The Prophylactic Treatment of COVID-19 in a Renal Failure and Hodgkin Lymphoma Patient with Convalescent Plasma

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

Case Study

ABSTRACT

COVID-19 is a viral infectious disease that is thought to have emerged from an animal market in Wuhan, People's Republic of China, in December 2019, and subsequently caused a pandemic. Despite the fact that one year has passed since the onset of the epidemic and many treatment agents have been tried, there is still no approved treatment. Convalescent plasma therapy is a passive immunization method and holds promise in the treatment of COVID-19. In this study, we observed that asymptomatic COVID-19 infection was effectively treated with convalescent plasma in a young patient with a diagnosis of Hodgkin lymphoma, acute renal failure also who received R-DHAP (Rituximab – Cisplatin – Cytarabine - Dexamethasone) chemotherapy treatment. We think that this treatment may be more effective when it is administered in an earlier stage of disease in asymptomatic patients.

Keywords: COVID-19; convalescent plasma; hodgkin lymphoma.

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1. INTRODUCTION

In the last two decades, infections belonging to the coronavirus family have led to outbreaks. Among them, SARS (Severe Acute Respiratory Syndrome) and MERS (Middle East Respiratory Syndrome) caused fear in 2002 and 2012 and the recent pandemic was SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) who is a new member of the coronavirus family. It made this under the name COVID-19 [1].

Convalescent plasma therapy is a passive immunization method that was used for more than one hundred years as an effective and reliable treatment for various infectious diseases and holds promise in the treatment of COVID-19 [2]. Convalescent plasma therapy uses blood from people who've recovered from an illness to help others recover. The U.S. Food and Drug Administration (FDA) has given emergency authorization for convalescent plasma therapy with high antibody levels to treat COVID-19. Because of the lack of B- and T-cell-derived immunity, immunosuppressed patients may benefit more from convalescent plasma treatment. Here, we report the rapid and effective treatment of COVID-19 disease with convalescent plasma that in a patient with Hodgkin lymphoma who infected shortly after her chemotherapy.

Despite the fact that one year has passed since the onset of the epidemic and many treatment agents have been tried, there is still no approved treatment. Although the difficulties in treating immunocompetent individuals still remain [1], also effort in developing treatment modality continues in immunosuppressed individuals, especially in patients with hematological malignances.

2. CASE REPORT

A 22-year-old female patient received 6 cycles of ABVD (Adriamycin-Bleomycin-Vinblastin-Dacarbazine) treatment with the diagnosis of Hodgkin Lymphoma 2 years ago. She was followed up in remission until October 2020. R-DHAP (Rituximab – Cisplatin – Cytarabine-Dexamethasone) chemotherapy was started due to recurrence in the patient. In the second cycle of the treatment, drug-induced nephrotoxicity developed in the patient and she received hemodialysis and renal replacement therapy for 6 times. She was referred to our clinic for hematopoietic stem cell transplantation. She was admitted to our service and the COVID PCR test was sent from the nasopharyngeal swab sample in accordance with our transplant protocol. Because of the positivity of her test, Favipiravir treatment was initiated for the asymptomatic patient. Serum immunoglobulin levels were measured and levels were not detected. COVID convalescent plasma therapy was administered. First, antibody titer of the convalescent plasma donor was measured. Plasma was collected from the donor with an IgG level above 1/320. 200 cc plasma was administered in 15 minutes and there was no complication. The patient was followed up in the COVID ward. Renal replacement therapy of the patient was continued in this place. In the follow-up, intravenous meropenem 3x1000 mg/day treatment was started. On the 7th day of the convalescent plasma treatment, the COVID PCR test which was taken from the nasopharyngeal swab sample became negative. It is planned to continue autologous stem cell transplantation procedure after recovery of kidney function.

3. DISCUSSION AND CONCLUSION

The treatment of COVID-19 in immunosuppressed patients is still a mystery. Increased mortality and morbidity is an expected result in patients with hematological malignancies. It is obvious that in patients with hematological malignancies, both innate and humoral immunity weakens due to the primary disease and the agents used in disease treatment. Currently, there is no standard treatment for COVID-19. The agents used are mostly antiviral drugs such as favipiravir, remdesivir, lopinavir-ritonavir, oseltamivir. Immune convalescent plasma therapy is a promising treatment in this respect. The use of convalescent plasma is recommended in patients with solid organ transplantation, hematological malignancy and low immunity [3]. Adding to this, it is advised that antiviral therapy and convalescent plasma treatments are used in combination. When the current literature is reviewed, it has been observed that convalescent therapy is mostly used in patients with advanced-stage, such as acute respiratory distress syndrome [4]. Data on the use of convalescent plasma in the treatment of hematological cancer patients with COVID-19 infection is very limited. However, it has been reported as an effective and safe treatment [3]. Similar to our case, convalescent plasma can be used as a safer treatment in patients with comorbidities such as kidney failure.

