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Hazards Of Blood Transfusion: A Surgeon's Perspective

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ABSTRACT:

Blood transfusion is an integral part of surgical practice. The attending surgeon should be aware of the pathophysiologic mechanisms underlying the complications of blood transfusion. A surgeon's perspective to the hazards of blood transfusion is presented in this paper.

Key-words: Hazards, complications, blood transfusion

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INTRODUCTION

Blood transfusion (BT) continues to be the greatest support system in surgical practice. BT practice has greatly evolved over a period of time with the development of multiple products obtained by component separation. However the risk involved in usage of any of these blood products continues to remain the same. Awareness of the hazards of the blood transfusion is mandatory for safe surgical practice. The paper briefly outlines the various complications of blood transfusion.

Patho-Physiology And Manifestations Of Complications:

Hemolytic transfusion reaction is the most serious complication of BT. It results from immunological interactions between the antibodies in the recipient plasma and the antigens of the donor. Despite meticulous assessment for ABO and rhesus D blood groups, yet hemolytic reactions still occur. These hemolytic reactions can either develop immediately or after some time as a delayed response.[1]

Immediate reactions are due to incompatibility between the donor RBC antigens and recipient plasma antibodies producing an antigen-antibody complex, which leads to compliment fixation, intra vascular hemolysis and destruction of transfused blood. If the titer of antibodies in the recipient is high the reaction is more severe.[2,3] The reaction is manifest immediately after commencing the transfusion with symptoms of headache, flank pain, chest pain, and fever with chills, flushing nausea, vomiting, urticaria, dyspnea and hypertension. In an anesthetized patient a watch has to be kept over the development of hypotension, hemoglobinuria in the form of discoloration of urine and increase in bleeding tendency as a feature of disseminated intravascular coagulation. The clinical features need to be picked up immediately in order to prevent a serious fatality. In the event of a reaction the transfusion needs to be stopped immediately. Optimum cardiac and respiratory support needs to be administered. The most dangerous fallout is acute renal failure (ARF) caused by vascular thrombosis and deposition of hemoglobin in the renal tubules. This needs to be dealt with by increasing the urine flow. Aggressive intravenous fluid therapy coupled with administration of diuretics will maintain adequate urine output, thereby preventing blockage of the tubules. In the event of delayed diagnosis with the development of ARF hemofiltration may be required.[4] The

BT has to be stopped immediately in both established and suspected cases of mismatched transfusion. The involved unit of blood should be sent back immediately to the blood bank. Repeat blood grouping and cross matching is mandatory. A positive Coombs test confirms the diagnosis. Laboratory findings will include hemoglobinuria, hemoglobinemia and increase in both unconjugated bilirubin and LDH.[5,6]

Delayed reactions are due to incompatibility with minor blood groups such as Rh, Kidd and Duffy. The majority of these patients usually test negative for antibody titers, in view of extremely low antibody titers. Further exposure to the antigens leads to increase in antibody production described as an anamnestic reaction. These interactions are not severe enough to activate the compliment system. As a result the hemolysis is usually extracellular. RBC's coated by IgG antibodies are removed by the reticuloendothelial system. Therefore the RBC destruction is significantly delayed, usually manifesting on day 7 to 21. Clinically it may manifest in the form of unexplained fall in the hematocrit, transfusion accompanied with jaundice, and a positive Coombs test. These reactions are quite uncommon but awareness of these is extremely important to prevent a misdiagnosis.[6]

Non-hemolytic febrile reaction (NHFR) can be associated with any intravenous therapy. In the context of a blood transfusion reaction resulting from donor leukocyte antigen reacting with antibody in recipient plasma, the resultant leukocyte antigen-antibody complex binds with compliment with the release of various endogenous pyrogens.[5,7] NHFR may also accompany platelet transfusions, which are usually mediated by cytokines derived contaminated leukocytes in the bag. Symptoms of NHFR include fever with chills generalized malaise, myalgia and severe headache. In rare situations it may progress to respiratory distress, vomiting, and hypotension, which may be immediately or after a few hours of transfusion depending upon the rate of infusion and leukocyte load. The biggest dilemma arises in differentiating fever due to NHFR from that seen in a hemolytic transfusion reaction. A direct Coombs test resolves this issue, which is usually negative in NHFR. Treatment comprises of antipyretics with slow rate of infusion taking uttermost care to look for other forms of clinically manifest hemolytic transfusion reactions.

Allergic reactions quite commonly encounter in day to day practice. These are due to the presence of foreign proteins in the donor plasma and are IgE mediated.[2] Severe urticaria with or without fever are the pathognomic features. The transfusion needs to be stopped and antihistamines administered promptly. If the symptoms resolve one can continue transfusion. However, if the symptoms recur it would be a safe practice to discontinue the transfusion.

Anaphylactic reactions mediated by IgA antibodies are rare, although one should be aware of the clinical features in the event of them developing.[2,8] The clinical features include dyspnea, bronchospasm, laryngeal edema and cardiovascular collapse. Treatment comprises of prompt administration of epinephrine to restore vasomotor tone and relieve bronchospasm, followed by intravenous fluid resuscitation, antihistaminic and steroid administration with or without respiratory support. In patients who exhibit this type of reactions, but regularly require transfusions, washed RBC's are suitable solution.

