Can Cancer Survivors Donate Convalescent Plasma for the Treatment of COVID-19?

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Case Vignette

SS is a 50-year-old female treated for stage III colon cancer in 2010 and on a 6-monthly follow-up. She missed her scheduled review in July 2020 and informed that she could not come on for her appointment due to coronavirus disease 2019 (COVID-19) infection, which affected her whole family, all of whom had mild symptoms and recovered uneventfully. I suggested that she could now donate convalescent plasma (CP) for the treatment of seriously ill COVID-19 patients, and she was immediately interested. I advised her to go to the hospital's blood transfusion center and volunteer. Later, I had a call from the transfusion medical officer asking me to clarify whether cancer survivors can donate blood or blood products.

Introduction

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), the cause of COVID-19, is the latest virus in the long line of infectious agents that have challenged human beings through our history. The pandemic started with an outbreak of pneumonia of unknown origin in Wuhan in the Hubei province of China in December 2019. By January 7, 2020, Chinese scientists had isolated the causative novel coronavirus (CoV). The Chinese flu spread rapidly through China and was exported, initially to Thailand, Japan, Korea, the United States, Vietnam, and Singapore, and later to the rest of the world. As of August 03, 2020, there are over 18 million recorded cases with ~700,000 deaths in 213 countries (www.worldometer.info).

The methods of managing the COVID-19 patients have varied widely across the world and continue to evolve. There is a tacit understanding that the final control over the virus will be achieved only when there is herd immunity, either by active infection or by a vaccine (the exact percentage of immune population required for this remains a matter of controversy). In the meantime, prevention by measures such as social distancing, hand washing, and face masks has been recommended to “flatten the curve,” thus spreading out the cases, and avoid overwhelming the health-care facilities by unmanageable spikes in symptomatic cases needing active treatment. The role of pharmacological agents in prevention, such as hydroxychloroquine, is controversial.

Treatment of symptomatic cases depends on the severity, and in addition to the management of complications, is a two-pronged approach—antiviral agents (only remdesivir has a high level of evidence) and anti-inflammatory drugs (again, only dexamethasone has a high level of evidence). An indirect way of targeting the virus is by boosting host immunity with the use of CP.

Convalescent Plasma

Passive antibody therapy through transfusion of CP is a short-term strategy for conferring immediate immunity and has been used in the past for similar viral epidemics such as Middle East respiratory syndrome and SARS-1. Readers are referred to an excellent review by Bloch et al for details of this therapy. CP (or immune) is a plasma containing neutralizing antibodies (NAbs) to a specific infection collected from previously infected individuals after resolution of infection. Many of the initial studies displaying the positive effects of CP have been from China. A systematic review of five studies (four from China) confirmed the beneficial effects in almost all patients, including a rise in NAb titers and disappearance of circulating CoV-2 RNA, and possible reduction in mortality. However, a large Cochrane analysis of CP reported that the safety and efficacy of CP in COVID-19 patients were “uncertain,” and that data from the ongoing 98 studies (including 50 randomized trials) are awaited.

The CP donor must have had a molecularly confirmed COVID-19 infection (such as real-time polymerase chain reaction (RT-PCR) positive) and must be confirmed as full recovery. The Blood Transfusion Advisory Committee at the Royal Hospital approved the donation protocol. The patient was approached for donation with the approval of the Medical Ethics Committee. After a thorough explanation of the potential benefits and risk involved, she agreed to donate.

According to the current guidelines, CP is not contraindicated in cancer survivors. Cancer survivors have normal immunity, unlike the patients who are undergoing immunosuppressive therapy or suffering from acute infections. The cancer survivors might have a better prognosis than the patients undergoing chemotherapy or radiation therapy. Moreover, cancer patients are more susceptible to the COVID-19 infection due to the presence of pre-existing conditions and comorbidities such as diabetes, hypertension, obesity, and smoking.
reaction positivity of nasopharyngeal swab), recovery from symptoms of at least 14 days, and a negative test subsequently (to prevent transmission to blood transfusion department staff).

However, the last criterion is not absolute as it is accepted that most cases of mild infection will clear the virus by the 10th day.

A Chinese study6 of 175 patients who recovered from mild COVID-19 infection showed that most COVID-19 patients developed SARS-CoV-2-specific NAbs by the convalescent phase of infection. However, 30% had low titers and 10 of them had undetectable levels—it was not clear how they recovered without generating an antibody response.

The titers of NAbs reached their peak at 10 to 15 days after the disease onset and that antibodies targeting on different domains of S protein, including S1, receptor-binding domain (RBD), and S2, contributed to virus neutralization. These and other studies10 indicate that seroconversion of the donor occurs between day 8 and 21 after the onset of symptoms, and peak antibody titers are obtained 14 days after the resolution of symptoms. The relationship between total and NAbs is not clear.