Table 1. The table below shows the patient's results before and after convalescent plasma

Examination Name (Unit)	Normal value	02.12.2020	09.12.2020
White Blood Count (10³/цL)	4,3-10,3	7,79	12,51
Red Blood Count (10⁶/цL)	4,38-5,77	3,78	3,59
Hemoglobin (g/dL)	13,6-17,2	10,10	9,7
Hematocrit (%)	39,5-50,3	30,0	28,8
Mean Corpuscular Hemoglobin (pg)	27,2-33,5	26,7	27,0
Mean Corpuscular Hemoglobin Concentration (g/dL)	32,7-35,6	33,7	33,7
Lymphocyte (%)	19,4-44,9	8,7	8,0
Monocyte (%)	5,1-10,9	30,8	10,2
Neutrophil (%)	41-76	59,4	81,0
Eosinophil (%)	0,9-6,0	0,3	0
Basophil (%)	0,3-1,5	0,8	0,8
Basophil (10³/цL)	0-0,2	0,06	0,1
Eosinophil (10³/цL)	0-0,5	0,02	0
Neutrophil (10³/цL)	2,1-6,1	4,63	10,14
Monocyte (10³/цL)	0,3-0,9	2,4	1,27
Lymphocyte (10³/цL)	1,3-3,5	0,68	1,0
Mean Corpuscular Volume (fL)	80,7-95,5	79,4	80,2
Platelet Count (10³/цL)	156-373	86	145
Glucose(mg/dL)	70 – 100	79,0	92,0
BUN (mg/dL)	7 - 18,7	20,88	69,64
Creatinine (mg/dL)	0,57 - 1,25	8,81	5,66
Uric Acid (mg/dL)	2,6 – 6	6,36	6,57
Total Protein (g/dL)	6,4 - 8,3	5,8	5,7
Albumin (g/dL)	3,5 – 5	2,9	2,9
Total Bilirubin (mg/dL)	0,2 - 1,2	0,48	0,33
Direkt Bilirubin (mg/dL)	0 - 0,5	0,27	0,19
AST (U/L)	5 - 34	31	46
ALT (U/L)	0 - 55	27	71
ALP (U/L)	38 - 155	90	106
GGT (U/L)	9 - 36	47	81
Magnesium (mg / Dl)	1,6 - 2,6	1,83	1,67
LDH (U/L)	125 - 243	2056	882
Amylase (U/L)	25 - 125	26	47
Lipase (U/L)	8 - 78	101	34
Sodium (mmol/L)	136 - 145	138	138
Chlorine (mmol/L)	98 - 107	101	103
Potassium (mmol/L)	3,5 - 5,1	3,84	4,32
Calcium (mg/dL)	8,4 - 10,2	8,9	9,7
Phosphorus (mg/dL)	2,3 - 4,7	2,1	6,5
C Reactive Protein (mg/dL)	0-0,351	10,8	1,59
IL-6 (pg/mL)	0-7	34,420	8,01
Ferritin (ng/mL)	10-291	1650	1650
Fibrinogen (mg/dL)	150-350	543,12	221,27
INR	0,8-1,2	1,19	
PTZ (second)	10-14	14,2	
APTT (second)	24,6	23-35	
COVID-19 PCR		**Positıve**	**Negatıve**

In a study of 17 patients receiving anti-B-cell treatments, it was reported that the effectiveness of convalescent plasma treatment emerged in a short period of one week [5]. According to Senefeld's study, the majority of 54 patients who have hematological malignancies demonstrated improved clinical status and viral clearance within 48 hours of convalescent plasma transfusion [6]. In addition, it was reported that the convalescent plasma was administered in a non-Hodgkin Lymphoma patient who was seronegative and whose complaints continued even 88 days of

viral contamination. After the onset of plasma his complaints relieved immediately [7]. In another case, convalescent plasma was transfused to a patient who was on day 20 of hospitalization. Following this treatment, the patient became independent of ECMO within one day and was successfully weaned from mechanical ventilation within two days [8]. In addition, a report of 16 patients in USA says steady improvement in oxygenation levels was observed following each convalescent plasma infusion. All of the 5 intubated patients were extubated between one and 19-days post convalescent plasma infusion. The remaining 11 showed a dramatic decline in oxygen needs and did not require ventilatory support [9].

