Time-critical administration of corticosteroid rescue therapy for COVID-19 pneumonitis in a ward-based patient with chronic obstructive pulmonary disease

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Introduction

The COVID-19 pandemic is placing extraordinary pressure on healthcare resources worldwide, and is particularly overwhelming critical care units, with many difficult decisions about treatment escalation being made. Pharmacological therapeutic options for COVID-19 are limited at present, although steroid therapy looks to have the most potential of the agents tested so far. This case demonstrates successful use of high-dose glucocorticoids as potential rescue therapy for a patient with diagnosed severe COVID-19 pneumonitis with a secondary haemophagocytic lymphohistiocytosis. This was a moderately frail, medically multi-morbid patient who was not a candidate for intubation. Despite his severe illness, he responded rapidly to steroid administration with a rapid wean and was discharged from hospital at day 11 of admission close to his functional baseline.

Case report

A 77-year-old man presented with 14 days of progressive shortness of breath, fever, cough and coryzal symptoms. Comorbidities included chronic obstructive pulmonary disease with moderate obstruction (forced expiratory volume in 1 second (FEV_1) 1.48 litres (59% predicted), forced vital capacity (FVC) 2.61 litres (78% predicted), FEV_1/FVC 57%. residual volume 143%, Medical Research Council score 3), hypertension, type 2 diabetes, chronic kidney disease stage 3 and ischaemic heart disease. His clinical frailty score was 4 (Walston et al, 2018). Based on this significant baseline comorbidity, it was felt that he would not be a candidate for escalation to level 3 treatment (intubation and ventilation) or cardiopulmonary resuscitation.

His admission chest X-ray showed diffuse bilateral opacification. There was high clinical suspicion of COVID-19 infection and empirical antibiotics were started for suspected bacterial chest infection. A COVID-19 polymerase chain reaction test was positive.

Within 48 hours his oxygen requirement rapidly increased from 2 litres (28%) to 15 litres humidified oxygen. Repeat chest X-ray at this time demonstrated worsening appearances (Figure 1). This was paired with a marked clinical deterioration and significant biochemical inflammatory response: his ferritin level peaked at 12 500 ng/ml (normal range 30–400 ng/ml) and C-reactive protein level at 217 mg/litre (normal range 0–4 mg/litre) (Table 1), consistent with the second phase of the disease (Zhou et al, 2020). Despite profound hypoxia, the patient remained alert, although severely dyspnoeic.

The clinical picture was felt to be consistent with secondary haemophagocytic lymphohistiocytosis phenotype (HScore 191) (Mehta et al, 2020). As a result, the patient was started on intravenous methylprednisolone 40 mg (0.5 mg/kg) on day 3 of admission. He improved substantially and his oxygen requirements progressively reduced. He no longer required oxygen therapy at day 6 of steroid treatment.

He completed an 8-day course of intravenous methylprednisolone followed by oral prednisolone wean, completing a total of 16 days. He was successfully discharged home on day 11 of his admission close to his functional baseline with no oxygen requirement. Steroid-induced hyperglycaemia was observed as an adverse effect, which was well controlled with supplemental insulin.

The patient has since been followed up in the respiratory clinic. He has made a good recovery although he remains at baseline more easily breathless on exertion. His follow-up high resolution computed tomography scan of the chest shows post-infection fibrotic change. This is being managed with close monitoring and pulmonary rehabilitation.

How to cite this article:
Kuzeva A, Dost S, Lams B, Agarwal S, Furmedge DS. Time-critical administration of corticosteroid rescue therapy for COVID-19 pneumonitis in a ward-based patient with chronic obstructive pulmonary disease. Br J Hosp Med. 2020. https://doi.org/10.12968/hmed.2020.0372

