CASE REPORT

JIACM 2020; 21(3-4): 170-74

Treatment of Covid-19 Pneumonia with Convalescent Plasma Therapy: A Case Series

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Abstract

Introduction: The entire globe is currently experiencing a pandemic by SARS-CoV-2 virus resulting in Covid-19. Management of this disease still remains largely supportive. Convalescent Plasma Therapy is still under investigation for efficacy in this disease.

Case studies: In this case series we have followed five patients who have received Convalescent Plasma Therapy along with systemic corticosteroids and two of the patients also received an antiviral agent in form of remdesivir. All five patients were above 35 years of age, all had severe Covid-19 pneumonia according to MoHFW guidelines and four patients had comorbidities (diabetes and/or hypertension).

Results and conclusion: All five patients showed clinical as well as radiological improvement in Covid-19 pneumonia after Convalescent Plasma Therapy. Inflammatory markers also started to decline following plasma transfusion. Convalescent Plasma Therapy could be an effective treatment for severe Covid-19. However, further randomised clinical trials the require to confirm its efficacy.

Key words: Covid-19, convalescent plasma therapy, case series.

Introduction

Coronavirus disease 2019 (Covid-19) caused by SARS-CoV-2 (formerly known as novel coronavirus 2019) has emerged from Wuhan city of China and infected approximately 16.3 million people, with death toll over 650,800 lives across the globe (as of 28 July 2020)[1]. The current treatment of Covid-19 is limited to general supportive care and provision of critical care[2]. The clinical data for the studies involving Covid-19 are still limited and available from China, Spain, Italy, United States of America, Germany, France and The United Kingdom. It is rapidly evolving and changing as new clinical data emerges. This will be a problem when predicting treatment outcomes.

Convalescent Plasma Therapy (CPT) is a form of adaptive immunisation. It provides an indirect method to protect a susceptible individual by granting immunity against a specific pathogen via preformed antibodies. A patient who is recovered from an infectious disease is screened for neutralising antibodies against the particular microorganism. Following identification of recovered individuals with high titers of these neutralising antibodies, convalescent plasma containing neutralising antibodies are administered to individuals with specified clinical disease. CPT has shown to reduce symptom severity as well as mortality.

Currently, Convalescent Plasma Therapy (CPT) is an attractive therapeutic option in the wake of this pandemic[3]. It has recently been suggested by Food and Drug Administration (FDA) in United States that administration and study of investigational CPT may provide a clinical benefit in treatment of Covid-19. Studies regarding effectiveness of CPT in Covid-19 are still lacking particularly in Indian settings. Here we present a case series of 5 cases of severe Covid-19 who received Convalescent Plasma Therapy. Our patients were categorised in severity grade and managed according to the Indian Council of Medical Research (ICMR) and Ministry of Health and Family Welfare (MoHFW) guidelines[5]. Clinical grading of severity of Covid-19 according to MoHFW guidelines:-

Mild: Patients with uncomplicated upper respiratory tract infection, may have mild symptoms such as fever, cough, sore throat, nasal congestion, malaise, headache. But no evidence of pneumonia.

Moderate pneumonia: Adolescent or adult with no signs of severe disease, but presence of clinical features of dyspnoea and or hypoxia, fever, cough, including SpO2 < 94% (90 - 94%) and/or respiratory rate > 24/min.

Severe pneumonia: Adolescent or adult with clinical signs of pneumonia, plus one of the following: respiratory rate > 30 breaths/min, severe respiratory distress, SpO2 < 90% on room air.

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Case 1

A 60-year-old diabetic male presented with complaints of fever and breathing difficulty for 5 days. On physical examination, he was tachypnoeic with oxygen saturation of 86% on room air. Chest X-ray was suggestive of bilateral pneumonia with peripheral consolidation. SARS-CoV-2 PCR of patient came out to be positive. Patient was started on non-invasive ventilation (NIV) in view of tachypnoea and type 1 respiratory failure, empirical antibiotics, and methyl prednisolone 80 mg IV once daily. Patient also received Convalescent Plasma Therapy on the second day of admission. IV methyl prednisolone was given for 5 days. Patient became asymptomatic by 4th day of admission but he still required low flow oxygen support. By 10th day of admission, he was off oxygen, maintaining saturation at room air. Patient completely recovered with non-detectable RNA copies on PCR by 20th day of admission and discharged. His CRP levels were 210 mg/dl, 130 mg/dl and 4.5 mg/dl on day 1, day 3, and day 15 respectively.

