

TA-GVHD, a Fatal Complication Following Blood Transfusion from a First-Degree Relative

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Introduction

Transfusion-associated graft-versus-host disease (TA-GVHD) is a devastating one, usually leading to fatal complication of blood transfusion that results from the engraftment and clonal expansion of allogenic donor lymphocytes. TA-GVHD first reported in immunocompromised patients and later was described even in immunocompetent hosts following transfusion when the donor was a first-degree relative. In this case report, we describe a fatal case of TA-GVHD in a woman who underwent elective total abdominal hysterectomy and received one unit of blood transfusion from a first-degree relative.

Case Study

A 45-year-old woman presented to the emergency medicine department of our hospital with history of high-grade fever, oral ulcers, skin rash, and jaundice of 15 days, duration. Subsequently she developed shortness of breath and cough. She underwent total abdominal hysterectomy 20 days before admission at a private hospital for dysfunctional uterine bleeding. She was transfused one unit of B-positive packed red cells donated by her son. At admission, she was found to be very sick looking, icteric, conscious, and coherent. There were milia, exfoliation, and erosions on the skin involving face, neck, arms, forearm, abdomen, and legs. Examination of the oral cavity revealed thrush and cheilitis. She had tachypnoea with a respiratory rate of 40 per min and pulse rate of 120 per min. Blood pressure recorded at the time of admission was 100/70 mmHg. Crepitations were heard all over the chest. Examination of the abdomen revealed a healed scar of the total abdominal hysterectomy.

Investigations at admission showed haemoglobin of 7.8 g/dl, with total leucocyte count of only 300 cells/cmm with an absolute neutrophil count of 30 cells/cmm and platelet count of 10,000/cmm. Blood urea and serum creatinine were within normal limits. Serum bilirubin was elevated; however, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and serum alkaline phosphatase were within normal limits. Blood culture after 24 h developed Gram-negative bacteria which were subsequently identified as *Pseudomonas aeruginosa*. Patient was

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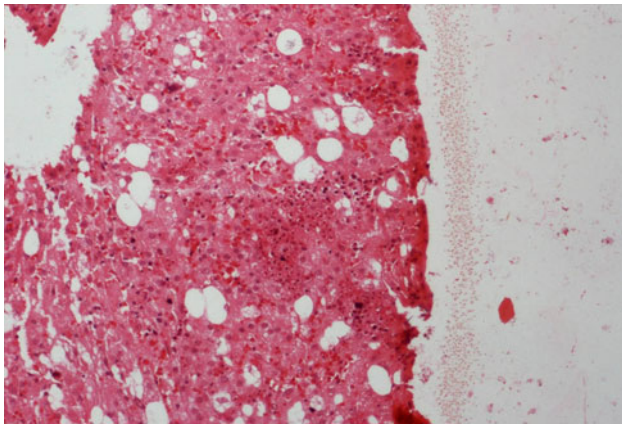


Fig. 1 Bone-marrow biopsy showing marked histiocytosis. H&E $\times 100$. Inset histiocytes showing erythrophagocytosis. H&E $\times 400$

started on intravenous antipseudomonal penicillin and aminoglycoside. She was transfused 2 units of packed red cells and single-donor platelets. In view of the history of transfusion from a first-degree relative 3 weeks before admission, a clinical diagnosis of TA-GVHD was entertained and bone-marrow aspiration and biopsy were done for pancytopenia. Bone-marrow aspiration and biopsy revealed hypocellularity, scattered histiocytes with erythrophagocytosis and lymphocytes (Fig. 1) which confirmed the diagnosis. Intensive care support in the form of ventilator and component transfusion as per requirement were given along with appropriate intravenous antibiotics. Despite close monitoring and supportive care, the patient continued to deteriorate and died after 5 days of hospital stay.

