Case Report

IgE- and IgG mediated severe anaphylactic platelet transfusion reaction in a known case of cerebral malaria

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Abstract:

Background: Allergic reactions occur commonly in transfusion practice. However, severe anaphylactic reactions are rare; anti-IgA (IgA: Immunoglobulin A) in IgA-deficient patients is one of the well-illustrated and reported causes for such reactions. However, IgE-mediated hypersensitivity reaction through blood component transfusion may be caused in parasitic hyperimmunization for IgG and IgE antibodies. **Case Report:** We have evaluated here a severe anaphylactic transfusion reaction retrospectively in an 18year-old male, a known case of cerebral malaria, developed after platelet transfusions. The examination and investigations revealed classical signs and symptoms of anaphylaxis along with a significant rise in the serum IgE antibody level and IgG by hemagglutination method. Initial mild allergic reaction was followed by severe anaphylactic reaction after the second transfusion of platelets. **Conclusion:** Based on these results, screening of patients and donors with mild allergic reactions to IgE antibodies may help in understanding the pathogenesis as well as in planning for preventive desensitization and measures for safe transfusion.

Key words:

Anaphylactic transfusion reaction, IgE mediated allergic transfusion reaction, investigation of transfusion reaction, platelet transfusion reactions

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Introduction

Severe anaphylactic transfusion reactions are uncommon events, occurring with an estimated incidence of 1.7 to 4.3 per 100,000 red blood cell (RBC) and plasma transfusions and 62.6 per 100,000 platelet (PLT) pools.[1] From 1968, more than 40 case reports have shown anti-IgA as one of the many reasons causing these reactions. Because of the rarity, the pathophysiology in non-anti-IgA-mediated reactions is less understood and based only on a few case reports.[1]

Here, we report a case of severe anaphylactic reaction in an 18-year-old male, a known case of cerebral malaria. The investigation of the transfusion reaction was carried out retrospectively, which revealed a significant elevation of serum IgE and IgG detected by gel column hemagglutination. This case merits reporting because of its classical presentation of severe anaphylactic reaction in a non -IgA-deficient, IgE- and IgG-mediated platelet transfusion recipient. It also emphasizes the role of prospective and complete investigation of transfusion reaction in mild allergic reactions.

Case Report

An 18-year-old male patient presented with the signs and symptoms of continuous, high-grade fever without chills and rigors since one week. He also had associated vomiting, altered sensorium, and was unconscious with delirium of one-day duration. On examination, the patient was unconscious, pulse: 82/minute, respiratory rate: 14/minute, blood pressure (BP): 110/60 mm of Hg. On auscultation, S1 and S2 were heard, and lungs were clear. There was no organomegaly, but tenderness in the right hypochondrium was present. Plantars were downgoing; he was started on antimalarial therapy. As per altered sensorium and deterioration, mechanical ventilation and intubation were done.

Basic laboratory investigations were done. Hemoglobin was 12.9g/dL, total leukocyte count was normal with normal differential count, and there was severe thrombocytopenia. Erythrocyte sedimentation rate (ESR) was normal. Plasmodium falciparum ring forms: 1/1000 RBC were seen. Complete urine examination showed trace amount of albumin. Biochemical analysis showed elevated serum bilirubin (2.4mg/dL), alkaline phosphatase, and transaminases. Disseminated intravascular coagulation (DIC) profile showed prolonged prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen -64mg/dL, and markedly reduced platelets. Lactate dehydrogenase was raised significantly.

The patient received blood components and platelets, and requested for fresh frozen plasma in view of DIC. Transfusion therapy received by the patient from day one of admission until death was reviewed [Table 1] and the description of the anaphylactic reaction [Table 2] was taken into consideration for investigating the adverse reaction. During the same period, plasma units of the same implicated platelet components were transfused to three different patients with bleeding, without any adverse transfusion reactions.

Investigation of transfusion reaction included clerical check of patient identification; labels of blood components, and grouping and typing, along with requisition forms revealed no misidentification. Visual inspection of the postreaction sample of the patient was negative for hemolysis. Pretransfusion testing done on day one of admission revealed 'O', Rh-positive blood group and negative antibody screening. On day five, the patient was transfused with 'O', Rh-positive platelets and no pretransfusion sample was available. Direct Coomb's test and IgG monospecific antibody were positive in the post-transfusion sample. In view of the positivity of the direct Coomb's test, antibody screening for any irregular or clinically significant red cell antibody was done to rule out immune-mediated hemolytic transfusion reaction. Indirect Coomb's test was negative. Antibody screening by commercial three red cell panel was also negative. Based on this workup, the possibility of immune-mediated hemolytic transfusion reaction was ruled out.

Blood components as well as the sample of the patient were submitted for culture, and the result was negative for both. The activity of anti-IgA, IgG, and IgM was tested by gel column hemagglutination method.[2] Gel column hemagglutination was positive for IgG antibodies and negative for IgA [Figure 1]. Serum imunoglobulins were measured by capture sandwich immunoassay using direct chemiluminescent technology and the results showed raised IgE antibody levels [Table 3].

