

Successful treatment of plasmapheresis followed by interferon beta-1a in a child with severe COVID-19

Rana Saleh¹, Hamid Rahimi¹, Amin Dehghan², Atefeh Sadeghizadeh³, Alaleh Gheisari⁴, Shima Saeidi¹, Zahra Pourmoghaddas¹

¹Department of Pediatric Infectious Disease, Isfahan University of Medical Sciences, Isfahan, Iran, ²Student Research Committee, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran, ³Department of Pediatric Intensive Care, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran, ⁴Department of Pediatric Nephrology Disease, Isfahan University of Medical Sciences, Isfahan, Iran

COVID-19 outbreak has become a global health concern due to challenges in treatment and high mortality rate; therefore, its therapeutic approaches play an important role in reducing the mortality rate and resolving this concern. Different therapies have been introduced, including interferon beta-1a and purification methods, for instance, plasmapheresis. In this article, we reported a child with severe COVID-19 who fully recovered after receiving plasmapheresis and interferon beta-1a.

Key words: COVID-19, interferon beta-1a, pediatric infectious disease, plasmapheresis

How to cite this article: Saleh R, Rahimi H, Dehghan A, Sadeghizadeh A, Gheisari A, Saeidi S, *et al.* Successful treatment of plasmapheresis followed by interferon beta-1a in a child with severe COVID-19. *J Res Med Sci* 2021;26:30.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) has become a global health concern due to pandemic and relatively high mortality rates, especially in severe and critical cases. Despite the lower incidence rate in children than in adults and the lower severity, COVID-19 in children could cause critical illnesses and even septic shock.

There is no consensus on the management of children with COVID-19. However, different treatment recommendations have been introduced and are being used in hospitals and ICUs based on patient's condition.^[1] Furthermore, supportive care, such as oxygen therapy, organ function support, maintaining water-electrolyte balance, and homeostasis are suggested.^[2] One of the controversial treatment is blood purification methods, for example, plasmapheresis. Some studies revealed a significant effect of plasma exchange on

cytokine/chemokine levels reduction.^[3,4] On the other hand, it was shown that hyperinflammation and cytokine storm played great roles in severe cases.^[4] However, there is no study on the treatment of plasmapheresis efficacy on children with COVID-19, based on our literature review.

In this article, we reported the first case of severe COVID-19 who fully recovered after receiving plasmapheresis and interferon beta-1a in addition to the Iranian protocol of COVID-19 treatment for children in Isfahan, Iran.

CASE REPORT

A 13-year-old girl was admitted with fever for 5 days, productive cough, hemoptysis, and diarrhea. In initial physical examinations, she was alert with respiratory distress and tachycardia. Chest indrawing and decrease lung sound on the right side were two obvious signs in the chest examination. The rest of the examinations was

Access this article online

Quick Response Code:



Website:

www.jmsjournal.net

DOI:

10.4103/jrms.JRMS_756_20

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

Address for correspondence: Dr. Zahra Pourmoghaddas, Department of Pediatric Infectious Disease, Isfahan University of Medical Sciences, Isfahan, Iran. E-mail: za.pourmoghaddas@gmail.com

Submitted: 14-Jul-2020; **Revised:** 13-Sep-2020; **Accepted:** 22-Dec-2020; **Published:** 27-May-2021

unremarkable. Her blood tests at the admission time showed lymphopenia and elevated C-reactive protein, procalcitonin, and lactate dehydrogenase [Table 1].

In order to confirm COVID-19, a chest computed tomography (CT) scan was done, and a nasopharyngeal swab sample was collected for the reverse transcription polymerase chain reaction (RT-PCR) test. The result of the RT-PCR test and chest CT scan findings confirmed the diagnosis of COVID-19 [Figure 1].

Therefore, based on the Iranian protocol of COVID-19 treatment, therapy began [Table 2].^[5] Furthermore, she went on BiPAP because of respiratory distress and decreased arterial oxygen saturation. Due to hemoptysis and suspicion

