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Letter to the Editor

# The successful management of an elderly Covid-19 infected patient by plasmapheresis

*Dear Editor,*

Coronavirus disease 2019 (COVID-19) is a pneumonia caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, China since December 2019. The epidemic spread rapidly worldwide, became a global threat and was characterized as a pandemic on March 11, 2020 by World Health Organization (WHO) [1]. It is not just a viral pneumonia, it can also cause a multisystemic disorder called COVID-19 immune syndrome [2]. In severe COVID-19 patients it was reported that the pro-inflammatory cytokins, mainly IL-6, IL-10, TNF-α were significantly increased around 7–14 days after onset, named as cytokine storm, which is also associated with the aggravation of disease and higher mortality [3,4]. Furthermore, most of these patients have already been in an induced-hypercoagulable state and predisposed to thrombosis. Currently, there isn't any specific effective and approved antiviral treatment for COVID-19 [5]. There aren't sufficient randomized controlled trials and so strong recommendations for the management of COVID-19 even from the international societies [2]. For better results and lower mortality rates, clinicians must both control the viral replication and also optimize the immun response. Plasmapheresis can take place successfully in the management of these patients with the use of anticoagulants and removal of both the inflammatory molecules and high molecular weight viscous components [6].

We want to emphasize the role of plasmapheresis by a critically ill Covid-19 patient whose clinical status worsen despite antiviral and tocilizumab treatments and who was successfully managed via performing plasmapheresis. A 65 year old female patient complaining of cough, myalgia and fatigue was admitted to our clinic who had a history of contact with a confirmed Covid-19 case. She had 3 comorbities: asthma, hypertension and type 2 Diabetes Mellitus. Her SARS-CoV-2 PCR test resulted negative, but her chest computed thomography(CT) revealed two small ground glass opacities in both lungs, which indicated COVID-19 pneumonia. According to our national Covid-19 treatment guidelines provided by the Ministry of Health, she was given hydroxychloroquine, azitromycine and oseltamivir. During hospital follow up, her maximum body temperature was 37.8 °C; all other vital signs were normal. Laboratory findings are summarized in Table 1. She completed the treatment schedule and was discharged from hospital after 5 days. On 10th day of the symptom onset she was readmitted to hospital with fever, cough, sputum and shortness of breath. Her fever was 38.5 °C, hearth rate was 118beats/min, respiratory rate was 26/min, blood pressure was 156/84 mmHg and oxygen saturation was 88 % at room air with intermittent prone positioning. Her thorax CT revealed bilateral multiple ground glass infiltrations (Fig. 1). Favipravir, enoxaparine prophylaxis, ceftriaxone and oxygen supplementation of 3 L/min were initiated. Laboratory tests showed elevated inflammation indicating cytokine storm with C-reactive protein 70 mg/L(reference 0−5) and IL-6 45.4 pg/mL(reference <7). Tocilizumab(8 mg/kg total dose) and prednisolone(1 mg/kg for five days) were also initiated. On the 14th day, patient complained of ongoing fever, dyspnea, haemoptyzis and became tachypneic(30 breaths/min), the oxygen need increased to 8 L/min to maintain oxygen saturation above 90 %. The patient was transferred to the intensive care unit (ICU). The D-dimer level increased to 1238 ng/mL. Chest CT-angiography showed that ground glass opacites were enlarged and turned to consolidation areas without thromboembolism (Fig. 2). Plasmapheresis was performed to control excessive inflammation by using 10 units of fresh frozen plasma. The plasmapheresis process was conducted with a Fresenius Medical Care device of Multifiltrate model with 7ML62939 serial number. The set used was Multifiltrate-Kit 16 MPS P2dry. On the following days tachypnea and fever were dissolved gradually. Significant improvement in the general

**Table 1**
Changes in laboratory parameters according to days after admission.

| Lab parameters (reference values) | Day1 | Day 10 | Day 14 | Day 24 | Day 38 |
|---|---|---|---|---|---|
| WBC (X1000)/uL | 8810 | 3920 | 2800 | 6540 | 5950 |
| Lymphocyte (X1000)/uL | 2300 | 1660 | 430 | 2770 | 2200 |
| CRP (0−5)mg/L | 9.5 | 70 | 8.7 | 0.2 | 0.3 |
| Procalcitonin (0−0.5) ng/mL | 0.2 | 0.1 | 0.1 | 0.1 | 0.1 |
| LDH (125−220) U/L | 154 | 272 | 453 | 208 | 170 |
| D-dimer (0−300)ng/mL | 338 | 318 | 1218 | 498 | 193 |
| Ferritin (4.6−204)ng/mL | 21 | 166 | 106 | 37 | 13 |
| ALT (0−55) U/L | 21 | 33 | 61 | 36 | 19 |
| AST (5−34) U/L | 13 | 32 | 56 | 19 | 12 |