Theoretically, the CP should be tested for antibody titers before transfusion, but tests for specific NAbs are not generally available and quantitative assays for total antibodies (such as ELISA) have not yet been validated. The Indian government guidelines11 suggest that in the case of nonavailability of tests for NAbs, plasma immunoglobulin G titer (against S–protein RBD) above 1:640 should be used.

The collection and administration of CP follow standard procedure, but it is recommended thatapheresis be used rather than whole blood donation; this will yield 400 to 800 mL of plasma, enough for two to four units of CP.6 The units are frozen after collection while awaiting standard procedure, but it is recommended that apheresis be used rather than whole blood donation; this will yield 400 to 800 mL of plasma, enough for two to four units of CP.6 The units are frozen after collection while awaiting standard procedure, but it is recommended that apheresis be used rather than whole blood donation; this will yield 400 to 800 mL of plasma, enough for two to four units of CP.6 The units are frozen after collection while awaiting standard procedure, but it is recommended that apheresis be used rather than whole blood donation; this will yield 400 to 800 mL of plasma, enough for two to four units of CP.6 The units are frozen after collection while awaiting standard procedure, but it is recommended that apheresis be used rather than whole blood donation; this will yield 400 to 800 mL of plasma, enough for two to four units of CP.6 The units are frozen after collection while awaiting standard procedure, but it is recommended that apheresis be used rather than whole blood donation; this will yield 400 to 800 mL of plasma, enough for two to four units of CP.6 The units are frozen after collection while awaiting standard procedure, but it is recommended that apheresis be used rather than whole blood donation; this will yield 400 to 800 mL of plasma, enough for two to four units of CP.6 The units are frozen after collection while awaiting standard procedure, but it is recommended that apheresis be used rather than whole blood donation; this will yield 400 to 800 mL of plasma, enough for two to four units of CP.6 The units are frozen after collection while awaiting standard procedure, but it is recommended that apheresis be used rather than whole blood donation; this will yield 400 to 800 mL of plasma, enough for two to four units of CP.6

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at higher risk for second primary malignancy, both due to inherited genetic defects and effects of cancer drugs, and with long-term immune abnormalities. Immunization schedule for cancer patients and survivors is different from that of general population and includes contraindication to live vaccines.\(^{30,31}\) It is assumed that cancer and its treatment could lead to lowered immunity, which raises the question whether COVID-19/ cancer survivors can generate sufficient antibody titres. At present there is no direct data on this, but as recent papers indicate equivalent survival in cancer patients affected by CoV,\(^{19}\) it can be assumed that they too generate an adequate antibody response.

Poor antibody responses to vaccines are common in patients of hematological malignancies, especially those who receive anti-B cell agents such as rituximab.\(^{32}\) Among patients with Hodgkin lymphoma, for example, vaccine responses remain impaired for as long as 7 years after treatment.\(^{33}\) However, such survivors of hematological malignancies are automatically excluded from CP donation. On the other hand, patients with solid tumors are classically given myelosuppressive rather than immunosuppressive therapy. Hence, the degree of immunosuppression is expected to be minimal. Consistent with this, no deficiency in serologic response was noted in patients with solid tumors, such as gastric and colorectal cancers, vaccinated with pneumococcal vaccine,\(^ {34}\) or influenza vaccine.\(^ {35}\)

They have responded with adequate antibody titers. Thus, both direct and indirect evidence suggests that survivors of solid tumors who recovered from COVID-19 will have equivalent NAbs. However, this requires confirmation.

**Conclusions**

Cancer survivors who survive COVID-19 (double survivors) are expected to have sufficient NAb titres in their plasma to be considered for CP donation. The risk of transmitting cancer through blood or blood products is negligible to nonexistent. Recent data indicate that patients recovering from mild CoV infection (representing ~85% of the infected population) have a limited period for donating their plasma due to rapid decay of antibody titres; this suggests that the donor pool is smaller than estimated. Cancer survivors form a not-so-negligible percentage of the population and they are well aware of the importance of blood transfusion by personal experience.

Consequently, they are well motivated to donate. It can be concluded that CP donation by survivors of solid tumors who are free of recurrences for at least 12 months after treatment is safe and of equivalent efficacy. In the meantime, there is an urgent need to revise the guidelines by the Indian regulatory authorities banning donation of blood and blood products by cancer survivors.

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Nil.

**Conflicts of Interest**

There are no conflicts of interest.

**References**

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