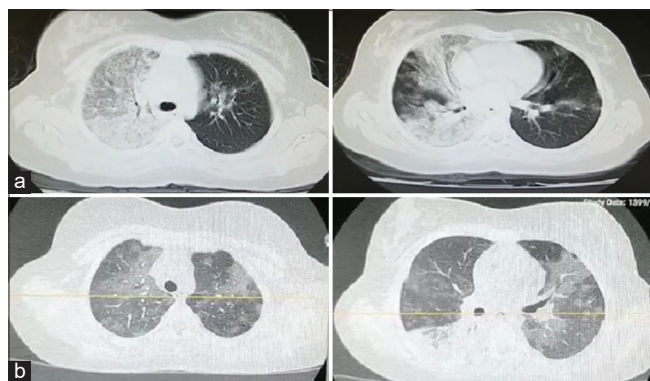


Figure 1: Chest computed tomography scans at (a) 1st day and (b) 7th day of admission. (a) Pulmonary infiltrations in the right lung and (b) the pulmonary infiltrations decreased in the right lung

of acute respiratory distress syndrome, she was admitted to ICU, and Atazanavir and interferon beta-1a were prescribed. Despite the therapy, signs worsened and arterial oxygen saturation decreased. Thus, plasmapheresis was performed four times in 2 days, and each time the patient received fresh-frozen plasma as replacement fluid.^[6]

After 2 days, a chest X-ray revealed a significant change in her lungs [Figure 2], and her general condition improved. Arterial oxygen saturation with BiPAP changed from 80% before the plasmapheresis to 94% after the fourth time of plasmapheresis. After that, interferon beta-1a was injected every 48 h for three times between the 3rd day and 7th day of hospitalization. Tachypnea and tachycardia disappeared on the 5th day.

Serial laboratory tests revealed an elevated WBC count with a predominance of PMNs in the 7th day. This leukocytosis remained until discharge time [Table 1]. Furthermore, repeated chest CT scans represented a dramatic change in pulmonary infiltrates compared to the 1st day [Figure 2].

The patient was transferred from the ICU to ward after the 8th day of hospitalization. On the 9th day, her oxygen therapy changed from BiPAP to a nasal cannula. Over the next 5 days, respiratory distress disappeared gradually which allowed tapering of supplemental oxygen.

Finally, she was discharged from the hospital after 14-day hospitalization with good condition, normal

Table 1: Daily physical examination and laboratory tests findings

Parameters	Day 1	Day 2	Day 4	Day 7	Day 9	Day 14
Pulse rate (/min)	121	110	70	86	80	82
Respiratory rate (/min)	40	65	38	30	28	24
Arterial oxygen saturation (%)	81	80	88	98	98	98
WBC ($\times 10^3$ / μ l)	6300	6800	6700	20,400	21,200	18,700
Neutrophil (%)	89.8	92.5	90	88	90	85
Lymphocyte (%)	8	6	9	7	7.9	11
Hemoglobin (g/dl)	13.4	13	12.6		13.2	12
Platelet count ($\times 10^3$ / μ l)	181,000	186,000	201,000		314,000	270,000
AST (IU/L)	37	31	117	41	37	36
ALT (IU/L)	18	14	108	87	57	206
T-Bilirubin (mg/dl)			3		0.8	
D-Dimer (ng/mL)	3240				1575	
Ferritin (ng/mL)					410	
Lactate dehydrogenase (IU/L)	701			988	988	
C-reactive protein (mg/dL)	46					47
ESR 1 st h	19					69
Procalcitonin (μ g/l)	10					
Creatinine (mg/dl)	0.9	0.9	0.8			
pH*	7.46	7.38	7.48	7.48		
Bicarbonate* (mmol/L)	21	22.2	32	25.1		
pCO ₂ * (mmHg)	30	38.5	43	34		

*Findings were resulted of venous blood gas tests. WBC: White blood cell, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

Table 2: Daily supportive care and treatment

Treatments	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14
Intensive care unit	✓	✓	✓	✓	✓	✓	✓	✓						
Oxygen therapy	BiPAP	BiPAP	BiPAP	BiPAP	BiPAP	BiPAP	BiPAP	BiPAP	Nasal cannula	Nasal cannula	Nasal cannula	Nasal cannula	Nasal cannula	Room air
Plasmapheresis	✓	✓												
Interferon beta 1-a			✓		✓		✓							
Hydroxychloroquine	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Lopinavir/ritonavir*	✓													
Ceftriaxone/cefotaxime	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Vancomycin	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Atazanavir*	✓													
Ciprofloxacin	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

*Atazanavir and lopinavir/ritonavir were discarded, because liver function tests and bilirubin level became abnormal at the 2nd day

