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Case Report

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Short period corticosteroid therapy related multifocal ostonecrosis: a case report

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ABSTRACT

Corticosteroid therapy is the most common iatrogenic etiologic factor for osteonecrosis and is most commonly seen in the femoral head. When osteonecrosis occurs in 3 or more regions, it is called multifocal osteonecrosis. The fact that corticosteriod treatment was administered in very large groups of patients during the coronavirus (COVID-19) pandemic indicates that large groups of patients with osteonecrosis will be encountered in a certain period. Despite the large patient masses treated with corticosteriod, the low number of reported cases of multifocal osteonecrosis suggests that it may be clinically asymptomatic. The paucity of studies reporting multifocal osteonecrosis despite extensive corticosteroid use suggests that it may be asymptomatic. The aim of this article is to present a case of multifocal osteonecrosis after short-term low dose corticosteroid use and to describe its clinical features. There is a variable relationship between the risk of osteonecrosis and steroid use. Multifocal osteonecrosis is a treatment complication that can develop even after short-term low-dose corticosteroid use. The widespread use of corticosteroids during the COVID-19 pandemic appears to be a risk factor for increased incidence of osteonecrosis.

Keywords: Multifocalosteonecrosis, COVID-19, facial paralysis, glucocorticoid

INTRODUCTION

Osteonecrosis (ON) is ischemia and tissue death in bone that develops in many different situations.[1] Corticosteriod (CS) use is the most common cause of iatrogenic ON[2,3] and is frequently seen in the femoral head.[4] ON occurring in three or more sites is termed multifocal osteonecrosis (MFON). The incidence is around 3%.[5] The most important risk factor for MFON is CS use. Systemic lupus erythematosus (SLE), coagulation disorders, renal failure, inflammatory bowel diseases, multiple sclerosis, sickle cell anemia, and hematologic malignancies may cause MFON.[6]

Glucocorticoid use varies in terms of dosage, route of administration or duration depending on the current diagnosis and the patient's condition. Calculated on prednisone, there are low (<7.5 mg/day), intermediate (7.5-30 mg/day), high (30-100 mg/day), very high dose (>100 mg/day) and pulse therapy alternatives.

The fact that CS treatment was applied in very large patient groups during the coronavirus (COVID-19) pandemic period indicates that patient groups with clinical signs and symptoms related to ON and the mechanical failure and joint destruction it causes will be encountered.[7]

Although there are many patients treated with CS, there are few case reports of MFON, suggesting that MFON may be asymptomatic and the number of patients who develop degenerative joint disease in the future may be high.

The aim of this case report is to raise awareness about the risk of encountering a high number of patients with sequelae of MFON in the near future and to draw attention to the detection of asymptomatic cases through a patient who developed ON in four extremities, which occurred approximately 2 years after methylprednisolone treatment for facial nerve paralysis.

CASE PRESENTATION

A 37-year-old male patient presented with rest pain in the left shoulder that increased with movement. It was learned that the patient was diagnosed with facial paralysis with facial numbness, inability to close the eyelid and asymmetry around the mouth 2 years ago and 16 mg/day methylprednisolone treatment was started and the drug was tapered and discontinued within one month.

On physical examination, range of motion was complete and Neer, Hawkins, Yergason and Speed tests were negative. Neurovascular examination was normal. Radiography revealed density loss, local osteopenic areas and patchy sclerotic appearance consistent with ON without collapse of the humeral head. While the patient was being evaluated, the same complaints started in the right shoulder and the patient was hospitalized in our clinic again. Radiographs of the right shoulder showed findings compatible with

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ON. Magnetic resonance imaging (MRI) revealed diffuse bone marrow edema in both shoulders and double line findings compatible with stage 2 ON according to Cruess classification (Figure 1).[8]

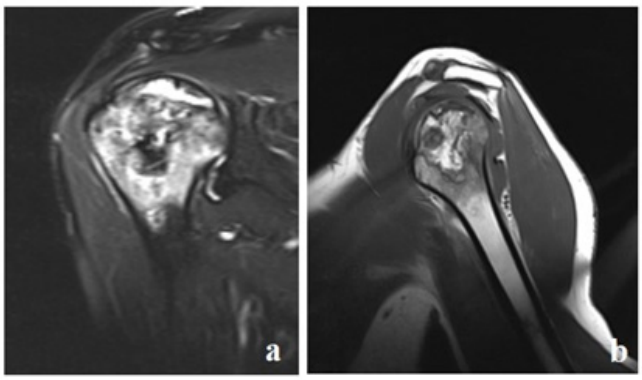

Figure 1. MR images in different planes and modalities showing Stage-2 osteonecrosis in both shoulder joints.

