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Case Report

Convalescent plasma therapy in obese severe COVID-19 adolescents: Two cases report

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ABSTRACT

Background: In Indonesia, 175 cases resulted in death in children from March to December 2020. Studies regarding Convalescent Plasma Therapy's (CPT) safety and efficacy in children are scarce. Our case report was the first to write CPT in Indonesian children.
Case presentation: In our case, two obese children with progressive shortness of breath, worsening cough, and high fever, the findings met severe COVID-19 criteria. We performed CPT for these patients and the patient's condition was improved and able to be discharged.
Discussion: Severe COVID-19 with or without comorbid was the indication of CPT which had been approved by the U.S. FDA and Indonesian Pediatrics Society. The key factors associated with CPT efficacy were the donor's titer antibody, the treatment time point, and the patient's comorbidities. The clinical impact showed an improvement by the combination therapy of CPT and remdesivir.
Conclusion: We noted that CPT might be well tolerated, could improve the clinical impact of severe COVID-19 in adolescents, and have no adverse events as well. CPT for severe COVID-19 cases in children had the potential to be developed in studies with better designs and stronger levels of evidence.

1. Introduction

In Indonesia, 175 cases resulted in the death of a total of 37,706 confirmed COVID-19 cases in children from March to December 2020, the highest mortality was aged 10–18 years [1]. Antivirals are given selectively to pediatric patients with confirmed severe or moderate degrees of COVID-19 accompanied by comorbidities [2]. Some adjuvant therapies given to adults are not necessarily applicable to children because of limited studies on this matter [3,4]. The use of Convalescent Plasma Therapy (CPT) has been proven successful in several adult COVID-19 patients [5]. Few studies regarding CPT's safety and efficacy in children were found and only in case reports or case series. However, some studies include the adolescent age group, only a few moderate or severe cases received CPT [6,7]. Based on the description above, we report two cases of COVID-19 in children who received the first CPT reported in Indonesia. The report is based on the Surgery Case Report (SCARS) 2020 Guideline [8].

2. Case presentation

2.1. Case 1

A 10-year-old obese boy weighing 60 kg was referred after being treated for eight days in a type D hospital for ICU admission due to rapidly progressing acute respiratory failure due to COVID-19. The patient has been commencing favipiravir for three days. The patient presented with progressively shortness of breath, worsening cough, and high fever for three days. The patient had close contact with the confirmed COVID-19 mother. The patient was febrile, tachycardia, tachypnea, and respiratory distress. The chest radiograph (CXR) and chest CT-Scan were performed (Fig. 1). Laboratory findings on admission showed lymphopenia, elevated alanine aminotransferase (ALT), C-reactive protein (CRP), Interleukin-6 (IL-6), ferritin, and D-dimer. Blood gas analysis (BGA) showed a fully compensated metabolic acidosis with severe hypoxemia. Following medium-flow nasal oxygen (15 L/min, FiO2 100%) for 12 hours, his condition had not improved.

Therefore, the patient was started on non-invasive ventilation (NIV)

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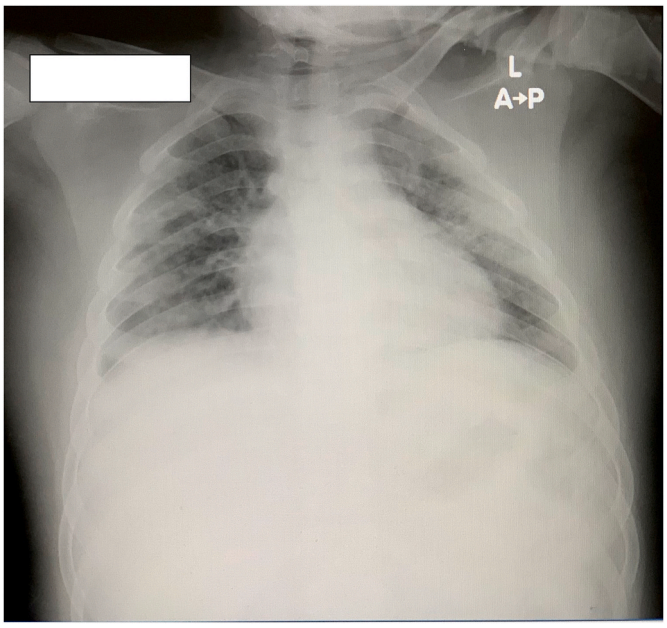

Fig. 1. Chest x-ray demonstrated bilateral infiltrates in the middle and lower lung fields, increased bronchovascular markings, pulmonary edema, bilateral pleural effusions without cardiac enlargement.

with CPAP setting Positive End Expiratory Pressure (PEEP) 7 cmH2O and 100% FiO2 (Table 1). The patient received remdesivir with a loading dose of 200 mg continued with 100 mg daily, systemic methylprednisolone 30 mg a day, Low Molecular Weight Heparin (LMWH) 1 mg/kg/day, and four units (2 × 400 mL) of CPT for two days was given on day 2 in our hospital. The improvement was noted of inflammatory markers and D-dimers on day 4. The patient could wean from NIV to NRM on day 6. The patient was stable on room air on day 8. The patient was discharged home on day 10 after undergoing physiotherapy and negative PCR results from two consecutive times (Fig. 2).