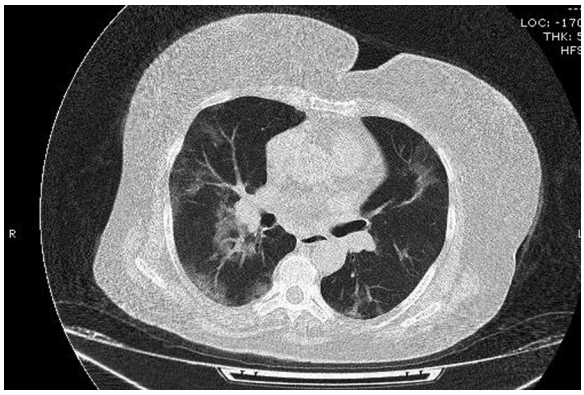

**Fig. 1.** Thorax CT showing bilateral multiple ground glass opacities on 10th day.

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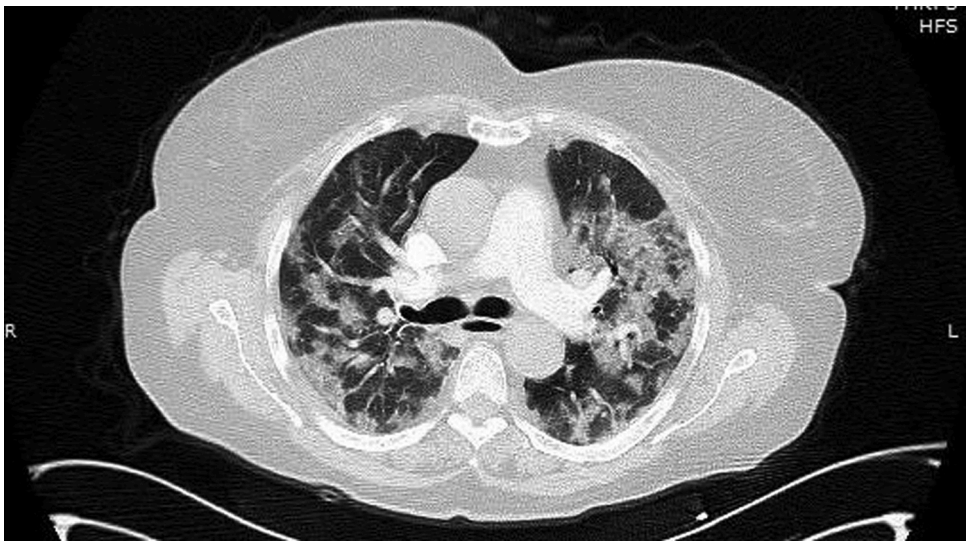


**Fig. 2.** Thorax CT showing bilateral multiple consolidations on 14th day.

health status of the patient was observed and transferred to standard care ward. Favipravir and prednisolone were terminated at 5th day, ceftriaxone was given for 10 days. Oxygen supplementation was decreased gradually and stopped. She was discharged from the hospital 24 days after first admission.

Currently, none of the therapies has showed definite efficacy for patients with COVID-19. Antiviral as well as anti-inflammatory treatment options, such as favipravir, remdesivir and tocilizumab, have been recently brought evidence forward. Yet, data upon optimal choice of one over the other, or combination formulas, remains an unanswered question [7]. It is known that, antiviral therapy is most beneficial when initiated earlier during the experience of the diseases both in influenza and in SARS [5]. The median duration from disease onset to ICU admission was 10.5 days, mostly associated with covid-19 immun syndrome. Tocilizumab is a recombinant anti-human IL-6 receptor monoclonal antibody. Thus it blocks IL-6 to bind its receptor, alleviates the inflammatory responses and prevents immune damage [8]. The half-life of inflammatory molecules in circulation is too short just as a few minutes. This suggests that plasmapheresis and other blood purification treatment options targeting inflammatory factors should be considered at an early stage in these patients as a 'window of opportunity' [9,10]. Because after the cascade effect of inflammatory factors, the efficiency of deposition may be limited. Timing of immunomodulatory treatments in cases with hypercytokinemia is crucial, and early initiation of treatment is in line with better outcome [3]. Nonetheless, in need, the administration of existing autologous antibodies collected from recovered COVID 19 patients, to provide immediate passive immunity, must always be kept in mind [11].

During this fight against pandemic, to reduce mortality it's inevitable that novel treatment and passive immunity options for severe cases are urgently needed until vaccines for COVID-19 are available [3]. We believe that plasmapheresis and convalescent plasma plays crtitical role in the management of severe COVID- 19 patients without suppressing immune system or in combination with immunsupressive agents.

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