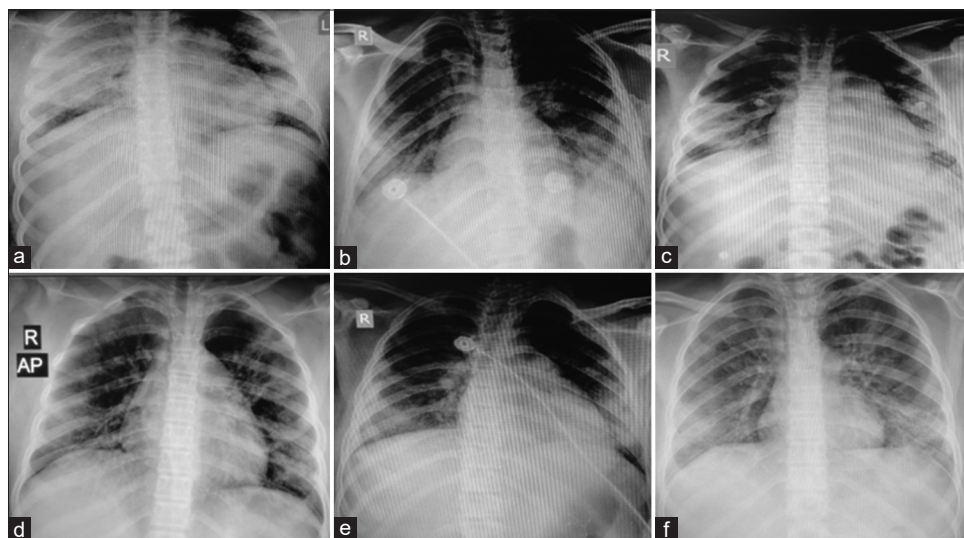


Figure 2: Serial chest X-rays revealing response to treatment, (a) 1st day, (b) 2nd day, (c) 3rd day, (d) 10th day, (e) 11th day, and (f) 13th day of admission

oxygen saturation in room air, and without fever. She had a good condition without any problem in a 2-week follow-up.

DISCUSSION

We reported the child with severe COVID-19 that received plasmapheresis in addition to standard therapy and ultimately was discharged in good condition. Her clinical characteristics, including respiratory rate, arterial oxygen saturation, and lymphopenia, were consistent with the literature review.^[2] However, her platelet count is normal, contrary to the literature review.^[7] Her diagnosis was made after the positive result of RT-PCR and typical lesions seen in the chest CT scan.

Up to the present, COVID-19 treatment consists of^[1] supportive care and^[2] reducing the severity of injuries caused by virus infection. Hyperinflammation and cytokine storm are among the causes of SARS-CoV-2 infection-associated lesions. On May 15, 2020, the World Health Organization announced the

diagnostic criteria of multisystem inflammatory syndrome related to COVID-19 (multisystem inflammatory syndrome in children [MISC]).^[8] At that time, we did not know this term in pediatric patients and now following this knowledge, the presented case suffered from MISC because of persistent fever, diarrhea, and elevated D-Dimer.

Early control of MISC can improve outcomes. In this regard, different theoretical methods, including IFN- λ , corticosteroid therapies, intravenous immunoglobulin, IL-1 family antagonists, TNF blockers, chloroquine and blood purification treatments, are recommended.^[9] Few studies introduced blood purification treatment as a therapeutic method for severe and critical adult cases.^[10,11] A case report showed convalescent plasma therapy as an efficient treatment in severe COVID-19 cases.^[12] Furthermore, plasma exchange and plasmapheresis are among new treatments in patients with severe COVID-19 based on theories;^[10,13] however, their outcomes are not completely known, especially in children. In our case, we performed two times/day plasmapheresis in the first 2 days of admission for our case, which caused a significant

diminishing of lung infiltration in chest X-ray. A single-center clinical trial showed that interferon beta-1a positively affected on adult patients' conditions.^[14] In our case, three doses of interferon beta-1a in 6 days were administered after performing plasmapheresis. Furthermore, hydroxychloroquine was introduced to reduce the severity of cytokine storm,^[15] and it was prescribed for our case. All of these, along with the Iranian protocol of COVID-19 treatment and respiratory support [Table 2] improved her severe COVID-19.

CONCLUSION

Up to now, there is no established treatment for COVID-19. Reports from the different parts of the world showed that children with MISC need immunomodulatory treatment. Control of them can survive patients' lives. In this article, we reported the successful use of plasmapheresis to control MISC and prevent its consequences.