Cor decompression was planned for treatment and pain management and range of motion exercises were started. During this period, the patient presented with pain in the left hip that increased with walking. Physical examination revealed full but painful range of motion of the left hip joint. The patient had an antalgic gait. FABER and FADIR tests were positive. There was no active complaint in the right hip joint. Range of motion was full and painless. FABER and FADIR tests for the right hip joint were normal. MR imaging revealed stage 2 CON in both hip joints according to Steinberg classification (Figure 2).[9] Core decompression surgery was performed on all 4 extremities of the patient at different times. In the second postoperative year, the patient had full motion in all joints. Harris scores were 77 (fair) and 89 (good) for the left and right hip joints respectively, Quick DASH scores were 30 for both shoulders and DASH-work module was 50. Written informed consent was obtained from the patient for this case report.

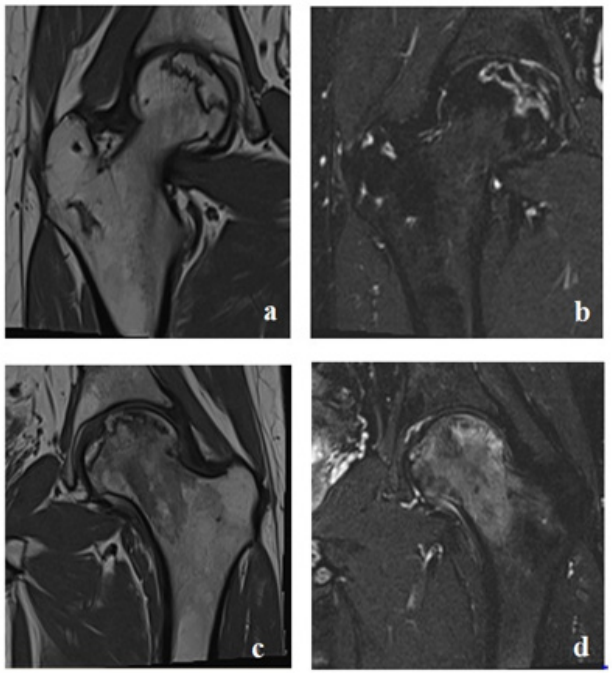

Figure 2. MRI images obtained in the coronal plane showing Stage-2 osteonecrosis in both hip joints.

DISCUSSION

In this case report, 3 main features of ON due to steroid use are presented.

The first feature is that ON may occur as late as 2 years after steroid use. Koo et al.[10] emphasized that the risk is high in the first 12 months after the start of treatment and close follow-up is required in this period. Oinuma et al. SLE, Saito et al. found ON between 3-12 months with MR follow-up after CS in renal transplantation patients. In our case, ON developed 2 years later with a short-term (1 month) treatment. It has been reported that the risk of ON development increases with increasing duration and dose of CS use (above 20 mg/day), while short-term low-dose or low-dose cumulative CS treatment does not lead to a significant increase in the risk of ON.[11,12] Our case shows that short-term treatment also carries this risk.

Based on this case, we think that patients should be followed up for at least 2 years for ON after CS treatment, and if the duration of treatment is long and the dose taken is high, follow-up should be performed at more frequent intervals.

The second feature of this case is that ON is multifocal and affects more than one joint. Krez et al.[3] in their study of 55 patients who developed MFON after CS, Krez et al. showed that the highest risk was SLE (45%) and the risk was increased in patients with hematologic malignancy, HIV, alcoholism and deep vein thrombosis receiving CS. Sun et al.[6] in their 96-case MFON series, SLE and hematologic diseases were the top two risk factors. In both MFON series, neuropathies were not reported as a risk factor. The absence of risk factors in our case suggests that MFON may develop due to CS use in every diagnosis. In Sun's series, 78% of the patients received high doses of CS over 20 mg/day and 24% over 80 mg/day. Unlike these data, an important finding of our case is that MFON may develop even at a dose of 16 mg/day. Krez et al.[3] found the mean duration of treatment to be 300 days and the shortest duration to be 90 days. Our case shows that even short-term treatments such as 30 days may be risky in terms of the risk of MFON development.

The third finding regarding the development of ON after CS in our case is that ON may be asymptomatic. In studies evaluating risk factors for MFON, it has been shown that involvement in one joint carries a risk of ON in the symmetrical joint.[1,3,6] When this information is combined with the asymptomatic clinic, we think that when ON is detected in one joint, the symmetrical joint should be evaluated in detail in terms of ON. Although MRI is the most sensitive imaging method known in the diagnosis of ON, we think that bone scintigraphy, which gives the chance to detect MFON at an earlier stage and has the potential to reveal multifocal involvement including asymptomatic involvement, may have a place in the diagnosis.[2]