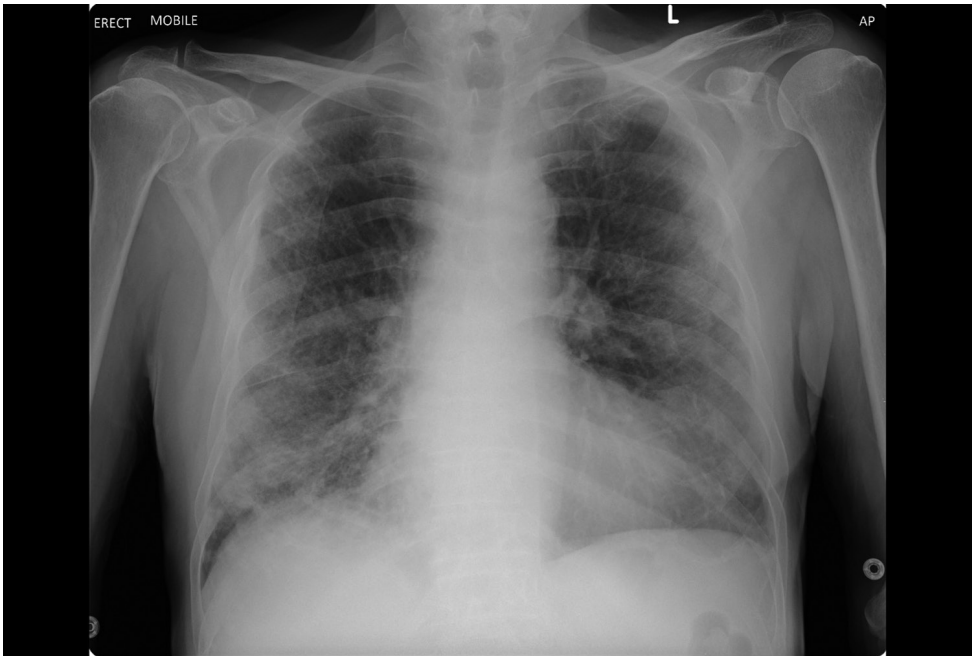

Figure 1. Chest radiograph taken on day 3 of admission.

Table 1. Course of disease parameters

Day from admission	1	2	3	4	6	11
Day from onset of symptoms	14	15	16	17	19	24
Day of intravenous methylprednisolone treatment			1	2	4	
White blood cells ($\times 10^9$/litre) (normal range 4.0–11.0 $\times 10^9$/litre)	5.8	6.0	5.5	7.0	11.1	9.3
Lymphocytes ($\times 10^9$/litre) (normal range 1.2–3.5 $\times 10^9$/litre)	2.9	0.7	0.7	2.1	2.6	2.8
C-reactive protein (mg/litre) (normal range 0–4 mg/litre)	217	186	178	200	96	15
Ferritin (ng/ml) (normal range 30–400 ng/ml)			12 500	9610	6324	1846
Oxygen requirement (litre/min)	2 litres	4 litres	15 litres	10 litres	2 litres	0
Temperature (°C)	37.1	38.6	38.3	37.0	36.1	36.4
Respiratory rate	29	24	30	22	20	19

Discussion

This case describes a deteriorating patient with a clinical picture suggestive of haemophagocytic lymphohistiocytosis and acute respiratory distress syndrome, in the context of COVID-19 pneumonitis with inflammatory markers suggestive of poor prognosis (Ruan et al, 2020). It appears that 17–41% of patients with COVID-19 develop acute respiratory distress syndrome, linked to a dysregulated systemic inflammatory response (Huang et al, 2020; Villar et al, 2020). Downregulation of systemic and pulmonary inflammation responses via corticosteroids plays an essential role in the recovery of damage caused by acute respiratory distress syndrome (Annane et al, 2017) and therefore corticosteroids are a good treatment option in patients treated at general ward level.

Corticosteroids are cheap, globally available, have a well-known side-effect profile and have had a targeted role in the treatment of acute respiratory distress syndrome since its first clinical description (Ashbaugh and Maier, 1985). Corticosteroids were used in Middle East respiratory syndrome and severe acute respiratory syndrome outbreaks, and the results from the majority of those studies were inconclusive, although a small number showed some benefits (Sung et al, 2004). At the beginning of the COVID-19 pandemic,

Learning points

- High-dose steroid therapy should be considered as rescue therapy for COVID-19 pneumonitis in those with evidence of a secondary haemophagocytic lymphohistiocytosis phenomenon (>day 10 from symptom onset, ongoing fever, persistently high C-reactive protein level and hyperferritinaemia).
- In particular, patients who are not candidates for escalation to critical care, who are multi-morbid or are moderately frail may benefit from high-dose rescue therapy with glucocorticoids, although patient selection needs careful thought.
- Care must be taken because of the risks associated with the use of corticosteroids, such as increased susceptibility to other pathogens and deranged hyperglycaemic control. However, the high benefit/risk (therapeutic index) ratio supports this intervention.
- Following the findings of the RECOVERY trial, which supports dexamethasone therapy in all patients with COVID-19 who require oxygen, further research is indicated in patients with COVID-19 who have a secondary haemophagocytic lymphohistiocytosis phenotype.

the World Health Organization did not support the use of corticosteroids in patients with COVID-19, based on an observational study showing decreased viral clearance in those taking glucocorticoids (Arabi et al, 2018). However, there is no evidence to suggest that delayed viral clearance is linked to an increase in mortality.

A recently released statement from the Chief Investigators of RECOVERY (Randomised Evaluation of COVid-19 thERapY) – a randomised clinical trial comparing 2104 patients treated with low-dose dexamethasone and 4321 patients randomised to usual care alone – showed that treatment with dexamethasone reduced the mortality by one third in patients on mechanical ventilation and by one fifth in patients on oxygen therapy (Recovery Trial Chief Investigators, 2020), although these data have not yet been peer reviewed. A small pre-printed study in Wuhan, China, assessing the effectiveness of early low dose methylprednisolone, showed that those taking it exhibited faster improvements in oxygen independence and temperature spikes (Wang et al, 2020). Another retrospective study in China found that methylprednisolone decreased mortality among those with acute respiratory distress syndrome (Wu et al, 2020).

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