

Aplastic Anemia: Non-COVID Casualties in the COVID-19 Era

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Abstract

With the emergence of COVID-19 pandemic, health care for many non-COVID illnesses has inadvertently slid back. For most patients with life-threatening illnesses, the directive from the Ministry of Health and Family Welfare to continue the treatment for essential health services has come as a relief. However, for certain life-threatening illnesses such as aplastic anemia, the situation has been grim. We discuss the poor outcome of 2 children followed up at our center for aplastic anemia and analyze the reasons for the same.

Keywords: Aplastic anemia, non-COVID, non-malignant hematology

INTRODUCTION

COVID-19, the global pandemic has captured the attention of all in the most unprecedented manner. It has forced most countries to dedicate its health-care resources to fight the crisis, leaving little if not none for patients suffering from other diseases. From the beginning of this pandemic, there have been advisories from various professional groups for hematology-oncology patients regarding tele-consultations and for postponing elective surgeries, hospital visits, chemotherapy, and immunosuppression.^[1] These decisions were made based on the risk of increased mortality if these patients contract COVID-19 due to their co-morbid status. However, as we move ahead into the 3rd month of travel restrictions imposed by COVID-19, decisions regarding non-COVID patients need reevaluation as their risk of death without receiving treatment is substantial. We describe two patients with very severe aplastic anemia who succumbed to the disease during this period and analyze reasons for the same.

CASE REPORT

A 17-year-old boy with on-and-off fever, gum bleeding, and melena for 3 months, presented to us in December 2019 and was evaluated and diagnosed to have very severe aplastic anemia. Bone marrow cellularity was <5% and absolute neutrophil count was persistently <100 cells/ μ L. Based on these investigations, the family was counseled regarding the treatment options of bone marrow transplantation (BMT)

and immunosuppressive therapy (IST). Human-leukocyte antigen (HLA) typing for siblings was done; no match was identified. He was posted for IST with anti-thymocyte globulin (ATG) and cyclosporine. Due to financial constraints, the sanction of government funding was awaited for starting treatment. During this period, he received multiple packed red cells and platelet transfusions in view of recurrent anemia and thrombocytopenia with mucosal bleeding. He had multiple episodes of life-threatening infections including agranulocytosis with mass obstructing the upper airway during this period. He also developed sudden onset of vision loss in both eyes followed by generalized seizures which was suggestive of intracranial hemorrhage with bilateral retinal hemorrhages. Following these, he received ATG with cyclosporine as per protocol just prior to the COVID-19-related travel restrictions in our city. He was discharged and followed up daily from home over teleconsultation. In view of anemia, he was advised hospital visit for red cell transfusion. However, the family was not able to come to the hospital, and he succumbed to severe anemia with respiratory distress. He was taken to the emergency department of a government hospital

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Submitted: 20-May-20 **Accepted:** 21-May-20

Published: 30-Jun-20

Access this article online

Quick Response Code:



Website:
www.jpalliativecare.com

DOI:
10.4103/IJPC.IJPC_152_20

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How to cite this article: Radhakrishnan N, Shankar R, Singh S. Aplastic anemia: Non-COVID casualties in the COVID-19 era. Indian J Palliat Care 2020;26:S145-7.

near home, but could not be transfused due to unavailability of blood products.

Another 13-year-old boy also presented to us in December 2019 with fever following an episode of jaundice 8 months prior. He also had mucosal bleeding, difficulty in walking and repeated infections. Bone marrow cellularity was < 10% and he also had severe neutropenia and thrombocytopenia warranting repeated admissions. He was HLA matched with his brother and was awaiting sanction of funds for undergoing BMT. During the follow-up at our center, he had multiple transfusions and febrile neutropenic episodes which required admissions. His last admission was for bilateral periorbital bleeding with left periorbital cellulitis which required antibiotics and antifungals. He was discharged on oral medication and was advised regular follow-up. However, further follow-ups were not possible due to travel restrictions and 2 weeks later he died following suspected intracranial hemorrhage at his native place.