One of the reasons for presenting a case of MFON due to CS use is that in the last 3 years, during the COVID-19 pandemic, CS treatment has been applied in large masses and the possibility of encountering single or multifocal ON patients with an increasing incidence in the clinic has emerged in this process. One follow-up study that in the literature, highlights the importance of MRI for evaluating the origin of hip and knee pain and timely detecting ON after the combined treatment with corticosteroids. The authors diagnosed ON at 2-year follow-up of 8 corticosteroid-naïve subjects exposed to variable doses and durations of

corticosteroid therapy.[13] In the literature, it has been reported and recommended that the use of methylprednisolone (1-2 mg/kg/day for 5-7 days) in patients with severe COVID-19 pneumonia is associated with better radiographic findings and shorter duration of supplemental oxygen therapy. And in daily practice there have been many COVID-19 patients treated with this and higher doses of corticosteroid.[14,15] Shetty demonstrated that in addition to the use of systemic CS, the hyperinflammatory state and activation of the coagulation cascade caused by SARS-CoV2 virus infection, endothelialitis and cardiac dysfunction will contribute to the development of ON with its direct effect on blood flow and multiply the risk.[16] Based on these findings, we would like to emphasize that ON should be kept in mind in the differential diagnosis of joint pain in patients with a history of COVID-19 who have received CS treatment, and that the possibility of developing ON is higher compared to the general population.

CONCLUSION

MFON may occur even with short-term and low dose CS treatment. Multifocal involvement may develop in ON and MFON may be asymptomatic. CS treatment during the COVID-19 pandemic is a risk factor that may lead to an increase in the number of patients developing ON.

ETHICAL DECLARATIONS

Informed Consent: All patients signed and free and informed consent form.

Reviewer Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: During the course of this study, no financial and/or moral support was received from any company that provides and/or manufactures any drugs, medical devices, equipment and supplies, or from any commercial company.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Pavelka K. Osteonecrosis. *Best Prac Res Clin Rheum,* 2000;14(2):399-414.
2. Chan KL, Mok CC. Glucocorticoid-induced avascular bone necrosis: diagnosis and management. *Open Orthop J.* 2012;6(1):449-450.
3. Krez A, Lane J, Heilbronner A, et al. Risk factors for multi-joint disease in patients with glucocorticoid-induced osteonecrosis. *Osteoporos Int.* 2021;32(1):2095-2103.
4. Chang C, Greenspan A, Gershwin ME. The pathogenesis, diagnosis and clinical manifestations of steroid-induced osteonecrosis. *J Autoimmun.* 2020;110(3):102460.
5. Group CO. Symptomatic multifocal osteonecrosis. A multicenter study. *Clin Orthop Relat Res.* 1999;369(3):312-326.
6. Sun W, Shi Z, Gao F, Wang B, Li Z. The pathogenesis of multifocal osteonecrosis. *Scient Rep.* 2016;6(1):1-6.
7. Zhan Y, Shang J, Gu Y, Huang Q, Xie J. Efficacy of corticosteroid in patients with COVID-19: a multi-center retrospective study and meta-analysis. *J Med Virol.* 2021;93(7):4292-4302.
8. Mercado JSC, Lievano JR, Zaldivar B, Barajas C, Fierro G, González JC. Atraumatic osteonecrosis of the humeral head: pathophysiology and current concepts of evaluation and treatment. *JSES Rev Rep Tech.* 2022;2(3):277-284.
9. Sultan AA, Mohamed N, Samuel LT, et al. Classification systems of hip osteonecrosis: an updated review. *Int Orthop.* 2019;43(1):1089-1095.
10. Koo KH, Kim R, Kim YS, et al. Risk period for developing osteonecrosis of the femoral head in patients on steroid treatment. *Clin Rheuma.* 2002;1(1):299-303.
11. Mont MA, Pivec R, Banerjee S, Issa K, Elmallah RK, Jones LC. High-dose corticosteroid use and risk of hip osteonecrosis: meta-analysis and systematic literature review. *J Arthroplasty.* 2015;30(9):1506-1512.
12. Dilisio MF. Osteonecrosis following short-term, low-dose oral corticosteroids: a population-based study of 24 million patients. *Orthop.* 2014;37(7):631-639.
13. Veizi E, Erdoğan Y, Sezgin BS, Karaman Y, Kılıçarslan K, Fırat A. The painful joint after COVID-19 treatment: a study on joint osteonecrosis following COVID-19-related corticosteroid use. *Joint Dis Rel Surg.* 2023;34(1):75.
14. Wang Y, Jiang W, He Q, et al. A retrospective cohort study of methylprednisolone therapy in severe patients with COVID-19 pneumonia. *Signal Transduct Targeted Therapy.* 2020;5(1):57.
15. Recovery collaborative group. Dexamethasone in hospitalized patients with Covid-19. *NEJM.* 2021;384(8):693-704.
16. Shetty GM. Double trouble-COVID-19 and the widespread use of corticosteroids: are we staring at an osteonecrosis epidemic? *Indian J Orthop.* 2021;56(2):1-11.