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## Case Report

# First case of convalescent plasma transfusion in a child with COVID-19-associated severe aplastic anemia

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## ARTICLE INFO

## Keywords:

Transfusion  
Convalescent plasma  
SARS-CoV-2  
Children  
Pancytopenia

## ABSTRACT

We present the case of a six-year-old girl with severe COVID-19, in whom SARS-CoV-2 was successfully eliminated after convalescent plasma transfusion. Children show a variable clinical course of COVID-19, from asymptomatic to critical. In our patient, we diagnosed COVID-19-associated aplastic anemia with severe pancytopenia. The correlation between SARS-CoV-2 infection with aplastic anemia remains unclear. At the beginning of the disease, we used antiviral drugs and immune modulators as therapy but without any positive results. After providing a transfusion of convalescent plasma, the elimination of SARS-CoV-2 was observed. We did not observe any adverse events of this treatment. The girl still has a diagnosis of aplastic anemia and requires specialist therapy.

## 1. Introduction

In December 2019, a novel coronavirus disease (COVID-19) caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) arose unexpectedly in China. It rapidly spread worldwide [1]. COVID-19 can occur in patients of all ages [2]. In children, the most common symptoms are fever (36–41.5 %), cough (19–48.5 %), diarrhea (9–12 %), and upper respiratory infection as well as fatigue, myalgia, headache, anosmia, and dysgeusia [3]. Most children appear to have an asymptomatic, mild, or moderate disease and recover within one to two weeks [2,4]. In pediatric patients with a severe or critical course of COVID-19, acute respiratory distress syndrome (ARDS) can occur; toxic shock is also observed. In some of patients, the clinical features are similar to those of Kawasaki disease, a multisystem inflammatory syndrome in children (MIS-C) [5]. Evidence suggests that most patients with severe COVID-19 have cytokine storm syndrome and/or cytopenia [6]. Therapeutic options available for children with COVID-19 have weak recommendations, involving potential antiviral drugs and/or immune modulators [7]. Here, we present a case of using a convalescent plasma transfusion as a therapeutic method for severe pediatric COVID-19-associated aplastic anemia.

## 2. Case report

A 6-year-old girl was admitted to our hospital because of fever, headache, sore throat, and rash in the form numerous small purple dots on the skin of both forearms and legs. Three days earlier, she began to feel fatigued and had an elevated temperature with a maximum of 39.0 °C. She received oral paracetamol at a dose of 10 mg/kg three to four times a day. In anamnesis, the child had no underlying condition. She lived in a region of Poland where cases of COVID-19 had been recently reported, so she could have been exposed to the virus in the community. On admission, vital signs were as follows: blood pressure 100/62 mmHg, temperature 36.5 °C, heart rate 102/min, respiratory rate 14/min, oxygen saturation 99 %. Physical examination was notable for many petechiae on the skin, and hepatomegaly. In laboratory tests, leukopenia, neutropenia, erythrocytopenia, and thrombocytopenia were noted, along with an elevated level of C-reactive protein and elevated activity of alanine and asparagine aminotransferase (Table 1). We noted severe pancytopenia, with extreme neutropenia ( $0.00 \times 10^3/\mu\text{l}$ ), a low number of natural killer cells ( $0.01 \times 10^3/\mu\text{l}$ ), decreasing number of helper T-lymphocytes, and an increasing number of cytotoxic T-lymphocytes (Table 2). Additionally, there was an elevated level of ferritin, a moderate elevated level of interleukin 6 and fibrinogen. In the fourth and fifth weeks of treatment, we observed bradycardia with a heart rate of 48–50/min and increased level of brain natriuretic

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**Table 1**  
Laboratory parameters tested during therapy in a six-year-old girl with COVID-19-associated aplastic anemia.