Transfusion related infections can be transmitted by blood and its individual components. These include bacterial, viral and prion disease.[9,10] Bacterial contamination of blood at 4°C predisposes to contamination with gram negative bacteria

such as Yersinia and pseudomonas species.

Gram. Positive Staph. Epidermis, Staph. Aureus and bacillus species usually proliferate at room temperature. There are no screening tests to check for bacterial contamination. However, close inspection of the bag may reveal an abnormally dark color of the content or the presence of gas bubbles. In the event of septic phenomena developing by virtue of influence of contaminated blood, diagnosis can be made only by culture of blood from both the recipient and the implicated blood component.

Viral: Viral contaminants are most hazardous in BT practice. The commonest viral diseases that are implicated are HBV, HCV, HIV I and II, HTLV, syphilis and cytomegalovirus. Health authorities have made it mandatory to screen potential donor for HBV, HCV and HIV I and II and with screening for syphilis. However the biggest challenge to effective screening is the concept of the window period wherein the donor is highly infectious but does not test positive by standard screening tests. Therefore the recipient runs the increased risk of acquiring the viral disease through transfusion. Nucleic acid amplification testing has evolved into an effective confirmatory test to diagnose blood samples in patients within the window period. However, availability of this test has limited its widespread use as a routine screening test for all blood donors.

Prion's disease: Creutzfieldt- Jacob (CJ) disease is a human prion disease traditionally described as a slow progressing viral sub-acute spongiform encephalopathy. Leucodepletion of blood may perhaps reduce the chances of transmitting this disease. The disease is incurable.[11,12]

Transfusion associated graft versus host reaction (GvH) is a fatal complication of BT.[13] Although it is rare, one needs to be aware of this entity. Donor derived immune cells, particularly T-lymphocytes mount an immune response against host tissue. The clinical features include a maculopapular rash affecting the palms, soles and the face accompanied by abdominal pain and loose motions. Liver function test may be abnormal. The bone marrow stem cells are completely destroyed by the donor T-lymphocytes leading to severe pancytopenia. Irradiation of the blood product may inactivate these destructive T-lymphocytes.

Immunomodulation is a therapeutically useful side effect of BT. This effect is usually mediated by type I & II HLA antigens on the donor leukocytes.[14] The net result is in natural killer cell activation with interleukin production and an increase in CD_4/CD_8 ratio's with phagocytic activation of macrophages. Its biggest therapeutic application is with prolonged survival of renal allografts in patients who have received pre-transplantation BT.

The negative implication of immunomodulation is that it increases the risk of post op-infections, increased tumor recurrence and activation of latent viral infections.[13,14]

Massive transfusion which is referred as replacement of total blood volume within 24 hours can lead to a series of complications.[15] These include hypocalcaemia, hyperkalemia, acid base imbalance (metabolic acidosis), hypothermia and DIC.[15,16,17] Close monitoring of coagulation profile, serum electrolytes and core body temperature is essential to predict the development of these complications. Meticulous adherence to standard massive blood transfusion protocols is the only way of preventing this untoward sequelae.

Transfusion associated lung injury (TRALI) is one of the commonest causes of morbidity and death following BT. Two mechanisms have been proposed.[18,19,20] An immune or antibody mediated and a non-immune mechanism. The immune mechanism is by virtue of the presence of leukocyte antibodies in the plasma of the

donor blood directed against HLA and human neutrophil allograft in the recipient. Antibody present in the recipient rarely causes TRALI. In a patient leukocyte antigens are absent or undetected. It is in these cases that reactive lipid products released from broken membranes of donor blood cells act as an initiating factor. This explains the non-immune mechanism for TRALI.[20,21] Effectively the target cell in TRALI is always the neutrophil granulocytes. The clinical features are breathlessness and severe pulmonary edema which can be life threatening. Such patients require immediate respiratory support. The pulmonary edema is non cardiogenic as compared to hydrostatic pulmonary edema as seen in transfusion associated circulatory overload (TACO).[22] TRALI is usually associated with FFP's and platelets as well. In fact the incidence of TRALI is high when associated with FFP's and platelet transfusions.[23,24]

Prognosis

Antibody mediated acute hemolytic reactions are severe and can have a fatal outcome. Whereas non antibody mediated acute hemolytic reactions usually run a benign course.[1,2,22,23,24]

Nonhemolytic febrile reactions are benign with no mortality.[7,8,23] Allergic and anaphylactic though bothersome are non-fatal.[23] Bacterial contamination of the transfused blood can lead to serious endotoxaemias with a high possibility of a fatal outcome.[12] Immunological hazards like graft versus host reaction and modulation require close observation as they can have a poor prognosis.[13] Massive blood transfusions can be fatal if proper protocols are not followed meticulously.[17] TRALI continues to be a serious hazard with poor outcome in quite a few cases.[20,21,22]

CONCLUSION

Blood transfusion continues to be the greatest challenge in surgical practice. Awareness of all the complications is important for the surgeon. Clinical manifestations, prompt diagnosis and immediate administration of required therapy can only prevent mortality in transfusion reactions. In view of the wide spectrum of morbidity and lethal implications associated with transfusion, a judicious judgment needs to be made as to the need and the volume of blood or its components to be transfused.

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