DISCUSSION

The prognosis of severe aplastic anemia in our country is dismal. The incidence of 4–6 per million population of childhood aplastic anemia in India and other Asian countries is higher than what is observed in the West.^[2] A significant proportion of patients of aplastic anemia (around 30%) die before any definitive treatment is initiated. In a recent series of patients followed up at AIIMS, Delhi, out of 1501 patients diagnosed over 7.5 years, only 303 (20%) received the definitive treatment modalities (i.e., either BMT or IST with ATG and cyclosporine).^[3] This is unlike other hematological illnesses including cancers, where access to treatment has improved and majority of patients are able to receive standard of care. In aplastic anemia, the factors interfering with treatment are mostly delay in diagnosis, delay in initiation of treatment due to monetary constraints, noninclusion of the disease under government schemes such as Ayushman Bharat and National Health Mission and delay in sanction of money from other government schemes such as Rashtriya Arogya Nidhi, Chief Minister and Prime Minister's relief fund often due to lack of proper documents. The cost of treatment for a 45–50 kg child (as in both of our patients) would be around 8–10 lakhs INR for BMT and 5–6 lakhs for immune suppressive treatment.

Delay in treatment often amounts to failed treatment. The response to HLA identical sibling donor BMT ranges from 70% to 90%, whereas that of IST ranges from 35% to 60%.^[4] Although complete response with IST is seen in only around 20%–30%, 2/3rd of patients achieve transfusion independence and are continued on cyclosporine long term.^[3-5] The delay in treatment occurs while waiting for a donor or while awaiting financial help. During this period, patients often receive multiple nonirradiated red cell and platelet transfusions resulting in allosensitization to leukocytes present in the donor blood. This generates HLA or non-HLA antibodies which can result in platelet refractoriness as well as increased risk of graft rejection following BMT.^[4] So also, as the duration of neutropenia increases, the risk of contracting

fungal infections and drug-resistant bacterial infections increase which further hamper the treatment.

With the global outbreak of COVID-19 infection, the situation of these patients has moved “*out of the frying pan into the fire.*” For most patients with life-threatening illnesses, the directive from the Ministry of Health and Family Welfare to continue treatment for essential health services has come as a relief.^[6] These essential services include reproductive and maternal health services, newborn care, severe malnutrition, vector-borne diseases, and noncommunicable diseases which include cancer care, palliative care, dialysis, and care of disabled. Under blood diseases, thalassemia, hemophilia, and sickle cell disease patients are being provided care under this guideline. Aplastic anemia, however, has not been mentioned as an essential health service. These patients are at the highest risk of death following a break in the treatment of few weeks.

COVID era has also resulted in delays in sanction of usual grants due to the lockdown of offices and inability in generating documents such as income certificate from the tehsils. Both our patients received the government grant after around 3–4 months of applying for the same; both children died before they could reach the hospital for treatment. Blood donations have taken the worst hit. Due to the norms of social distancing, regular camps conducted by blood banks have stopped. Voluntary blood donors also fear visiting hospitals and blood banks for risk of contracting the viral infection. Even those who are motivated to donate face difficulty to travel owing to restrictions.

Compared to aplastic anemia, what has helped patients with other blood disorders are patient support organizations that become the spokespersons for their rights. Their role has been instrumental in providing expensive (e.g., clotting factor concentrates for hemophilia, BMT and chelation therapy for thalassemia) and safe treatment (leukoreduced blood for thalassemia) for patients and for inclusion of these diseases under government schemes such as Ayushman Bharat (cancer) and National Health Mission Blood Cell (for hemophilia and hemoglobinopathies). Upfront inclusion under these schemes ensures smooth treatment for the above patients rather than having to wait for release of grants as in the case of aplastic anemia. Until recently, those eligible for Ayushman Bharat could not apply for other schemes. This thankfully has been relaxed for diseases such as aplastic anemia where no definite treatment package is yet available under the scheme.

CONCLUSION

As we await the peak of COVID-19 in our country and possibly secondary and tertiary waves thereafter, patients with aplastic anemia who are the sickest among all hematological illnesses would benefit greatly from urgent intervention from the government to ensure timely 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.

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