Commentary

IgA deficiency: Implications for transfusion

Anaphylactic transfusion reactions are acute, potentially life-threatening events with generalized signs and symptoms. Usually IgE mediated they may also result from antigen-antibody reaction involving non-IgE antibodies which fix complement and generate anaphylatoxins. The best documented reactions of the latter type result from presence of anti IgA antibodies in IgA deficient patients who receive transfusion of blood/components containing donor plasma. Anti IgA usually belongs to the immunoglobulin class IgG, less commonly IgM and rarely IgE. Anti IgA of the IgE type has been detected in patients with hypogammaglobulinaemia and not selective IgA deficiency who had developed anaphylactic reaction to blood products. IgA is the predominant immunoglobulin in various human external secretions, but it also constitutes 10 to 15 per cent of the total concentration of serum immunoglobulins. It exists in two subclasses, IgA1 and IgA2. The IgA2 subclass has two allotypes designated as IgA2m (1) and IgA2m (2). Secretary IgA prevents entry of pathogens across mucosal surfaces. From immunological point of view, individuals with serum IgA levels <5 mg/dl are considered IgA deficient and are potentially at risk for recurrent respiratory and gastrointestinal infections. However, the spectrum of clinical symptoms of IgA deficiency is wide; majority of those affected are asymptomatic, while others suffer form recurrent respiratory and gastrointestinal infections and have increased propensity to develop malabsorption, allergic and autoimmune disorders.

For purposes of transfusion medicine individuals with serum IgA levels <0.05 mg/dl may be considered IgA deficient on two accounts. Firstly, as recipients they are at risk of developing class-specific anti IgA when exposed to IgA and hence anaphylactic transfusion reactions. Secondly, only individuals with IgA <0.05 mg/dl are suitable as “IgA-deficient” blood donors. Blood components containing <0.05 mg/dl IgA are not associated with anaphylactic reactions. An occasional patient with IgA deficiency may also develop serious reaction after intramuscular administration of IgG. Most of the immunoglobulin preparations contain 95 per cent or more IgG, but some amount of IgA is usually present. Some individuals with normal IgA levels also develop IgA antibodies. These have been subclass specific (anti IgA1 or anti IgA2) or allotype specific [anti IgA2 m (1) or anti IgA2 m (2)], i.e., antibodies with limited specificity. Patients with ‘limited specificity’ anti IgA tend to develop less severe anaphylactoid reactions.

The prevalence of IgA deficiency depends on the sensitivity of the assay used as well as the population under study. In healthy Finnish blood donors, tests using a gel diffusion method that could not detect less than 10 mg/dl IgA levels, one out of 396 donors appeared IgA deficient. Repeat testing with radioimmunoassay with detection sensitivity of 0.001mg/dl showed only one out of 800 donors being IgA deficient. In another study by Vyas et al., the incidence of IgA deficiency was 1 in 650 using gel diffusion and 1 in 886 using haemagglutination inhibition technique with a sensitivity of 0.05 mg/dl.
IgA levels in 3818 blood donors were estimated by an in-house ELISA with a sensitivity of 0.05 mg/dl. Thus, the test system has the requisite sensitivity to detect IgA deficient donors for transfusion purposes. If healthy blood donors are taken to represent a population sample then IgA deficiency may not be a significant clinical problem in our country. However, subclass specific or allotypic antibodies may occur with normal IgA levels. This aspect needs to be studied further. Passive haemagglutination and ELISA based techniques are available but given the range of IgA antibodies- class specific/subclass specific/allotype specific and their titration, the optimum test system for anti IgA detection, in terms of its sensitivity, feasibility and cost-effectiveness and clinical significance needs to determined.

Passive haemagglutination detected class-specific anti IgA in 61 out of 80 (76.3%) IgA deficient patients who had a history of anaphylactic transfusion reaction. However, the same test system also identified class specific anti IgA in 27 out of 87 (31.0%) random untransfused IgA deficient volunteer blood donors. Anti IgA titres of individuals in donor and patient groups overlapped; thus further discriminatory criteria/test are required to categorize high risk individuals.

ELISA based test system can no doubt be readily adapted in blood banks as suggested by Chandran et al especially for screening of donors for IgA deficiency. However, detection, characterization and titration of anti IgA are more time consuming and laborious and reference laboratories may be required. Research is now needed in patients with anaphylactic reaction to blood components or immunoglobulin preparations to determine the role of IgA deficiency and presence of anti IgA in the causation of these reactions. Establishment of rare donor registry of IgA deficient blood donors would then be the next appropriate step.

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References