Table 1
Demographics and clinical characteristics.

Patient	Case 1	Case 2
Age	10.7	17.7
Sex	Male	Female
BMI	27.8	32.4
Ethnicity	Malaysia	Batak
Comorbidities	Obesity, asthma	Obesity
O2 Support	NIV PEEP 5, 100%	Non-rebreathing mask, O2 15 L/Min
Hospital LOS	10	10
Hospital day of CCP	2	3
CPP units transfused	400	400
Additional therapies	Remdesivir, Methylprednisolone, LMWH	Remdesivir, Methylprednisolone, LMWH
Outcome	Discharge home 6d after CCP	Discharge home 5d after CCP
Laboratory at admission		
C-reactive protein (mg/L)	35.6	131
Interleukin-6	28.32	N/A
Ferritin (ng/mL)	845.16	N/A
Lactate dehydrogenase (U/L)	N/A	692
D-Dimer (ng/mL)	608.1	1320
WBC	10,040	6810
Lymphocyte (/mm^3)	18.5	17.2
Platelet count (/mm^3)	395,000	293,000
Aspartate aminotransferase/ Alanine aminotransferase (U/L)	225/495	64/42
Blood group	B+	A+
pH	7.41	7.34
pCO2	49	42
pO2	56	52
HCO3	30.1	23
BE	4.1	−3
SpO2	88	84

2.2. Case 2

A 17-year-9-month-old obese teenage girl weighing 72 kg presented to Emergency Unit due to progressive shortness of breath for three days. For seven days, the complaint was preceded by fever, cough, rhinorrhea, chest pain, malaise, and nausea. We could not identify the case index of COVID-19 from close household contact. The patient was alert, tachycardia with normal blood pressure and perfusion, respiratory distress, rhonchi in both lung fields, and 80% oxygen saturation in room air. The CXR and chest CT-Scan was performed (Fig. 3). Laboratory results were showed lymphopenia, elevated CRP, LDH, D-Dimers, slightly elevated ALT, and BGA results showed fully compensated metabolic acidosis with severe hypoxemia (Table .1).

The patient received 15 L/min oxygen by NRM; therefore, ICU and NIV were occupied. The patient received remdesivir with a loading dose of 200 mg continued with 100 mg daily, systemic methylprednisolone 40 mg a day, LMWH 1 mg/kg/day, and two units (2 × 200 mL) of CPT for two days which are given on the third days of hospitalization. Following CPT initiation of remdesivir, the patient had improvement in laboratory value and oxygen requirement on day 6. In addition, the CXR showed infiltrate improvement. The patient was discharged on day 10 after undergoing physiotherapy, and PCR examination showed negative results two consecutive times (Fig. 1).

3. Discussion

Studies regarding CPT's safety and efficacy in children are minimal and are only in case reports or case series. A case series of 4 patients admitted to the PICU diagnosed with COVID-19 and ARDS who required a high flow nasal cannula at admission. All patients had a complete recovery and found no adverse effect from CPT [6]. In late 2020, a systematic review about the use of CPT in children was published and concluded that the efficacy of CPT was still uncertain due to the limited number of samples [2].

CPT is classic adoptive immunotherapy that has been given to prevent and treat many infectious diseases for more than one century [9]. CPT obtained from recovered COVID-19 patients who had established humoral immunity against the virus contains many neutralizing antibodies that can neutralize SARS-CoV-2 and eradicate the pathogen from the blood circulation and pulmonary tissues [10]. Antibodies from donor plasma can bind to SARS-CoV-2 and exhibit neutralizing properties directly or through other mechanisms, such as complement activation, antibody-dependent cellular cytotoxicity, and phagocytosis [10,11]. It accelerates the healing process when administrated prophylactically or immediately after symptom onset [12,13]. Thus, the administration of passive antibodies is a short-term strategy to provide immediate immunity to susceptible individuals [11]. Things to watch out for and monitor after convalescent plasma therapy are possible side effects: transfusion-related lung injury (TRALI), transfusion-associated circulatory overload (TACO), and anaphylaxis [6].

In the United States, CPT is given through the Emergency Use Authorization (EUA) from the FDA. However, the safety and effectiveness of CPT in the pediatric patient population have not been evaluated [14]. The Indonesian Pediatric Society (IPS) recommends giving convalescent plasma therapy for children weighing >40 kg at a dose of 200–500 mL and a dose of 10–15 mL/kg BW for children weighing <40 kg [15]. There are three critical factors associated with CPT efficacy. Firstly, the neutralizing antibody titer [9,12]. Therefore, it is necessary to find eligible donors who have high levels of neutralizing antibodies.

