Investigation and Clinical Management of Suspected Reactions to Immunoglobulin A (IgA)

1. Introduction

Immunoglobulin A (IgA) deficiency is relatively common, occurring in approximately 1:700 individuals. Severe anaphylactic transfusion reactions have rarely been described in IgA deficient individuals. They are stated to be more common in individuals with antibodies against IgA, although some authors disagree. Between 2005 and 2010, there has been only one report to SHOT of a transfusion reaction in which a recipient had antibodies against IgA: The patient had a normal level of IgA and the antibody was low-titre. It has been suggested that some of the more severe case reports and series previously published were in fact due to TRALI. There is therefore little current evidence on which to base guidance on the transfusion of patients with IgA deficiency.

Previously, the approach adopted in England, during the period when no reports implicating IgA deficiency in transfusion reactions were reported to SHOT, could be summarised as follows:

When the need for blood was urgent, IgA deficient patients, with or without IgA antibodies could receive standard components. In less urgent circumstances, transfusion dependent patients, and those with IgA antibodies could receive components from IgA deficient donors. IgA deficient individuals who were likely to need transfusion as a “one-off” and who had been shown to be without antibodies could be given standard components.

The current guidance takes into account the fact that the majority of individuals identified as having IgA deficiency have been identified outside the field of transfusion medicine and that the number of reports of anaphylaxis or severe allergy linked to IgA deficiency appears very low. The most important guiding principle is that urgent treatment should not be denied or delayed because IgA deficient components are not immediately available.

2. IgA and anti IgA assays

Patients are likely to have an initial screening test for IgA deficiency for the following reasons:

- As part of the investigation of suspected coeliac disease. This is likely to be the commonest indication at present.
- Investigation of possible immuno-deficiency syndromes
- Investigation of acute allergic or anaphylactic transfusion reactions

Initial screening for IgA deficiency is usually performed using nephelometry, and low levels should be confirmed using a more sensitive technique. NHSBT currently uses a haemagglutination inhibition test for confirmation and for the detection of antibody to IgA. Selective IgA deficiency is defined by the European Society of Immunodeficiencies as “serum IgA level of <0.07 g/L, and normal levels of serum IgG and IgM, when other causes of hypogammaglobulinemia have been excluded”. The importance of anti-IgA antibodies in patients with IgA deficiency is unclear, although past studies do suggest a higher incidence of reactions in patients with high-titre, class-specific anti-IgA antibodies.
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If a patient has an anaphylactic or severe allergic reaction to blood components, immunoglobulins including IgA levels can be measured in most hospital pathology departments. If the levels are normal the reaction is unlikely to be due to IgA. If the levels are low (less than 0.5g/L), and levels of IgG and M are normal, the case should be discussed with the Red Cell Immunohaematology (RCI) laboratory which performs reference testing for your hospital and samples sent to them for testing. The local RCI lab will forward the samples to RCI Colindale or Sheffield who will quantify the amount of IgA present and screen for anti-IgA.

Check with your local pathology department for the samples required for immunoglobulin levels including IgA (usually a clotted sample)

Samples required for RCI investigation of IgA levels and anti-IgA are 2 x 6ml EDTA

3. Choice of blood components for IgA deficient patients with a previous history of severe allergic/anaphylactic reactions (Patients in this category would be expected to be rare)

- In non-urgent cases, IgA deficient components should be used if available.
- In urgent cases, where IgA deficient red cells are not available and there is insufficient time to prepare washed red cells, red cells in SAG-M optimal additive solution (standard red cells) should be used.
- If platelet components are required in an emergency, standard platelets should be used.
- Platelets in PAS can be provided if the risk of delay in provision does not outweigh the need for urgent platelet transfusion (manufacturing will take approximately 2 hours followed by transport to the hospital). PAS suspended platelets may still be a dangerous product for a patient with a history of anaphylaxis as they still contain appreciable amounts of IgA.
- IgA deficient platelets are collected by arrangement and require notice (see below). This is therefore not an option when platelets are required urgently

4. Components for patients with confirmed IgA deficiency, with or without IgA antibodies, who have previously never been transfused, or who have received standard blood components with no reaction

There is no current evidence on which to base guidance. As the incidence of adverse reactions in this group of patients is likely to be extremely low, patients without any history of allergy or anaphylaxis may be transfused with standard components. However, patients with a history of severe allergy (even if unrelated to transfusion) may be at increased risk of anaphylactic transfusion reactions and consideration can be given to the use of IgA deficient components, or washed red cells and platelets in PAS. Patients with IgA deficiency who are likely to receive multiple transfusions may also be considered for washed red cells or platelets in PAS, although there is no evidence base for this decision

All patients in these categories, whether receiving IgA deficient components or not, must be transfused in a setting where there is immediate access to skilled clinical help, and where staff have been trained in anaphylaxis management and have access to IM adrenaline. In addition, staff monitoring the patient must be aware of the symptoms & signs of anaphylaxis that might occur in IgA deficient patients.
5. Follow up of patients with IgA deficiency

IgA deficiency forms part of the spectrum of common variable immunodeficiency, and a significant percentage of patients will go on to develop infections, allergies and autoimmune disease. It is therefore advisable for individuals with confirmed IgA deficiency to be discussed with a clinical immunologist at some stage. It is also possible that a desensitisation procedure may be an option for the small number of patients who have had transfusion reactions and may require further transfusion. A consultant immunologist would be able to advise on this.

6. Stocks of IgA deficient components

- IgA deficient red cell units are kept at NHSBT Sheffield (tel Sheffield Hospital Services: 0114 358 (4) 4817).
- IgA deficient plasma, is available from Sheffield, contact details as above, or Colindale Hospital Services: 0208 957 (6) 2800.
- IgA deficient platelets are collected from a small panel of donors in London. These are not available for urgent cases. To arrange these, contact the medical PAs on 0208 258 (6) 2928 during working hours, to be transferred to a member of the donor clinical support team.
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References


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