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Research Article

Transfusion and Immunosuppression: An Update

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Abstract

Major advances in the treatment of cancer have resulted in improved survival rates. However, serious infections continue to be a major source of morbidity and mortality in the immunocompromised patients these are patients who have one or more defects in their natural defense mechanism that put them at an increased risk of developing infections. Not only the infections risk is greater in these people, but also once they get infection it is often severe, rapidly progressive and life threatening.

Introduction

Immunocompromised patients are usually seriously ill and many such patients, especially those undergoing stem cell transplantation, have prolonged periods of pancytopenia and consequently, heavy transfusion requirements. All transfusion are potentially hazardous but transfusion to immunocompromised patients cause additional problems, which may be immunological or infectious.

Problems such as haemolytic transfusion reactions and HLA alloimmunisation leading to transfusion refractoriness are well known and common to all patients. Less well known (but of particular importance to immunocompromised patients) is transfusion associated graftversus-host disease (TA-GvHD), mediated by donor derived, "passenger" T lymphocytes in cellular components, and immunomodulation that may increase the risk of infection and cancer recurrence.

Every blood transfusion interferes with the immune system of the recipient. However, patients who are already immunocompromised often require frequent blood transfusion and pose special challenges for blood transfusion service. Some additional issues which need to be considered in patients with congenital or acquired deficiencies of the immune system are blood grouping discrepancy, transfusion associated graft verus host disease (TA-GvHD), CMV transmission, increased risk of bacterial and other infections from the blood components and anaphylactic reactions in IgA deficient patients [1].

The management and treatment of patients who are immunosuppressed require the commitment and involvement of the transfusion service and he transfusion medicine physician. This objective can be achieved only by a thorough understanding of the needs and clinical situation of each patient and a high level of interactivity among the primary care team, the transfusion service, and the transfusion medicine physician. Patients who are immunosuprressed cannot be managed solely by preestablished rigid transfusion guidelines. Each patient requires an approach that is individually designed. The transfusion medicine physician must be the driving force that case for these patients [1].

Transfusion services have acquired the sophistication to support the needs of immunosuppressed patients. As such therapies as high-dose chemotherapy, BMT, or PBSCT have become more common, many large centers routinely deal with issues related to the screening of blood components for cytomegalovirus (CMV) and problems of alloimmunization, leukoreduction, and irradiation of blood products. Patients who are immunosuppressed are especially susceptible to infection from any microorganism that may contaminate the blood components. We must avoid this problem in all patients who are transfusion dependent. Care must be taken to prevent and minimize the bacterial contamination of blood products, especially for platelets. The immune systems of immunosuppressed patients are incapable of recognizing foreign cells. This situation can lead to the development of fatal transfusion associated graft-vs-host disease (TA-GVHD) when patients are infused with immunocompetent effector T-Lymphocytes and monocytes present in the transfused blood components [2].

The transfusion services should obtain a complete transfusion history including details of antibody workups, type and number of blood components infused, special handling requirements, and transfusion reaction events and results and interpretation of the causes and resolutions of such events so that consistent and coherent support can be provided. Also, it is important to learn from the patient whether intravenous immunoglobulin (IVIG) was administered during the previous 6to 8 weeks, because RBC isoagglutinins and alloantibodies contained in IVIG may interfere with pretransfusion testing [3].

Blood transfusion is a potential source of transmission of viruses, bacteria and parasites. The severity of reaction to bacterial contamination of blood components is dependent on immune status of the patient. While immune-competent recipients may present with only mild to moderate reaction, this may lead to life threatening sepsis in immunocompromised patients. Approaches for prevention include donor screening, skin disinfection, initial aliquot diversion, and pretransfusion bacterial detection [4].

Transfusion-transmitted CMV is of particular concern in immunocompromised patients as both primary infection and reactivation disease can be overwhelming and even fatal. CMV is transmitted primarily through leukocytes contained in cellular blood components. The sites of CMV latency are thought to include CD34+ progenitor cells and CD13+ and CD14+ monocytes. Patients who are at highest risk include foetuses receiving intrauterine transfusions, low birth weight premature infants born to CMV seronegative mothers and CMV seronegative recipients of solid organ or hematopoetic stem cell transplants from seronegative donors. The risk of transmission depends on the immunosuppressed state of the patient, viral load transmitted by the blood component, and preventive measures taken against CMV. Strategies to reduce the risk of transfusion transmitted CMV include use of blood from CMV seronegative donors, reduction of leukocytes in the blood components, and postdonation treatment of the blood components to inactivate the virus. It may be difficult to provide CMV negative blood components from donor populations where prevalence of CMV is high. A residual leucocyte level of 5X106 is said to mitigate the risk of CMV transmission [4].