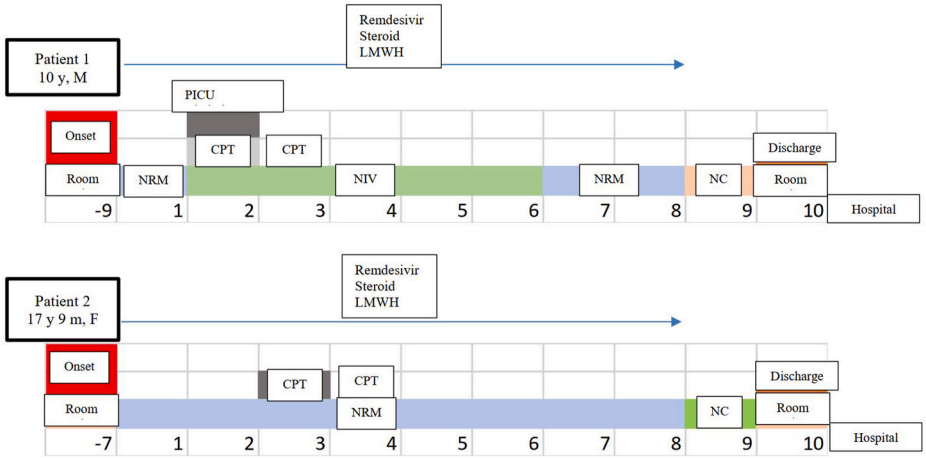

Fig. 2. Timeline of hospital course including treatment strategies employed, respiratory support, and outcome. CPT = convalescent plasma therapy, NIV = non-invasive ventilation, NRM = non-rebreathing mask, NC = nasal cannula, LMWH = low molecular weight heparin, y = year, m = month, m = male, f = female.

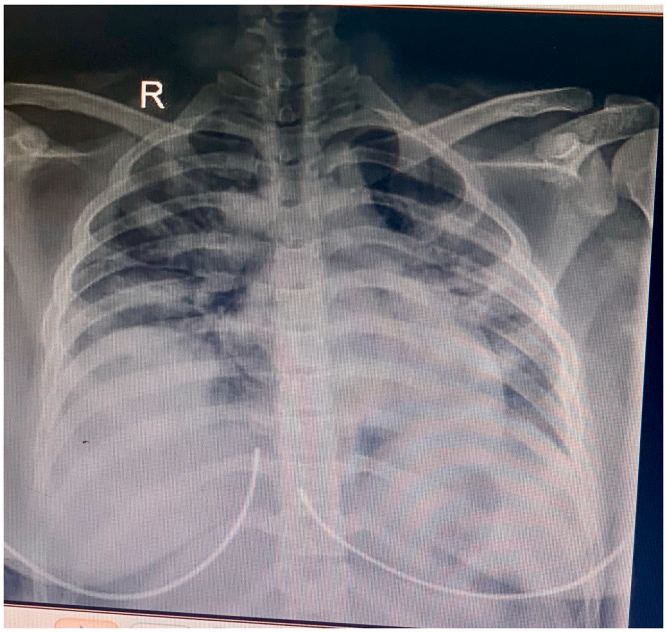

Fig. 3. Chest x-ray was showed hazy and patchy bilateral pulmonary infiltrates in the middle and lower lobe of both lung fields.

Secondly, the treatment time point. Data from other respiratory infections suggest that convalescent plasma provides the most practical effect early in the disease process [9].[7] Thirdly, the presence of comorbidities in inpatients. The earlier the administration of convalescent plasma therapy will be very beneficial for managing severe and critical COVID-19, but comorbid diseases will significantly affect the prognosis of COVID-19 in children, which requires further research [12].

Both of our patients had obesity as a comorbidity. Obesity is a common metabolic disorder globally [13]. It has been reported that obese patients are more vulnerable to COVID-19 and have a higher risk of worse clinical outcomes [13,16]. Several hypotheses may explain the relationship between obesity and severe COVID-19. Obesity, characterized by adipose tissue (AT) expansion that affects the inflammatory response [17–20]. Cytokine storm is the hyperactivation of the inflammatory response with elevated interferon γ, IL- 6, and other pro-inflammatory cytokines also aggravate COVID-19 severity [17]. In addition to this, severe patients appeared to have a higher portion of $CD14^{+}CD16^{+}$ inflammatory monocytes than non-severe patients, suggesting an elevated inflammation level in severe COVID-19 patients [19,20]. The weakened immune system in obese patients may lead to higher viral load, rapid viral replication, and spreading [17,19,20].

The limitations of this study are the small number of participants and the comparison of giving CPT to COVID-19 patients. Future studies are expected to complement the limitations of our report.

4. Conclusion

We note that CPT at a dose of two or more 200-mL, with combination therapy, might be likely well tolerated and could improve the clinical impact of severe COVID-19 cases in adolescents with no adverse events identified. The optimal dose, time point, and comorbidities are the key for the clinical benefit of CPT need further study in more extensive, well-controlled trials. The CPT with the combination of remdesivir and steroid may have led to a rapid resolution of the infection.

Ethical approval

We have conducted an ethical approval base on Declaration of Helsinki at Ethical Committee.

Sources of funding

None.

Author contribution

All authors contributed toward data analysis, drafting and revising the paper, gave final approval of the version to be published and agree to be accountable for all aspects of the work.

Registration of research studies

Not applicable.

Guarantor

Citra Cesilia.

Consent

Written informed consent was obtained from the patient or guardian for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this

journal on request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

The author declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.103084.

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