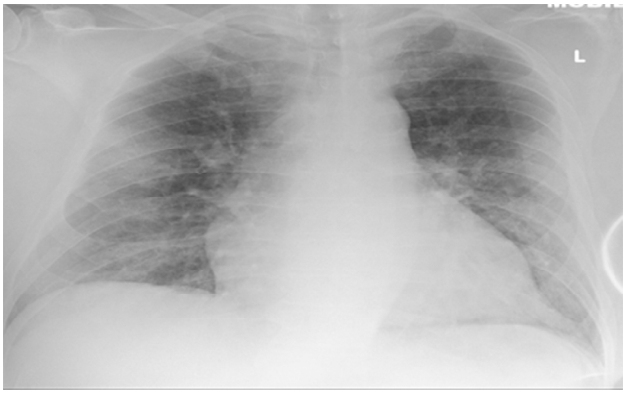

Fig. 1.1: *Chest X-ray showing bilateral middle and lower zone opacities (case 1) before plasma therapy.*

Fig. 1.2: *Chest X-ray showing right middle and lower zone minimal peripheral opacities with clearing (Case 1) after plasma therapy.*

Case 2

A 50-year-old male with diabetes mellitus, presented to the emergency department with complaints of fever for 7 days, dry cough for 4 days, and breathing difficulty for 3 days. He was tachypnoeic with saturation of 90% on room air and his chest X-ray had bilateral infiltrates with peripheral consolidation involving more than half the lung fields. PCR for SARS-CoV-2 was positive. Patient had severe category Covid-19. Patient stared on NIV with oxygen, empirical antibiotics, IV methyl prednisolone and hydroxychloroquine. Patient also received Convalescent Plasma Therapy on the day of admission. Patient was afebrile after 72 hours maintaining saturation at room air without oxygen support by the 5th day of admission. Patient was discharged after 10 days of admission period as he was asymptomatic and repeat RNA PCR was also negative. His CRP levels were 56 mg/dl, 84 mg/dl and 3.3 mg/dl on day 3, day 4 and day 5 of admission.

Fig. 2.1: *Chest X-ray showing bilateral middle and lower zone consolidation (Case 2) before plasma therapy.*

Fig. 2.2: *Chest X-ray showing resolution (Case 2) after plasma therapy.*

Case 3

A 49-year-old diabetic patient presented with complaints of fever and dry cough for 4 days and generalised weakness for 3 days. On initial assessment his saturation was 88% on

room air and chest X-ray suggestive of left middle and lower zone pneumonia with mainly peripheral consolidation. His throat and nasopharyngeal swabs turned out to be positive for SARS-CoV-2. Patient was started on oxygen inhalation and empirical antibiotics. Patient received Convalescent Plasma Therapy on second day of admission. Patient became asymptomatic and he was maintaining saturation on room air by 72 hours of admission. Patient was discharged after 15 days of admission period with non detectable viral RNA copies on RT-PCR. His CRP levels were 30 mg/dl on day 1 which decreased to 8 mg/dl and 4.8 mg/dl thereafter.

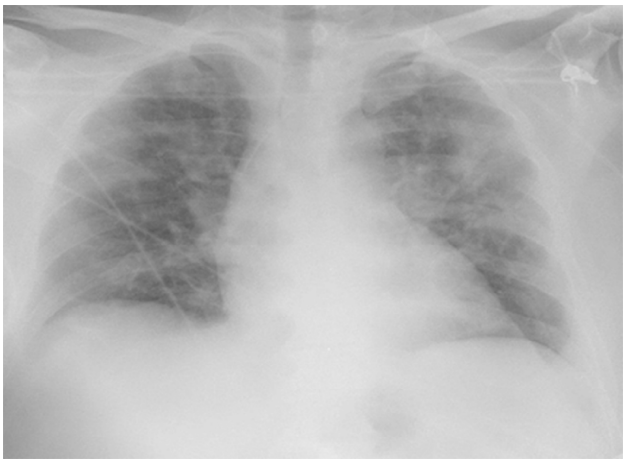

Fig. 3.1: *Chest X-ray showing bilateral opacities in peripheral distribution and left upper lobe consolidation (Case 3) before plasma therapy.*

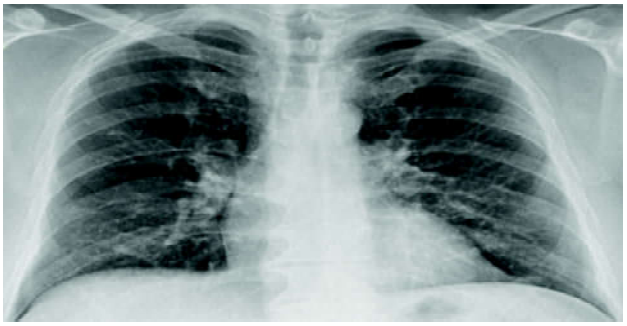

Fig 3.2: *Chest X-ray showing no significant abnormality with resolution (Case 3) after plasma therapy.*