Post-transfusion EBV infection may lead to EBV associated lymphomas if patient is immunocompromised Coagulation factor concentrates may transmit parvovirus B19 which may lead to pure red cell aplasia in some immunocompromised patients. Morbidity and mortality due to transfusion transmitted malaria is particularly severe in immunocompromised and splenectomised patients because of high parasitemia in these groups. Some centres in malaria endemic areas practice premedication of vulnerable recipients with chloroquine, routinely before transfusion [5].

IgA deficiency has been recognized as most frequent immunodeficiency in humans. The individuals with IgA deficiency are mostly asymptomatic and no further investigation is warranted unless blood transfusion is required [6]. They may develop class specific alloantibodies to IgA and anaphylactic reactions occur when blood components containing IgA are transfused. If anaphylaxis related to blood transfusion is suspected, administration of any additional plasma-containing blood component should be avoided, and an appropriate diagnostic evaluation should be performed [7].

Grouping discrepancy occurs when the results of cell grouping are not in agreement with serum grouping. Weak or missing antibodies may give rise to false negative reactions on serum grouping of patient's blood sample. Several case reports have been published where patient's primary disease came into light only when no or weak reaction was seen on serum grouping, warranting investigations of immunoglobulin levels [3].

Immunosuppressed patients may require frequent transfusions of RBCs owing to the disease process itself or as a consequence of the myelosuppressive effects of therapy. As the patient enters the hospital or outpatient clinic, we recommend type and screen as a baseline to determine the presence of RBC alloantibodies [8].

Furthermore, as the patient is admitted to our institution for allogeneic BMT or PBSCT, we perform an RBC phenotype to document the presence or absence of clinically significant antigens, such as those in Rh, Kell, Duffy, or Kidd blood group systems. While the disease is developing and therapy is instituted, the patient who is immunosuppressed may have undetectable levels of anti-A and anti-B isoagglutinins, which gives the impression of an ABO discrepancy during a routine immunohematologic workup. We routinely conduct detailed RBC antibody screens, and crossmatches include an antihuman globulin phase at each transfusion event [9].

Patients who are immunosuppressed may be transfused with random or single-donor platelets as the supply allows and is available. To obtain a reliable therapeutic response, it is important that platelet concentrates be dosed according to a patient's body weight and blood volume. It is preferable to transfuse ABO-compatible platelets that are 1 to 3 days old. Data suggest that rate of bacterial contamination and cytokine-induced reaction increases as the storage time of platelets increases [10]. It is also important to infuse those platelets as soon as they are pooled and released from the transfusion service, because the likelihood of bacterial contamination may lead to such negative effects as increased morbidity and mortality due to sepsis, or the contamination of blood and components with bacteria. When transfusing platelets, it is helpful if no other therapy is given through another IV line. Such therapies include antibiotics or other biochemical agents that may inhibit platelet function and render the transfusion ineffective [11].

Fresh frozen plasma and cryoprecipitate are transfused to immunosuppressed patients when an objectively documented coagulopathy exists. Such derivatives are administered according to institutional guidelines and ABO blood group congruency, but they are neither irradiated nor leukoreduced [12].

Conclusion

An immunocompromised patient receives more transfusions. Transfused leucocytes cause special problems. TA-GvHD is caused by donor T cells. Irradiating cellular components prevents TA-GvHD. Leucocytes cause immunomodulation increasing infection and tumour recurrence [13]. Leucodepletion reduces problems due to immunomodulation. CMV latent in leucocytes can cause disseminated infection. CMV negative blood or effective leucodepletion prevent CMV transmission. EBV may cause B cell lymphoma and parvovirus B19 can effect haemopoiesis. Pre-storage is better than post-storage leucodepletion [14].

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Conflict of Interest

None

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