Table 1: Blood component utilization by the patient

Patient's stay	Indication for transfusion	Blood component utilization
Day 1	Platelet count: 20,000/μL	Platelets (RDP): 3 units
Day 2	Platelet count: 20,000/μL	Platelets (RDP): 3units
Day 4	Platelet count: 20,000/μL, PT, APTT prolonged	RDP: 4
Day 5	DIC	Platelets (RDP)-2 units (FFP – 3 units ordered but not transfused)

RDP: Random donor platelets; FFP: Fresh frozen plasma; DIC: Disseminated intravascular coagulation; PT: Prothrombin time; APTT: Activated partial thromboplastin time

Table 2: Adverse transfusion reaction signs and symptoms, time of onset

Hospital course	Adverse reaction description	Time course of the event
Day 1	Itching and rashes all over the body	Immediately after the transfusion of three units of RDP
Day 5	Rashes all over the body, bronchospasm, increased endotracheal secretions, hypoxia, breathlessness, tachycardia, and hypotension	Immediately after the transfusion of two units of RDP

RDP: Random donor platelets

Signs and symptoms of transfusion reaction such as rashes all over the body, bronchospasm, endotracheal secretions, hypoxemia, tachycardia, and breathlessness developed immediately after the platelet transfusions. As the gel hemagglutination assay was positive for IgG and serum IgE levels were raised, we considered non-IgA-mediated or IgE- and IgG-mediated severe anaphylactic transfusion (alternate pathway) reaction.[3]

Based on some of the pulmonary signs and symptoms like breathlessness, hypoxia, and chest radiograph with lung infiltrates, transfusion-related acute lung injury (TRALI) might have been considered as the important differential diagnosis. However, the underlying critical illness of the patient with ventilator-associated pneumonia may explain the cause for acute lung injury. Subsequent transfusion of the plasma units of the implicated platelet components was uneventful.[4]

Discussion

Anaphylaxis is an acute, potentially life-threatening systemic reaction with various mechanisms, clinical presentations, and severity that result from the sudden systemic release of mediators from mast cells and basophils.[5] Allergy is a hypersensitivity reaction mediated through immunological mechanisms in a predisposed individual.[6]

The first allergic transfusion reaction was described in 1919.[7] Ever since, the possible mechanisms that produce the allergic transfusion reactions are pre-existing IgE or IgG antibody in the recipient which reacts with allergens or proteins in the transfused blood [e.g., drugs or chemicals (ethylene oxide), plastics, albumin, haptoglobin, and complement components], class- or subclass-specific anti-IgA

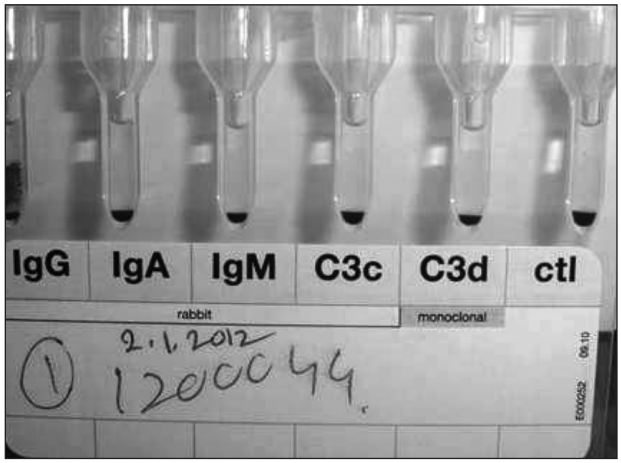

Figure 1: Gel column hemagglutination with IgG weak positive reaction

Table 3: Post-transfusion serum immunoglobulin levels

Immunoglobulin	Serum level	Normal range
IgA	389 mg/dL	44–441 mg/dL
IgG	1930 mg/dL	528–2190 mg/dL
IgE	798 mg/dL	(UPTO 160) mg/dL
IgM	173 mg/dL	48–226 mg/dL

antibody in the recipient reacting against IgA in the transfused blood,[8] passive transfer of IgE antibodies from the donor to the recipient, transfusion of complement-derived anaphylatoxins (C3a and C5a) produced during blood storage and transfusion of cytokines, bradykinins, histamines, or other biological mediators produced during blood storage.[9]

IgE or anti-IgA antibodies are often implicated in severe anaphylactic reactions, although the cause and effect are not always evident. In our case, the severe anaphylactic reaction was preceded by mild allergic reaction to the platelet transfusions. The patient was a diagnosed case of plasmodium falciparum cerebral malaria. Elevation of IgE antibody levels is a known phenomenon in plasmodium infections.[10] The IgE and IgG antibodies maybe protective or play a role in hypersensitivity reactions in malaria. In plasmodium infections, the IgE antibody response may vary depending upon the host genetic and parasite virulent factors.[11]

Platelets constitutively express functional receptors for the Fc fragment of IgE, both the low-affinity receptor (Fc–RII) and the high-affinity receptor (Fc–RI), and could be activated via IgE.[10] Flow cytofluorometric analysis revealed that 20% of the platelets express the Fc–RII receptor and the percentage increases up to 50 in patients with IgE-dependent allergic disorders or parasitic infections accompanied by high levels of circulating IgE.[12] Activated human platelets release platelet-derived inflammatory mediators, such as serotonin and chemokine-like RANTES (RANTES: Regulated on Activation Normal T Cell Expressed and Secreted). It is possible that activated platelets or platelet-derived microparticles are involved in anaphylactic transfusion reactions.[5] The high IgE levels in the serum of the patient may explain the pathophysiology of anaphylactic transfusion reaction occurring in platelet transfusions.

Conclusion

The principal contribution of this interesting case report is in describing uncommon transfusion-related anaphylaxis by well-known mechanisms (IgE-mediated). In addition, it emphasizes the role of thorough investigation of mild allergic transfusion reactions in patients with parasitic infestation. It also explains the fact that anaphylactic transfusion reactions are mainly caused by the antibodies produced in recipients who have been transfused repeatedly.[13] In such cases, pretransfusion testing for serum IgE and IgG levels may help in planning preventive measures like premedication, washed blood products and anti-IgE therapy to achieve safe transfusion.

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