severe adverse effect as well. Corticosteroid is a double edged sword, as additional supplement is required to protect the biological function of vital organs following any bodily insult, whereas there are relatively increased adverse effects following long-term therapy or high doses [5]. Bones are one of the most common regions for their adverse effect. Secondary osteoporosis and osteonecrosis are the serious orthopaedic adverse effect following corticosteroid therapy [6]. During the 2003 epidemic of severe acute respiratory syndrome (SARS) in China, 23.1% of patients treated with high-dose corticosteroid developed avascular necrosis (AVN) of femoral head during their follow-up [7].
Here, we present a case of symptomatic AVN of femoral head and osteoporosis, which developed following treatment of Covid-19.

Case
A 31years old female was diagnosed with Covid-19 pneumonia for which she was admitted and treated in general ward with oxygen supplementation. During the treatment she was given methylprednisolone 32 mg daily for initial 7 days but as improvement observed was minimal so it was further continued for 10 days more (Total dose 544 mg). After 1 month of asymptomatic period, she began to develop pain over bilateral hip joints radiating to knee region along with pain over the joints of elbow and wrist.

She also had generalized body weakness and easy fatiguability. For these symptoms she was advised to take rest and took some analgesics. However, her symptoms began to worsen; pain over her left hip joint was unbearable. In addition, she also had difficulty climbing stairs and motor vehicles. Her family member also noticed the limping gait.

She was evaluated by X-ray of pelvis with both hip joints (AP view), which showed crescent sign over left femoral head (Figure 1). MRI of both hip joint revealed AVN of both femoral head (Figure 2). DEXA scan of lumbar vertebra showed T-score of -2.9, whereas T-score was -1.7 & -1.8 in right and left hip, respectively. Other blood parameters are described in Table No 1.

Fig 1: X- ray of pelvis with both hip joints (AP view), showing crescent sign over left femoral head (arrow).

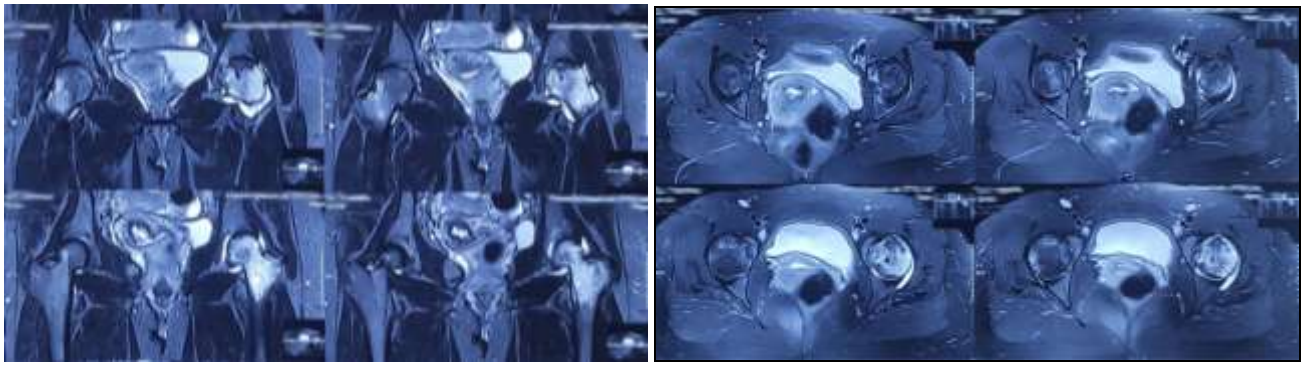

Fig 2: MRI of both hip joint, showing Bilateral AVN of femoral head (sagittal and axial view)

Table 1: Blood Parameters

Parameter	Values
Hb	12.5 gm%
ESR	23 mm at 1st hour
CBC	TC: 5.5×10^9/L, RBC: 4.34×10^{12}/L, Platelet: 3005.5×10^9/L
RBS	5.1 mmol/L
Creatinine	0.91 mg/dl
Calcium	8.1 mg/dl
CRP	3.02 mg/L
RA	9.19 IU/L
Parathyroid Hormone	36.5 pg/ml
Vitamin D	34.93 ng/ml
TSH (Thyroid Stimulating Hormone)	3.102 μIU/ml
Lipid Profile	Total cholesterol: 168 mg/dl, TG: 35 mg/dl, LDL: 118mg/ dl
ANA	Negative
Anti CCP	Negative
Anti- ds-DNA	Negative

Discussion

Morbidity related to osteoporosis and osteonecrosis are very frustrating for the patients. Steroid induced osteoporosis results in rapid loss of bone density of around 6- 12% within 3 months and 75% increase risk of fracture within 1 year; whereas, 9% to 40% osteonecrosis occurs due to long term steroid therapy which commonly involves the hip joints [6]. The femoral head is commonly affected due to the peculiarities of its blood supply. Wang and Niu discussed the two potential mechanisms for development of AVN of femoral head, where the release of inflammatory cytokines due to inflammatory response to virus, causes abnormal hemodynamics of femoral head, along with the hypoxia that cause imbalance between the demand and supply of oxygen to femoral head. Second mechanism is steroid induced femoral head necrosis; phenomenon related to steroid dose, cumulative dosage and individual genetic background [8].

Debate still exists regarding the dose and duration of

corticosteroid for the development of osteonecrosis. Chan *et al*. in their cohort showed that the cumulative dose of methylprednisolone >2000mg for more than 18 days had prevalence of 9.9% for development of osteonecrosis [9]. Similarly, Mont *et al*. also showed osteonecrosis incidence was 6.7% if the dose of prednisolone was >2000mg and increase in risk if the dose was >40mg/ day; also there was 3.6% increase in incidence for each 10mg/ day increase in dose of prednisolone [10]. A meta-analysis done by Staa *et al*. found out that osteoporosis occurs shortly after start of steroid therapy and comparatively at low dose, and increase in risk was observed with the dose of more than 5mg/day of prednisolone [11]. In our case patient had cumulative dose of 544mg methylprednisolone for duration of 17days.

The development of osteonecrosis occurs relatively within 6-8 months following corticosteroid therapy [12]. However, in a case series done by Agarwala *et al*. showed that the AVN in post Covid-19 patients developed at mean of 58 days (range 46- 67days). Similarly, in our case patient developed first symptoms at 1 month following the Covid-19 infection. The development of AVN should not only be focused on the corticosteroid therapy, as its course may have been expedited due to the disease process of Covid-19 as discussed earlier, where there is altered hemodynamics due to inflammatory cytokines and hypoxia over the femoral head.

High level of suspicion should be maintained for the patient who complains of hip joint pain and alteration of gait. The screening is recommended in all the patients who have been treated with steroids for a long duration and those who are at high risk of developing osteonecrosis and osteoporosis. The MRI can be used for screening as it is highly sensitive for early detection of osteonecrosis; along with bone mineral densitometry (BMD) for osteoporosis. Early stage of osteonecrosis can be treated conservatively with bisphosphonate or surgically by core decompression; whereas joint replacement surgery is reserved for the end stage of arthritis. Along with bisphosphonate, calcium and vitamin D supplements are also important. Though steroids have provided promising results in Covid-19 patients and have reduced the mortality rates, it is very crucial to use minimum effective doses and decrease the duration of steroids for maintaining clinical efficiency and to reduce the risk of adverse effects. Also the patients should be well informed regarding those adverse effects and should seek medical help immediately if such symptoms occur. Early detection of osteonecrosis and osteoporosis, and their prompt treatment is essential for decreasing morbidity and improving quality of living.

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