

Case Report

Contents lists available at ScienceDirect

Annals of Medicine and Surgery



journal homepage: www.elsevier.com/locate/amsu

Steroid-induced avascular necrosis: A case report on a patient treated with steroid therapy for COVID-19



Gyabina Maharjan^a, Stuti Yadav^{b,*}, Mandeep Kumar Yadav^c, Nirajan khati^d, Himal Bikram Bhattarai^e, Jaydev Joshi^a

^a Department of Internal Medicine, Kirtipur Hospital, Kathmandu, Nepal

^b Nepalese Army Institute of Health Sciences, Kathmandu, Nepal

^c Department of Internal Medicine, Nepal Bharat Maitri Hospital, Kathmandu, Nepal

^d Department of Internal Medicine, Vayodha Hospital, Kathmandu, Nepal

^e Gandaki Medical College Teaching Hospital and Research Center, Pokhara, Nepal

ARTICLE INFO	A B S T R A C T
Keywords:	Introduction: COVID-19 must get a combined approach that involves epidemiology, surveillance, accurate diagnosis, and prophylaxis. Corticosteroids use in the treatment of COVID-19, for a long time at high doses, can cause steroid-induced avascular necrosis.
COVID-19	<i>Case report:</i> The patient is a 22-year-old female. She came with a complaint of bilateral groin pain for 4 months. The pain was abrupt in onset, continuous, non-radiating, aggravated by walking and relieved with rest. We did an X-ray of the bilateral hips, blood tests, and MRI. With the investigations, we established the diagnosis of avascular necrosis of the femoral head.
Avascular necrosis	<i>Discussion:</i> Ischemia of the femoral head is caused by any interruption in the blood supply of the acetabulum. It is induced by high-dose and long-term steroid usage. Glucocorticoids affect the metabolism of lipids which results in the formation of fat emboli and lipoprotein globules. This blocks peripheral vessels and leads to necrosis of the bone due to ischemia.
Corticosteroid	<i>Conclusion:</i> Avascular necrosis of the femoral head has been reported in patients treated with corticosteroids while being treated for COVID-19. So, physicians should keep it as a possible diagnosis and enhance their knowledge on this topic.

1. Introduction

COVID-19 has devastated millions of lives. Hence, this pandemic must get a combined approach that involves epidemiology, surveillance, accurate diagnosis, and prophylaxis. The treatment of COVID-19 may involve the use of corticosteroids. The use of corticosteroids, for a long time at high doses, can cause steroid-induced avascular necrosis of the femoral head (SANFH) [1,2]. It is an aseptic and ischemic condition that can develop after steroid therapy [3]. Here, we discuss the case of a 22-year female who developed avascular necrosis of the femoral head after being treated for COVID-19 with corticosteroids. This case has been reported in line with SCARE's guidelines [4].

2. Case report

A 22-year female presented to the Out Patient Department with bilateral groin pain for 4 months. She developed pain in the right groin 4 months ago, which was abrupt in onset, continuous, non-radiating, aggravated by walking and relieved with rest. It was not associated with fever and swelling. She developed the same type of pain in her left groin, which was radiating towards her left knee joint. Regarding her past medical history, she had COVID-19 pneumonia seven months ago, for which she was treated with oral and parenteral steroids for six weeks. She was diagnosed with avascular necrosis of both femoral heads and underwent core decompression of both femoral heads with Bone Marrow Aspirate Concentrate (BMAC) injection.

https://doi.org/10.1016/j.amsu.2022.104226

Received 11 May 2022; Received in revised form 13 July 2022; Accepted 19 July 2022 Available online 31 July 2022

^{*} Corresponding author. Nepalese Army Institute of Health Sciences, Kathmandu, Nepal. *E-mail address:* stui4542@gmail.com (S. Yadav).

^{2049-0801/© 2022} The Author(s). Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

2.1. Investigation

2.1.1. Prominent laboratory findings include

SN.	Laboratory investigations	Laboratory values	References
1	Total Leucocyte count	5100	4000-11000
2.	Differential Leucocyte	N59L31M8E2BO	N 55–70 L 20–40 M 2-8
	count		E1-4
			B 0.5–1
3.	ESR	40mm/hr	Male: ≤15 mm/hr
			Female: ≤20 mm/hr
4.	CRP	27mg/L	CRP: <10 mg/L

2.2. X-ray of the bilateral hips

- Subchondral lucency and a crescent sign suggested avascular necrosis in the right femoral head.
- Normal findings in the left hip.

2.3. MRI of the bilateral hips

- It showed avascular necrosis of the bilateral femoral head.