We observed that asymptomatic COVID-19 infection was effectively treated with convalescent plasma in a young patient with Hodgkin lymphoma, acute renal failure and who received anti-CD-20 therapy. As stated in some studies in the literature, we saw that our patient turned negative for the COVID-19 PCR test within 1 week [10]. When it was given in 72 hours of admission, convalescent plasma recipients <65 years had 4-fold lower mortality and 4-fold lower deterioration in oxygenation on severe Covid-19 patients [11]. The other 3 studies, it was stated that when convalescent plasma is used at an average of 44 and 72 hours, it reduces mortality in elderly patients. It should be used in the early period especially before the cytokine storm begins [12,13]. In the meta-analysis of 17 studies, 5 of which were randomized, it was reported that the mortality rates of patients who received convalescent plasma were significantly lower than those who did not [14]. FDA announces best outcomes occur in those who receive a high-titer unit of convalescent plasma within 3 days of COVID-19 diagnosis or admission to the hospital [15]. Some guidelines report convalescent plasma therapy is risky because that it should be used very carefully especially use of the titer of COVID-19 convalescent plasma [16]. We think that the clinical improvement of the patient condition may be due to other drugs used in combination with convalescent plasma. Convalescent plasma can be used as an additive therapy agent in such patients where there is no standard treatment and the mortality rate is high due to the underlying disease. Finally, this treatment may be more effective in asymptomatic and immunosuppressed patients when it is given as soon as they are diagnosed.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Dhama K, Khan S, Tiwari R, et al. Coronavirus Disease 2019-COVID-19. Clin Microbiol Rev. 2020;33(4):e00028-20. Published 2020 Jun 24. DOI:10.1128/CMR.00028-20
2. O'Maley JJ, Hartman FW, Treatment of ınfluenzal pneumonia with plasma of convalescent patients JAMA. 1919; 4:34.
3. Senefeld JW, Johnson PW, Kunze KL, Bloch EM, van Helmond N, Golafshar MA, et al. Access to and safety of COVID-19 convalescent plasma in the United States Expanded Access Program: A national registry study. PLoS Med. 2021;18(12): e1003872. DOI:10.1371/journal.pmed.1003872. PMID: 34928960; PMCID: PMC8730442.
4. Baang JH, Smith C, Mirabelli C, et al. Prolonged severe acute respiratory syndrome coronavirus 2 replication in an immunocompromised patient. The Journal of Infectious Diseases, jiaa666. Available:https://doi.org/10.1093/infdis/jiaa666
5. Hueso T, Pouderoux C,Péré H,Beaumont AL, et al. Convalescent plasma therapyfor B-cell–depleted patients with protracted COVID-19. Blood. 2020;136(20):2290–2295. DOI: https://doi.org/10.1182/blood.2020008423
6. Senefeld JW, Klassen SA, Ford SK, et al. Therapeutic use of convalescent plasma in COVID-19 patients with immunodeficiency medRxiv 2020;11(08):20224790. DOI:https://doi.org/10.1101/2020.11.08.20224790

7. Moore JL, Ganapathiraju PV, Kurtz CP, Wainscoat BA. 63-year-old woman with a history of non-hodgkin lymphoma with persistent sars-cov-2 infection who was seronegative and treated with convalescent plasma. The American journal of case reports. 21;e927812. Available:https://doi.org/10.12659/AJCR.927812

8. Van Damme FAK, Tavernier S, Van Roy N, et al. Case Report: Convalescent Plasma, a Targeted Therapy for Patients with CVID and Severe COVID-19 Front. Immunol; 2020. | Available:https://doi.org/10.3389/fimmu.2020.596761

9. Ibrahim M, Pal P, Niu A, et al. COVID-19 convalescent plasma decreased oxygen requirement and hospital stay in COVID-19 hospitalized patients including those with hematological malignancies: A report of 16 patients. Presented at: The 62nd American Society of Hematology (ASH) Annual Meeting and Exposition; 2020. Abstract 101

10. Alsharidah S, Ayed M, Ameen R M, Alhuraish F, et al. 4COVID-19 convalescent plasma treatment of moderate and severe cases of sars-cov-2 infection: A multicenter interventional study. Int J Infect Dis. 2020;S1201-9712(20)32513-3. DOI: 10.1016/j.ijid.2020.11.198.

11. Yoon H ah, Bartash R, Gendlina I, et al. Treatment of Severe COVID-19 with Convalescent Plasma in the Bronx, NYC. medRxiv. 2020;12(02):20242909. DOI:https://doi.org/10.1101/2020.12.02.20242909

12. Libster R, Marc GP, Wappner D, et al. Prevention of severe COVID-19 in the elderly by early high-titer plasma. medRxiv 2020;11(20):20234013. DOI:https://doi.org/10.1101/2020.11.20.20234013

13. Salazar E, Christensen PA,Graviss EA, et al. Significantly Decreased Mortality in a Large Cohort of Coronavirus Disease 2019 (COVID-19) Patients Transfused Early with Convalescent Plasma Containing High-Titer Anti-Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Spike Protein IgG Am J Pathol. 2020;191(1):90-107. DOI: 10.1016/j.ajpath.2020.10.008.

14. Ahmad A, Salsabil M, Oliver T. Mortality rates in matched cohort, pseudo-randomised and randomised trials of convalescent plasma given to COVID-19 patients medRxiv. 2020;11(19): 20234757. DOI:https://doi.org/10.1101/2020.11.19.20234757

15. Clarifying the Emergency Use Authorization Framework For COVID-19 Convalescent Plasma: Considerations for Clinicians Prepared Jointly by The Infectious Diseases Society of America And AABB; 2020.

16. COVID-19 Treatment Guidelines (Last Updated: December 16, 2021) Available:https://www.covid19treatmentguidelines.nih.gov/therapies/anti-sars-cov-2-antibody-products/convalescent-plasma/

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