Laboratory parameters	Week of disease						Week of disease		
	1	2	3	4	5		6	7	8
WBC total 10 <sup>3</sup> /µl (4.00 – 12.00)	1.06	1.63	0.71	0.54	1.64	Convalescent plasma transfusion	3.57	3.47	0.98
Neutrocytes 10 <sup>3</sup> /µl (1.50 – 8.00)	0.16	0.02	0.02	0.01	0.01		0.00	0.02	0.00
Lymphocytes 10 <sup>3</sup> /µl (1.00 – 6.50)	0.86	1.61	0.68	0.53	1.62		3.55	3.45	0.97
RBC 10 <sup>6</sup> /µl (4.50 – 5.50)	3.39	3.52	4.47	3.35	3.97		3.63	3.07	3.56
HGB g/dl (12.0 – 15.5)	9.6	9.9	12.6*	9.6	11.0		10.1	8.4	10.4
HCT % (37.0 – 43.0)	26.6	26.1	33.8	24.8	29.4		27.2	22.4	28.2
PLT 10 <sup>3</sup> /µl (150 – 400)	5	48	32	28	22		57	22	34
CRP mg/dl (< 0.5)	2.93	0.49	2.08	0.08	< 0.2		0.30	0.72	12.84
ALT IU/l (< 39)	247	98	29	28			74	153	88
AST IU/l (< 47)	98	45	25	20			36	54	34
LDH IU/l (110 – 295)	171	143	318	196					271
Ferritin ng/mL (15.0 – 300.0)	173	408.3	5920.2	1485.0	1133.0			1524.0	1536.9
BNP pg/mL (< 100.0)				204.5	102.0			< 10.0	< 10.0
Fibrinogen mg/dL (180 – 350)	353	229	422	164	209		220		582
IL-6 pg/mL (1.5 – 7.0)			11	< 7.0					
SARS-CoV-2 RNA – RT-PCR	positive	positive	positive	positive	positive		negative	negative	negative

Legend to Table 1: WBC – white blood cells, RBC – red blood cells, HGB – hemoglobin, HCT – hematocrit, PLT – platelets, CRP - C-reactive protein, PCT– procalcitonin, ALT - alanine aminotransferase, AST - asparagine aminotransferase, LDH – lactate dehydrogenase, BNP - brain natriuretic peptide, IL-6 – interleukin 6, SARS-CoV-2 - severe acute respiratory syndrome coronavirus 2.

\*the level measured after the packed red blood cells transfusion.

**Table 2**  
Immunoprofile of white blood cells in a six-year-old girl with COVID-19-associated aplastic anemia in weeks 3 and 4.

White blood cells profile	week 3	week 4
WBC total 10 <sup>3</sup> /µl (4.00 – 12.00)	1.53	1.64
Neutrocytes % (25 – 60)	2	3
Eozynocytes % (1.0 – 5.0)	0	0
Bazocytes % (0.0 – 1.0)	0	0
Monocytes % (1.0 – 6.0)	0	0
<b>Lymphocytes</b>		
Total % (25 – 50)	97	90
Total 10 <sup>3</sup> /µl (1.2 – 4.7)	2.4	1.48
B % (4 – 33)	12	37
B 10 <sup>3</sup> /µl (0.1 – 0.8)	0.29	0.54
NK % (2 – 31)	1	1
NK 10 <sup>3</sup> /µl (0.07 – 0.6)	0.02	0.01
T % (55 – 97)	92	60
T 10 <sup>3</sup> /µl (0.77 – 4.0)	1.35	0.89
T-CD4 % (25 – 51)	22	44
T-CD4 10 <sup>3</sup> /µl (0.4 – 2.5)	0.33	0.65
T-CD8 % (13 – 47)	60	11
T-CD8 10 <sup>3</sup> /µl (0.2 – 1.7)	0.89	0.16
CD4:CD8	0.38	3.97

Legend to Table 2: WBC - white blood cells, NK – natural killer.

peptide. The chest X-ray indicated normal lungs and enlargement of the heart. Abdominal ultrasound confirmed hepatomegaly and enlarged kidneys bilaterally (right 9.8 cm, left 11.5 cm). Echocardiography and electrocardiography (Holter) were normal. We excluded an acute infection (PCR or/and serological methods) caused by herpes simplex viruses 1 and 2, varicella-zoster virus, Epstein-Barr virus, cytomegalovirus, human herpesviruses 6 and 7, enteroviruses, adenoviruses, influenza viruses type A and B, respiratory syncytial virus, parechovirus, parvovirus B19, human immunodeficiency virus, hepatitis B and C viruses, and *Toxoplasma gondii*. We found SARS-CoV-2 RNA in a nasopharyngeal swab (RT-PCR method). The test used was a CE IVD Bosphore Novel Coronavirus Detection Kit v2. (cut-off value 61.5 copies/mL for gen E; 193.5 copies/mL for gen ORF1ab). We confirmed an asymptomatic SARS-CoV-2 infection in the girl's mother. Based on all laboratory tests, bone marrow aspiration, and biopsy results, we established a diagnosis of COVID-19-associated severe aplastic anemia. We started therapy for COVID-19 with intravenous immunoglobulin (IVIG) in one dose of 2 g/kg. Additionally, we applied azithromycin 10