2.3.1. Treatment

In the aseptic condition, bone marrow was aspirated from the left ASIS. BMAC was prepared. Bilateral core decompression was done. BMAC was injected and the wound was closed in layers. Tab alendronate 70mg OD weekly for 2 months, Tab Zocef (cefuroxime and clavulanic acid) 500mg per oral BD for 2 weeks and Tab pantop(Pantoprazole) 40mg OD for 2 weeks were prescribed.

2.3.2. Outcome and follow-up

She was advised of non-weight bearing exercises. Mobilization on crutches was done for 1 month. Physiotherapy was done. On further follow-up, she is now mobilizing without crutches. Two follow ups were done. One after 2 weeks and another after 2 months of surgery.

3. Discussion

The acetabulum or socket of the hip is supplied by the acetabular branch of the obturator artery along with the pubic branches of the obturator artery and the deep branches of the superior gluteal artery. Any disruption in the blood supply could lead to ischemia and then necrosis [5,6].

It is very imperative to know the pathophysiology of COVID-19 and the role of corticosteroids. Firstly, the infected cellular debris augments the release of inflammatory cytokines like TNF-alpha, IL-1, and IL-6. The further cycle of immune activation with a subsequent hyperinflammatory state is triggered by uncontrolled viral replication. There is an accompanying "cytokine storm" that causes heavy vascular inflammation, hypotension, disseminated coagulation, and shock leading to multi-organ failure and death. The intervention of corticosteroids in COVID 19 was formulated with this pathophysiology [7,8].

Glucocorticoids inhibit cytokine storm by inhibiting the expression of IL-1, IL-2, IFN-gamma, and TNF-alpha which are pro-inflammatory proteins. It also inhibits the migration of leukocytes to the site of inflammation.

Ischemia is caused by glucocorticoids in several ways. Glucocorticoids affect the metabolism of lipids by disturbing the emulsification of VLDL in the blood. This results in LDL combining with lipoprotein globules and forming fat emboli, which block peripheral vessels and lead to necrosis of the bone due to ischemia. Moreover, FFA, which is formed by the hydrolysis of fat emboli, tends to damage endothelial cells of capillaries and cause diffuse vasculitis. It can further initiate intravascular coagulation and exacerbate ischemic necrosis [9-11].

Glucocorticoids regulate the local blood flow by controlling the response of vessels to vasoactive substances, which constrict the internal artery of the femoral head. Fu et al. revealed that the expression of microRNA 596 in the bone marrow of SANFH patients was up-regulated. The repair of osteonecrosis bone is impeded due to inhibition of proliferation and differentiation of BMSCs [12].

The glucocorticoid-induced Noxs expression, which may cause osteocyte apoptosis in the process, is a major source of oxidative stress [13-15]. ROS has been demonstrated to ONFH [16,17].

4. Conclusion

Many incidences of SANFH have been reported in convalescent SARS patients. Hence, physicians should keep it as a possible diagnosis in mind while dealing with patients with bone and joint pain. Physicians must enhance their knowledge about the prevention of avascular necrosis.

Ethical approval

Ethical approval was not required. Consent was taken.

Sources of funding

This research did not receive any grant, funds or sponserships.

Author contribution

Gyabina Maharjan: Providing resources, Visualization, Reviewing, and supervision. Stuti Yadav: Data Curation, Writing, Reviewing, and editing the manuscript. Mandeep Kumar Yadav: Writing, Reviewing, and editing the manuscript. Nirajan Khati: Writing, Reviewing, and editing the manuscript. Himal Bikram Bhattarai: Writing, Reviewing, and editing the manuscript. Jaydev Joshi: Writing, Reviewing, and editing the manuscript.

Consent

Written consent taken from the patient.

Research registration number

Not applicable.

Registration of research studies

- 1. Name of the registry: None
- 2. Unique Identifying number or registration ID: None
- 3. Hyperlink to your specific registration (must be publicly accessible and will be checked): None

Guarantor

Gyabina Maharjan.

Declaration of competing interest

No conflict.

Acknowledgment

None.

G. Maharjan et al.

Abbreviations

SANFH	steroid-induced avascular necrosis of the femoral head
OPD	out patient department
BMSCs	bone marrow stromal cells
ROS	reactive oxidative stress
ONFH	osteonecrosis of femoral head
VLDL	very-low-density lipoprotein
LDL	low-density lipoprotein

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.104226.