Case 4

A 50-year-old male with diabetes mellitus and hypertension presented with complaints of fever for 6 days and cough with breathing difficulties for 3 days. On examination, he was dyspnoeic with saturation 89% on room air and his chest X-ray was showing bilateral pneumonia with peripheral consolidation. His nasopharyngeal swab and throat swab sent for SARS-CoV-2 RT PCR, came out to be positive. The patient required NIV support with oxygen in view of tachypnoea and type1 respiratory failure. He was started on empirical antibiotics and antiviral IV remdesivir. Patient did not respond to the standard supportive care, so on 6th day of admission he was transfused with convalescent plasma. Patient become asymptomatic with significant clinical improvement and maintaining oxygen saturation at room air by 8th day of admission. Patient was discharged after 12 days of admission period with negative RT PCR for SARS-CoV-2. His ferritin level was 1,000 ng/ml which decreased to 499 ng/ml after 5 days.

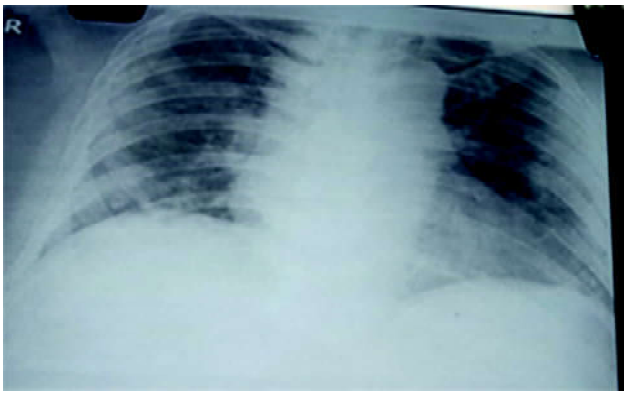

Fig. 4.1: *Chest X-ray showing bilateral peripheral consolidation (Case 4) before plasma therapy.*

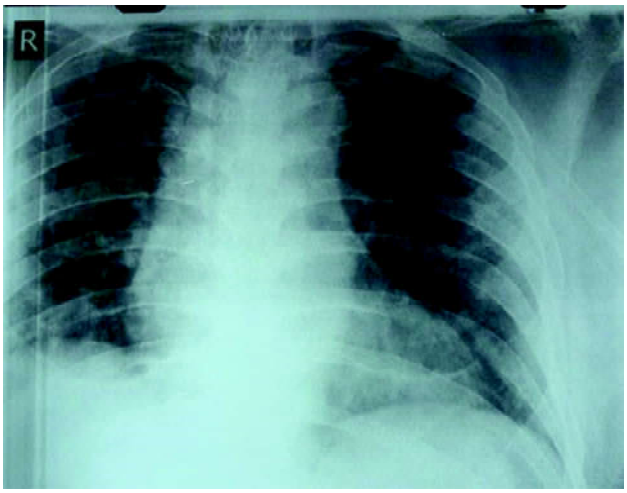

Fig. 4.2: *Chest X-ray showing resolution (Case 4) after plasma therapy.*

Case 5

A 37-year-old male came with complaints of fever since 14 days and cough with difficulty in breathing since 7 days. Patient was dyspnoeic with respiratory rate of 30 and SpO2 of 82 % on room air. Patient was given NIV support and antibiotics. Patient was administered with IV antiviral agent remdesivir. Patient was admitted on 25 July 2020. As patient did not improve on supportive treatment he was given

plasma therapy on day 3, and day 4 of admission. Gradually, he was off NIV support on day 6 and was maintaining saturation on room air on day 9 of admission. His LDH and CRP were 961 IU/L and 71 mg/dl on day 4 respectively, which

Fig. 5.1: *Chest X-ray showing bilateral patchy opacities with peripheral involvement (Case 5) before plasma therapy.*

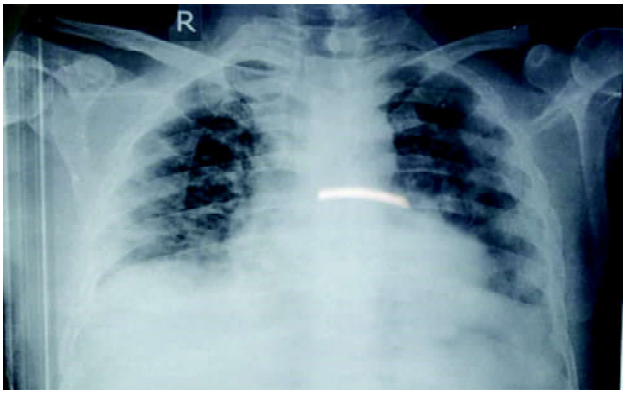

Fig. 5.2: *Chest X-ray showing bilateral peripheral opacities with clearing compared to previous X-ray (Case 5, after plasma therapy).*

reduced after Convalescent Plasma Therapy.