mg/kg/24 h once a day. After seven days, because of the poor effect of treatment, we repeated IVIG at the same dose, ceased azithromycin, and introduced lopinavir-ritonavir (10 mg + 2.5 mg twice a day). The therapy with lopinavir-ritonavir ended after five days because of an itchy rash on the skin. We administered intravenous methylprednisolone for 5 days (30 mg/kg) with an oral dexamethasone taper (0.1 mg/kg/24 h). The patient needed blood and platelet transfusions and a systematic evaluation because of the risk of serious bacterial, fungal, or new viral infection. She received antibiotics and antifungal drugs. We considered tocilizumab but the level of IL-6 was only slightly elevated, and we did not apply this treatment. For five weeks from the beginning of the disease, we repeated SARS-CoV-2 RNA detection tests at least once a week, and the results were always positive. Then, we transfused convalescent plasma (inactivated using methylene blue) with antibodies against SARS-CoV-2 IgG at a titer of 1:700 once in a 200 mL dose. We did not observe any adverse events. For the next three weeks, we repeated tests for the detection of SARS-CoV-2 RNA in nasopharyngeal swabs seven times. All these results were negative. The hematologic parameters did not improve after SARS-CoV-2 elimination.

### 3. Discussion

We present a case of using convalescent plasma in the therapy of a child with severe COVID-19. To our knowledge, no evidence of such treatment in COVID-19 has been previously reported in children. The results from small groups of adult patients showed that therapy was well tolerated and led to improving clinical symptoms and to the disappearance of viremia within few days [8]. Several studies present the clinical manifestation of COVID-19 in children with fever and signs of upper respiratory infection only [2,3]. A severe or critical course of the disease is described as ARDS, respiratory failure, toxic shock, or recently as MIS-C [2,5]. In our case, only at the beginning of the disease did this child have classic symptoms like fever, headache, and fatigue. However, she then developed rapidly occurring profound pancytopenia, with severe thrombocytopenia. Studies have shown that, indeed, about 25 % of children with COVID-19 have white blood cell counts below  $5.5 \times 10^3/\mu\text{l}$ , and lymphopenia, but usually they have thrombocytosis [3]. These parameters, according to current observations, are associated with increased severity or worse outcomes of COVID-19, like thrombocytopenia, elevated liver enzymes, elevated lactate dehydrogenase, and elevated inflammatory markers, as were present in our

patient [9]. Acquired aplastic anemia occurs in Europe and North America rarely (2 cases per million population per year). In the literature, idiopathic (80 %), post-hepatitis (9%), post-viral (7%), and post-drug and other toxins (4%) are reported etiologies [10]. Even though a post-viral etiology is possible, there have been no reports of acquired aplastic anemia triggered by SARS-CoV-2 in children up to now. In our patient, the etiology of aplastic anemia is still unclear. The current recommendation for the treatment of severe COVID-19 in children suggests, despite no evidence, monitoring and supportive care only. Antiviral or adjunctive therapy is a suggestion for selected patients in clinical trials [7]. The primary goal of therapy in our patient was the elimination SARS-CoV-2, while the secondary and future aim is a complete diagnosis and treatment of her aplastic anemia. We started therapy with potential antiviral drugs and immune modulators. Finally, we used plasma from a recovered COVID-19 patient with good results.

#### 4. Conclusion

We still do not know all the clinical manifestations of COVID-19. In the treatment of COVID-19 in children, we should individualize methods depending on symptoms and diagnostic findings. In patients with pancytopenia, when they are unable to form antibodies against the virus, transfusion of convalescent plasma could be the best choice.

#### Statement of ethics

The study was approved of the local Bioethical Committee affiliated with Poznan University of Medical Sciences (No 298/20; No 376/20).

#### Declaration of Competing Interest

None.

#### Acknowledgements

We thank all the co-investigations and study teams at each of the participating sites.

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