References

- P. Rai, B.K. Kumar, V.K. Deekshit, I. Karunasagar, I. Karunasagar, Detection technologies and recent developments in the diagnosis of COVID-19 infection, Appl. Microbiol. Biotechnol. 105 (2021) 441–455, https://doi.org/10.1007/ s00253-020-11061-5.
- [2] S. Zhang, C. Wang, L. Shi, Q. Xue, Beware of steroid-induced avascular necrosis of the femoral head in the treatment of COVID-19—Experience and lessons from the SARS epidemic, Drug Des. Dev. Ther. 15 (2021) 983–995, https://doi.org/ 10.2147/DDDT.S298691.
- [3] T. Kubo, M. Fujioka, M. Ishida, Clinical condition of steroid-induced osteonecrosis of the femoral head, Clin. Calcium 17 (2007) 856–862, https://doi.org/ clica0706856862.
- [4] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, for the SCARE Group, The SCARE 2020 guideline: updating consensus surgical CAse REport (SCARE) guidelines, Int. J. Surg. 84 (2020) 226–230.
- [5] J. Barney, N.S. Piuzzi, H. Akhondi, Femoral head avascular necrosis, in: StatPearls, StatPearls Publishing, Treasure Island (FL), 2022. http://www.ncbi.nlm.nih. gov/books/NBK546658/. (Accessed 3 May 2022).

- [6] Z.-Q. Fan, S.-C. Bai, Q. Xu, Z.-J. Li, W.-H. Cui, H. Li, X.-H. Li, H.-F. Zhang, Oxidative stress induced osteocyte apoptosis in steroid-induced femoral head necrosis, Orthop. Surg. 13 (2021) 2145–2152, https://doi.org/10.1111/os.13127.
- [7] R.M. Sweeney, D.F. McAuley, Acute respiratory distress syndrome, Lancet 388 (2016) 2416–2430, https://doi.org/10.1016/S0140-6736(16)00578-X.
- [8] F. Wang, J. Nie, H. Wang, Q. Zhao, Y. Xiong, L. Deng, S. Song, Z. Ma, P. Mo, Y. Zhang, Characteristics of peripheral lymphocyte subset alteration in COVID-19 pneumonia, J. Infect. Dis. 221 (2020) 1762–1769, https://doi.org/10.1093/infdis/ jiaa150.
- [9] C. Strehl, L. Ehlers, T. Gaber, F. Buttgereit, Glucocorticoids-all-rounders tackling the versatile players of the immune system, Front. Immunol. 10 (2019) 1744, https://doi.org/10.3389/fimmu.2019.01744.
- [10] K.-H. Koo, R. Kim, Y.-S. Kim, I.-O. Ahn, S.-H. Cho, H.-R. Song, Y.-S. Park, H. Kim, G.-J. Wang, Risk period for developing osteonecrosis of the femoral head in patients on steroid treatment, Clin. Rheumatol. 21 (2002) 299–303, https://doi. org/10.1007/s100670200078.
- [11] M.A. Kerachian, C. Séguin, E.J. Harvey, Glucocorticoids in osteonecrosis of the femoral head: a new understanding of the mechanisms of action, J. Steroid Biochem. Mol. Biol. 114 (2009) 121–128, https://doi.org/10.1016/j. jsbmb.2009.02.007.
- [12] L. Fu, H. Liu, W. Lei, MiR-596 inhibits osteoblastic differentiation and cell proliferation by targeting Smad3 in steroid-induced osteonecrosis of femoral head, J. Orthop. Surg, 15 (2020) 173, https://doi.org/10.1186/s13018-020-01688-5.
- [13] A. Latini, K. Scussiato, R.B. Rosa, S. Llesuy, A. Belló-Klein, C.S. Dutra-Filho, M. Wajner, D-2-hydroxyglutaric acid induces oxidative stress in cerebral cortex of young rats: D-2-hydroxyglutaric acid and oxidative stress, Eur. J. Neurosci. 17 (2003), https://doi.org/10.1046/j.1460-9568.2003.02639.x, 2017–2022.
- [14] E. Warwick, A. Scourfield, J. Quint, Systemic manifestations of chronic obstructive pulmonary disease, Br. J. Hosp. Med. 76 (2015) 324–329, https://doi.org/ 10.12968/hmed.2015.76.6.324.
- [15] N. Mizushima, B. Levine, A.M. Cuervo, D.J. Klionsky, Autophagy fights disease through cellular self-digestion, Nature 451 (2008) 1069–1075, https://doi.org/ 10.1038/nature06639.
- [16] Z. Li, W. Sun, H. Qu, Y. Zhou, B. Dou, Z. Shi, N. Zhang, X. Cheng, D. Wang, W. Guo, [Clinical research of correlation between osteonecrosis and steroid], Zhonghua Wai Ke Za Zhi 43 (2005) 1048–1053.
- [17] Y. Mao, J. Wei, L. Zhou, M. Wang, J. Su, [Related factor analysis of avascular necrosis of the femoral head after internal fixation with cannulated screws in femoral neck fractures], Zhonghua Yixue Zazhi 85 (2005) 3256–3259.