Discussion

In this case series, we have included five patients with severe category Covid-19 illness. All of these patients have received Convalescent Plasma Therapy between day 7 to day 20 of symptom onset. All patients turned negative on RT PCR for SARS-CoV-2 (undetectable RNA levels) following Convalescent Plasma Therapy.

A case series by Shen *et al* in March, 2020 showed improvement in clinical status and viral load after Convalescent Plasma Therapy in five patients who were critically ill Covid-19 patients. Out of these 5 patients, four patients were on mechanical ventilation[6]. However, such studies were lacking in Indian settings and we have included patients who are either on non-invasive ventilation or oxygen support rather than invasive mechanical ventilation.

In our study, we defined severe Covid-19 as clinical signs of pneumonia plus one of the following; respiratory rate > 30 breaths/min, severe respiratory distress, SpO_2 less than 90% according to MoHFW guidelines.

Out of 5 patients, four patients had co-morbidities, four patients were 45 years or above and four patient received NIV support. All patients received empirical antibiotics, but only two received methyl prednisolone, and one patient received oral hydroxychloroquine. Out of five patients, case 4 and case 5 also received IV antiviral agent remdesivir besides the standard care. Table I is showing clinical and treatment characteristics of patients. All patients also received therapeutic anticoagulation via subcutaneous enoxaparin administration.

All patients improved clinically after Convalescent Plasma Therapy in terms of symptom recovery, temperature reduction and oxygen requirement. C-reactive protein levels and ferritin levels were obtained before and after administration of Convalescent Plasma Therapy. Quantitative levels of these inflammatory markers reduced after plasma therapy. Patients also had radiographic improvement in terms of decreased infiltrates. RNA levels by RT PCR also became undetectable after plasma therapy. Table II and Fig. 1 shows pre- and post-transfusion CRP levels. These are showing significant decline in quantitative CRP levels

In our study, two of the patients received antiviral agent, remdesivir. A Case series published in JAMA network also had 5 patients with critical Covid-19 but all of these patients

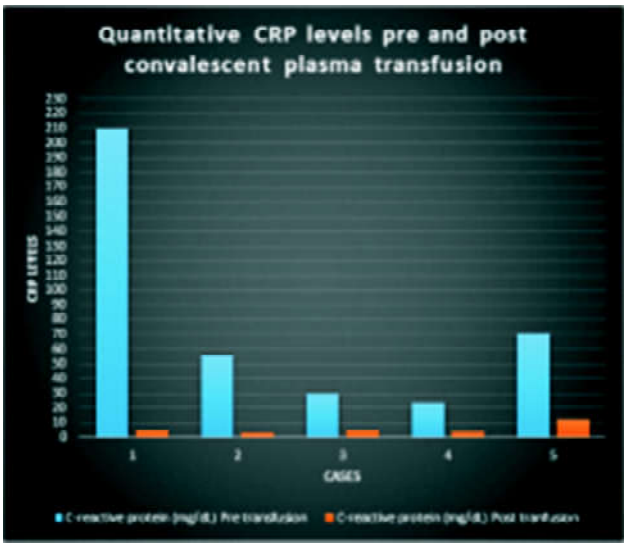

Fig. 1: *Quantitative C-reactive protein (CRP) levels before and after CPT.*

also received antiviral agents such as interferon, lopinavir-ritonavir beside convalescent plasma which may have affected outcome[6].

Table I: Clinical and therapeutic characteristics of cases.

Case	Age (years)	Co-morbidities	Duration of stay (days)	Saturation support/ presentation (%)	Oxygen methyl NIV	IV predniso-lone (Y/N)	Antivirals (IV Remde-sivir)
1	60	Diabetes mellitus	20	85	NIV	Y	N
2	50	Diabetes mellitus	11	90	NIV	Y	N
3	49	Diabetes mellitus	15	88	Oxygen	Y	N
4	50	Diabetes mellitus, hypertension	11	89	NIV	Y	Y
5	37	No	12	82	NIV	Y	Y

Table II: Quantitative CRP levels pre- and post-convalescent plasma transfusion.

Cases	C-reactive protein (mg/dl)	
	Pre-transfusion	Post-tranfusion
1	210	4.5
2	56	3.3
3	30	4.8
4	23.5	4.0
5	71	12.4

Conclusion

In this uncontrolled clinical case series, five patients with severe Covid-19 who received Convalescent Plasma Therapy, showed improvement in clinical status and inflammatory markers. However, a proper clinical trial should be carried-out to further investigate effectiveness of convalescent plasma in Covid-19.

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