High-dose steroids for the treatment of severe COVID-19: comment

Shuichi Tanaka¹ · Koichiro Yamamoto¹ · Hideharu Hagiya¹ · Kou Hasegawa¹ · Fumio Otsuka¹

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Dear editor,

We read with great interest the recent paper published by Piccica et al. regarding the effectiveness of high-dose steroid therapy for coronavirus disease 2019 (COVID-19) [1]. In this case series, 13 patients were introduced high-dose steroid pulse therapy for a median of 4 days (IQR 3–5); the median dosage of methylprednisolone was 250 mg. Interestingly, nine patients (69.2%) who were received high-dose steroids improved, while four of those did not. The authors suggested a necessity of investigation for appropriate dosage of steroid therapy with or without other treatment strategy. As the authors cited in the report, a meta-analysis revealed that a corticosteroid administration was effective to critically ill patients with COVID-19, which was associated with improvement of 28-day all-cause mortality [2]. In that study, dexamethasone had a statistically significant effect, while hydrocortisone or methylprednisolone did not. We herein present the case with severe COVID-19, to whom 6.6 mg per day of dexamethasone was ineffective but subsequent methylprednisolone pulse therapy improved respiratory condition and inflammation.

A 77-year-old woman, who was diagnosed with COVID-19 by PCR test to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), presented with a 6-day-long fever. The patient was obese (body mass index, 26.6 kg/m²) and had medical histories of hypertension, dyslipidemia, and Alzheimer's dementia. On admission, she was hyperthermic (38.4 °C) in severe respiratory distress with an oxygen saturation level of 70–80% at room air. Laboratory tests revealed elevations of serum inflammatory markers: C-reactive protein (CRP), 7.01 mg/dL; ferritin, 647 ng/mL; and lactate dehydrogenase, 587 U/L. Chest computed tomography showed bilateral multiple ground-glass opacities, which

were compatible with COVID-19 pneumonia. The patient was admitted at an intensive care unit, and oxygen supplementation via a facial mask with reservoir bag (10 L/min) and administration of favipiravir and 6.6 mg per day of dexamethasone were initiated. On the 4th day of hospitalization, her respiratory condition deteriorated to 96 of PaO₂/FiO₂ ratio, with remaining a high serum CRP level (7.70 mg/dL). Chest X-ray showed bilaterally spreading infiltration shadow with the right dominance (Fig. 1A). We intubated the patient and administered 125 mg per day of methylprednisolone for 3 days as a steroid pulse therapy. Her respiratory status as well as serum inflammatory markers ameliorated thereafter, and the steroid treatment was tapered. She was extubated on the 9th day of admission, when infiltrate shadows on chest X-ray improved (Fig. 1B).

There is no well-established treatment for the severe COVID-19 cases, although the latest researches and clinical guidelines recommend certain treatment options. In reaction to SARS-CoV-2 infection, macrophages and dendritic cells trigger an initial immune response such as lymphocytosis and cytokine release [3]. In critically ill patients with COVID-19, the inflammatory response results in the destruction of lymphocytes attempting to suppress SARS-CoV-2 proliferation, leading to unregulated cytokine production [3]. Cytokine storm damages healthy cells typically in the lungs, and causes diffuse alveolar damage, hyaline membrane formation, thrombus formation, fibrin exudates, and fibrotic healing [3]. Preliminarily, corticosteroid therapy (6.6 mg per day of dexamethasone) is considered to be effective for suppressing abnormal immune responses [4], and we initially treated the present case with it. However, her PaO₂/FiO₂ ratio and inflammatory markers deteriorated, indicating an ineffectiveness of the usual dose of steroid therapy. As Piccica et al. mentioned effectiveness of high-dose steroid therapy [1], Edalatfard et al. also suggested high-dose methylprednisolone therapy can reduce respiratory inflammation in the early phase before intubation [5]. In that report, patients treated with high-dose methylprednisolone therapy (250 mg per day for 3 days) had a better clinical course than those with the standard therapy (94.1% vs 57.1%); even the

✉ Hideharu Hagiya
hagiya@okayama-u.ac.jp

¹ Department of General Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Science, 2-5-1 Shikata-cho, Kita-ku, Okayama 700-8558, Japan

Fig. 1 Imaging of COVID-19 on admission. Chest X-ray pictures on day 4 (**A**, just before the intubation) and day 9 (**B**, soon after extubation). The infiltration shadow mainly at right lung dramatically improved

mortality rate was dramatically lower in high-dose methylprednisolone therapy (5.9% vs 42.9%) [3].

In conclusion, as Piccica et al. mentioned the potential efficacy of high-dose corticosteroid therapy [1], the present case shows that, in case the lower-dose corticosteroid therapy was unsuccessful for a patient with severe COVID-19, a high-dose corticosteroid therapy, i.e., 125 mg per day of methylprednisolone, may save the life in front of you.

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Declarations

Conflict of interest The authors declare no conflicts of interest.

References

1. Piccica M et al (2021) High-dose steroids for the treatment of severe COVID-19. *Intern Emerg Med*. <https://doi.org/10.1007/s11739-021-02707-x>
2. Sterne JAC et al (2020) Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: a meta-analysis. *JAMA* 324(13):1330–1341. <https://doi.org/10.1001/jama.2020.17023>
3. Bhaskar S et al (2020) Cytokine storm in COVID-19-immunopathological mechanisms, clinical considerations, and therapeutic approaches: the REPROGRAM consortium position paper. *Front Immunol* 11:1648. <https://doi.org/10.3389/fimmu.2020.01648>
4. Horby P et al (2021) Dexamethasone in hospitalized patients with Covid-19. *N Engl J Med* 384(8):693–704. <https://doi.org/10.1056/NEJMoa2021436>
5. Edalatfard M et al (2020) Intravenous methylprednisolone pulse as a treatment for hospitalised severe COVID-19 patients: results from a randomised controlled clinical trial. *Eur Respir J* 56(6). <https://doi.org/10.1183/13993003.02808-2020>

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