Discussion

TA-GVHD is under-reported and under diagnosed because of its rarity, clinical similarity to viral infection, drug eruption, or underlying disease [1]. Precise incidence of transfusion-associated GVHD is unknown in India but is higher than the assumed rate [1]. Routine blood transfusions are usually not matched for the major histocompatibility complex. However, when the donor and the recipient share human leucocyte antigen (HLA) haplotype, the donor T cells initiate a cell-mediated immune response directed at host tissue antigens, and the host does not recognize the transfused donor cells as foreign and is unable to reject them. Under normal circumstances, the host destroys the donor lymphocytes, thereby preventing them to mount a graft-versus-host response. Homozygosity for HLA types is more likely to occur among the first-degree family members (i.e. parents, children,

and siblings); therefore, such relative-to-patient-directed donations carry an increased risk of initiating TA-GVHD as seen in the above case. Likelihood of developing TA-GVHD is related to the number and viability of the transfused lymphocytes in cellular blood components and the extent of immunosuppression and degree of HLA antigen sharing between donor and recipient. It is suggested that the presence of a shared HLA haplotype in blood donors and recipients may be more important in the development of TA-GVHD than is the patient's immune status as seen in our case.

The diagnosis of TA-GVHD is usually made on the basis of history of recent blood transfusion and constellation of clinical features. Important differential diagnoses to be considered in this case were acute viral infection and hypersensitivity to drugs. Transfusion-associated viruses like HIV, hepatitis B, and cytomegalovirus can cause similar type of illness. Dengue fever and leptospirosis are another important differential diagnosis for a person living in endemic area, but such intense exfoliation of shin and oral thrush are unlikely in both [2].

TA-GVHD typically occurs 3–30 days after transfusion of blood products. Our patient started to develop symptoms after 10 days of transfusion of packed red cells. The initial manifestations are often a high fever, and an erythematous skin rash. Oral thrush, hepatitis, pancytopenia, and bone-marrow aplasia are also characteristic findings in TA-GVHD. Our patient had severe oral thrush, jaundice, hepatitis, exfoliating skin rash, tachypnea, and severe pancytopenia leading to severe leucopenia (total leucocyte count of 300 cells per microlitre) which led to bacteremia due to *Pseudomonas aeruginosa*.

TA-GVHD has an extremely poor prognosis; the mortality rate reaches up to 90 %. Unfortunately, there are no effective therapies currently for this condition except for supportive care. There are very few cases in the literature from India on patients surviving with this deadly complication as it is the case with our patient [3]. Apart from suspicion and early diagnosis, bacterial and fungal cultures, aggressive management with intravenous antibiotics along with supportive care from the beginning may help in improving the survival of the patient. Our patient had severe oral thrush which suggests that antifungals to be started at the early period of hospital stay. Apart from supportive care, the patients have to be managed like GVHD with barrier precautions as there is severe bone-marrow aplasia.

Both stored blood and fresh blood are implicated in the occurrence of TA-GVHD. Universal leucoreduction also does not prevent occurrence of TA-GVHD. Gamma irradiation abolishes the proliferative activity of the lymphocytes. Blood irradiators are capable of delivering 15–30 Gy over 1–5 min per unit; this dose effectively inactivates

immunocompetent T lymphocytes [1]. Gamma irradiation does not affect in vivo red cell, platelet, or granulocyte survival or function, but slightly decreases the ability of red cells to tolerate storage [1].

According to World Health Organization's strategy for promoting and practicing rational use of blood and blood products, the use of a single unit of blood should be strongly discouraged. Instead of single unit of packed red cells, some of the elective patients could receive treatment with hematinics few weeks before surgery and avoid transfusion-associated infections and complications.

There is a need for nationwide survey of HLA matching among donors and transfusion medicine practices in India to find out HLA homozygosity and the incidence of this fatal complication. Incidence of TA-GVHD declines with greater degree of HLA polymorphism among population, lower level of dependence on fresh blood with conservative transfusion practices followed.

Conclusions

It is suggested that blood donations from the first-degree relatives should not be permitted, unless the donation is irradiated to prevent TA-GVHD. It is also important to bring awareness among clinicians as well as general public about complications of receiving blood donation from the first-degree relatives and transfusion of fresh blood.

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