



Osteonecrosis amid the COVID-19 pandemic

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Received: 4 April 2023 / Accepted: 17 April 2023 / Published online: 25 April 2023

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The COVID-19 pandemic has changed our understanding of numerous autoimmune diseases, clinical conditions, and complications triggered by the novel coronavirus and related treatments. Numerous new clinical issues have emerged as a result. The latest evidence on osteonecrosis (ONC), or avascular necrosis, after combined COVID-19 treatment at the beginning of the pandemic, is one of the proofs of the emerging issues [1]. The global medical community is alerted on the risk of corticosteroid therapy of COVID-19 in corticosteroid-naïve subjects that may complicate with hip and knee pain and ONC at 1-year follow-up [1]. The follow-up study highlights the importance of MRI for evaluating the origin of hip and knee pain and timely detecting ONC after the combined treatment with corticosteroids. The authors diagnosed ONC at 2-year follow-up of 8 corticosteroid-naïve subjects exposed to variable doses and durations of corticosteroid therapy [1]. One of the eye-catching features of the study is the wide range of cumulative corticosteroid doses – 50–20,675 mg prednisolone, although it is unclear why the extremely high dose of 20,675 mg was used and whether it resulted in ONC. The cumulative dose of 400 mg prednisolone, or 6 mg/daily dexamethasone for 10 days, seems the highest acceptable extreme in severe COVID-19 in view of the RECOVERY trial outcomes [2].

The global medical community has been alerted on the likelihood of the ONC syndemic that can be prevented by more careful approach to corticosteroid therapy, supplementation of calcium and vitamin D, and personalized physical rehabilitation [3–6]. Regrettably, more and more general practitioners, rheumatologists, and orthopedic surgeons worldwide are now encountering post-COVID-19 patients with ONC involving the femoral head, knee, jaw, and other joints [7–9]. ONC is now viewed as a key manifestation of long COVID syndrome that may present within 2 months after COVID-19 treatment even with relatively low cumulative doses of corticosteroids [10, 11]. We think that ONC can be considered the main musculoskeletal manifestations of post-COVID-19 syndrome as myalgia, arthralgia, and arthritis [12].

ONC is a degenerative complication of corticosteroid therapy that commonly affects subjects on high-dose and prolonged therapies, although short-term exposure to lower doses and may also result in the same complication. Plausible mechanisms of ONC in genetically predisposed subjects include lipid abnormalities with fat embolism, coagulation defects with thrombosis, and osteocyte apoptosis [13]. Systemic inflammation, coagulation, and vasculitis with leucocyte activation and aggregation in COVID-19 may affect osteoblast proliferation and differentiation and augment pathways underlying ONC [14]. Early diagnosis of ONC by timely MRI is strongly advisable as it may help to choose the best non-interventional and interventional treatment modalities, particularly arthroplasty in collapsed femoral head [15, 16].

The open-label RECOVERY trial has demonstrated one-month mortality benefit of dexamethasone therapy in COVID-19 patients on invasive mechanical ventilation or oxygen therapy alone [2]. However, the same trial did not find any benefit of corticosteroid therapy in subjects without intensive respiratory support. Moreover, another large US-based study of COVID-19 hospitalized patients who did not require intensive respiratory support dexamethasone use within 48 h almost doubled the mortality risk at 90 days

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(Hazard Ratio 1.76, 95% Confidence Interval 1.47–2.12) [17]. Both studies stressed the importance of justified use of dexamethasone to avoid deaths, particularly in mild and moderate cases.

Regrettably, findings of these landmark studies have not been correctly interpreted across most COVID-19 clinics. As a result, a global increase of long-term complications of unjustified corticosteroid use in COVID-19 is expected. For instance, a tripled frequency of ONC of femoral head has been observed in subjects referred to Shymkent Medical Center of Joint Diseases (Shymkent, Kazakhstan) during the pandemic: 11, 22, and 31 cases in 2019, 2020, and 2021, respectively. Such a worrying dynamic can be due to routine administration of corticosteroids to all hospitalized patients in COVID-19 clinics across the country. Additionally, widespread corticosteroid exposure in outpatient COVID-19 cases and unauthorized self-administration by patients who refuse physician referrals may further complicate the issue.

Undoubtedly, well-designed cohort studies are warranted to uncover confounding factors of ONC during and after the pandemic. Patients with arthroplasties may form a special interest group in whom severe COVID-19 and non-infectious comorbidities and multi-morbidities may enhance the risk of operative interventions independently of corticosteroid therapies. Corticosteroid therapies should be reserved for critically ill COVID-19 cases only. Increasing the global awareness of the risk of ONC due to uncontrolled and unjustified corticosteroid therapies may help timely diagnose this complication and avoid operative interventions.

Declarations

Conflict of interest None.

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