Convalescent Plasma Rescued a Severe COVID-19 Patient with Chronic Myeloid Leukemia Blast Crisis and Myelofibrosis

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To the Editor,
Coronavirus disease 2019 (COVID-19) is now an unprecedented worldwide pandemic. However, there are no specific antiviral drugs available for its treatment. A handful of literature has summarized convalescent plasma (CP) transfusion in severe or critical case[1,2,3,4,5,6], whereas therapies for COVID-19 with hematologic cancers are rather limited. We first reported the initial clinical experience with CP transfusion administered to a severe COVID-19 patient with chronic myeloid leukemia blast crisis (CML-BP) and myelofibrosis.

A 46-year-old female patient presented with diarrhea, a cough with clear sputum, and fatigue for 3 days. Her previous history of treatment for CML-BP consisted of daunorubicin 45 mg/m² for 3d and cytarabine 200 mg/m² for 7d in a continuous infusion and then experienced discontinuation of tyrosine kinase inhibitor (TKI) therapy. She was given imatinib (600 mg/d) starting from November 2017, but a drug-related hematologic adverse event occurred quickly. As a result, dasatinib (150mg/d) was given instead. She did not achieve complete hematological remission (CHR) at diagnosis of COVID-19 due to poor responses to these therapies. At admission (February 21, 2020), the most relevant clinical findings included white blood cell (WBC) count of 4.93×10⁹/L with 78% neutrophils, 9.2% lymphocytes, 2.3% basophils, 0.4% eosinophils, and 10.1% monocytes, hemoglobin of 51g/L, platelet count of 79× 10⁹/L, high-sensitive C-reactive protein (CRP) of 57.43mg/L, and the interleukin 6 level was 59.25 pg/mL. The RT-PCR assay of throat swab was positive for SARS-CoV-2 infection. A chest CT obtained on February 21 revealed bilateral ground-glass opacities primarily distributed along the pleura (Figure. 1a, d). Bone marrow

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examination and flow cytometry suggested a blast crisis, with 20.5% of leukemic blasts (Figure. 2a) that expressed CD33, CD13, and partially CD41, CD34, HLA-DR, cMPO (Figure. 2c). Real-time polymerase chain reaction (RT-PCR) revealed a major chimeric BCR-ABL1 transcript. Fluorescence in situ hybridization (FISH) analysis confirmed the BCR-ABL1 fusion rearrangement signal. Gene sequencing showed no mutation in the ABL1 kinase domain. Cytogenetics were characterized as 46,XX,t(3;17)(q21;q21),t(9;22)(q34;q11)[19]/47,idem,+8[1] (Figure. 2d). A biopsy specimen detected grade 2 fibrosis (Figure. 2b) according to the marrow fibrosis scoring system. Computed tomographic (CT) scanning showed hepatosplenomegaly (21 cm in length). The disease was consistent with COVID-19 and CML-BP with myelofibrosis. The patient developed worsening hypoxemia, with oxyhemoglobin saturation (SaO2) oscillating between 90% and 93%, after receiving conventional antiviral therapy, such as arbidol (200 mg three times daily), oseltamivir (75 mg twice daily), ribavirin (500 mg every 12 hours), and interferon-alpha-2b inhalation (5 million units twice daily). A follow-up chest CT showed increased consolidation and extended opacities (Figure. 1b,e). On February 26, the patient received a transfusion of 200 ml CP derived from a donor recovered from SARS-CoV-2 infection in January 2020 with the neutralizing antibody titer above 1:640. No immediate adverse reactions were observed after plasma infusion. One day later, her SaO2 increased to 98% with OI of 200 mmHg. At the same time, clinical symptoms and pathological criteria improved rapidly within 3 days. The patient's condition improved to stable, thus treatment with pulsed dasatinib was administered (100 mg once daily). Three repetitive RT-PCR test results were negative from 6th to 8th day after CP transfusion. Chest 2 images showed absorption of opacities within 10 days (Figure. 1c, f). The patient recovered and was discharged on 14th day of admission. A recent study showed a 10% case rate of COVID-19 amongst 128 patients with hematological cancers in Wuhan[7]. The treatment of severe COVID-19 has been challenging. This pilot study on CP therapy shows it can serve as a promising rescue option for hematologic cancer patients with severe COVID-19, which warrants further investigation by randomized trials.

Keywords: COVID-19, chronic myeloid leukemia; blastic crisis, convalescent plasma therapy

Informed Consent: It was received.

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Authors' contributions
References
**Figure 1.** Representative chest CT scans of this patient. **a, d** Chest CT obtained at admission showed multiple ground-glass opacities with uneven density involving both upper lungs and right lung. **b, e** Chest CT obtained on February 25 before CP transfusion, multiple shadows
of high density in both upper lungs and patchy consolidation in the right lung were observed.  
C, f CT image taken on March 6 showed the absorption of bilateral ground-glass opacity after  
CP transfusion.
Figure 2. Morphology, flow cytometry, and cytogenetics of the patient at admission. a Bone marrow aspirate smear (Wright-Giemsa stain, original magnification $\times 1000$) showed
leukemic blast cells. b Bone marrow biopsy (H&E stain, original magnification ×100) showed fibrosis. c Flow cytometry plots showed single cluster of blasts with positivity for CD33, CD13, and partial CD41, CD34, HLA-DR, cMPO. d Karyotype of bone marrow showed t(9;22) and t(3;17) abnormality in the same leukemic clone cells.