RS contributed in the conception of the work, revising the draft, approval of the final version of the manuscript, and agreed for all the aspects of the work. HR contributed in revising the draft critically for important intellectual content, approval of the final version of the manuscript, and agreed for all aspects of the work. AD contributed in the conception of the work, drafting, revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. AS contributed in revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. AG contributed in revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. SS contributed in revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. ZP contributed in revising the draft critically for important intellectual content, approval of the final version of the manuscript, and agreed for all aspects of the work.

Acknowledgments

We would like to thank Dr. Hamid Melali and Dr. Mohammad Shammam Esfahani for their assistances as President and Chief Executive Officer of Amin Hospital, the ones who helped our team to perform this successful treatment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Alhazzani W, Møller MH, Arabi YM, Loeb M, Gong MN, Fan E, *et al.* Surviving Sepsis Campaign: Guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). *Intensive Care Med* 2020;46:854-87.
2. Chen ZM, Fu JF, Shu Q, Chen YH, Hua CZ, Li FB, *et al.* Diagnosis and treatment recommendations for pediatric respiratory infection caused by the 2019 novel coronavirus. *World J Pediatr* 2020;16:240-6.
3. Liu X, Zhang Y, Xu X, Du W, Su K, Zhu C, *et al.* Evaluation of plasma exchange and continuous veno-venous hemofiltration for the treatment of severe avian influenza A (H7N9): A cohort study. *Ther Apher Dial* 2015;19:178-84.
4. Lorenz G, Schul L, Schraml F, Riedhammer KM, Einwächter H, Verbeek M, *et al.* Adult macrophage activation syndrome-haemophagocytic lymphohistiocytosis: 'Of plasma exchange and immunosuppressive escalation strategies' – A single centre reflection. *Lupus* 2020;29:324-33.
5. Karimi A, Rafiei Tabatabaei S, Rajabnejad M, Pourmoghaddas Z, Rahimi H, Armin S, *et al.* An algorithmic approach to diagnosis and treatment of coronavirus disease 2019 (COVID-19) in children: Iranian expert's consensus statement. *Arch Pediatr Infect Dis* 2020;8:e102400.
6. Nakanishi T, Suzuki N, Kuragano T, Nagasawa Y, Hasuike Y. Current topics in therapeutic plasmapheresis. *Clin Exp Nephrol* 2014;18:41-9.
7. Yasri S, Wiwanitkit V. Platelet count among the patients with novel coronavirus 2019 infection: An observation on 46 cases. *J Res Med Sci* 2020;25:58.
8. Multisystem Inflammatory Syndrome in Children and Adolescents Temporally Related to COVID-19: The World Health Organization; 2020. Available from: <https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19>. [Last accessed on 2020 Jun 10].
9. Ye Q, Wang B, Mao J. The pathogenesis and treatment of the 'Cytokine Storm' in COVID-19. *J Infect* 2020;80:607-13.
10. Keith P, Day M, Perkins L, Moyer L, Hewitt K, Wells A. A novel treatment approach to the novel coronavirus: An argument for the use of therapeutic plasma exchange for fulminant COVID-19. *Crit Care* 2020;24:128.
11. Shi H, Zhou C, He P, Huang S, Duan Y, Wang X, *et al.* Successful treatment of plasma exchange followed by intravenous immunoglobulin in a critically ill patient with 2019 novel coronavirus infection. *Int J Antimicrob Agents* 2020;56:105974.
12. Ahn JY, Sohn Y, Lee SH, Cho Y, Hyun JH, Baek YJ, *et al.* Use of convalescent plasma therapy in two COVID-19 patients with acute respiratory distress syndrome in Korea. *J Korean Med Sci* 2020;35:e149.
13. Pourahmad R, Moazzami B, Rezaei N. Efficacy of Plasmapheresis and Immunoglobulin Replacement Therapy (IVIG) on Patients with COVID-19. *SN Comprehensive Clinical Medicine*. 2020;2:1407-11.
14. Payandemehr P, Azhdarzadeh M, Bahrami-Motlagh H, Hadadi A, Najmeddin F, Shahmirzaei S, *et al.* Interferon beta-1a as a candidate for COVID-19 treatment; An open-label single-arm clinical trial. *Adv J Emerg Med* 2020;4:e51.
15. Chen J, Liu D, Liu L, Liu P, Xu Q, Xia L, *et al.* A pilot study of hydroxychloroquine in treatment of patients with moderate COVID-19. *Zhejiang Da Xue Xue Bao Yi Xue Ban* 2020;49:215-9.