Scottish National Blood Transfusion Service
Policy Record

Ref: NATP CLIN 034 02
Cat: Clinical

Title: The transfusion management of patients found to be IgA deficient

Background:

This policy describes the management of transfusion support for patients with IgA-deficiency with or without preceding allergic transfusion reactions.

It does not provide advice on the general management of IgA-deficiency.

Key Change From Previous Revision:

Scotland no longer carry out anti-IgA testing

Policy Agreement	CGSC: 1st May 2018	BBWG 30.4.2018; PSOG 2..5.2018
Supersedes Policy Ref:	NATP CLIN 034 01	
Date Of Implementation:	27th August 2018	

Management of transfusion support for patients with IgA-deficiency

Background

Definition of IgA-deficiency: "*Definitive*" IgA-deficiency (IgAD) as defined by the European Society of Immunodeficiencies is a *selective* deficiency of IgA (i.e. normal levels of IgG and IgM) at a level below 0.07g/l in patients over 4 years of age, in whom other causes of hypogammaglobulinaemia have been excluded. In *probable* IgAD the serum-level of IgA is at least 2 SD below normal for age (1).

Selective IgAD is mainly *primary*, i.e. genetically determined, but can also be secondary or acquired, e.g. due to other diseases or drug effects (2).

Patients with IgAD can also be classified by the *degree* of their IgAD into patients with *relative* IgAD (IgA level below the laboratory's reference range, which is usually around < 0.05g/l) and *absolute* IgAD (<0.0005g/l).The degree of IgAD correlates with an individual's risk of formation of class-specific allo-anti-IgA-antibodies and transfusion reactions, and transfusion reactions are mainly confined to patients with absolute IgAD (4). In England, patients with IgAD and transfusion reactions have been found to have IgA-levels <0.0016g/l (HT, verbal communication).

Frequency of IgA-deficiency: Primary IgAD is the most common immunodeficiency in humans. In Caucasians, primary IgA-deficiency occurs at a frequency of about 1:500 (2).
Many individuals with IgAD are asymptomatic; however, long-term follow-up studies of IgA-deficient individuals have shown an increased incidence of infections, allergies, autoimmune disease, coeliac disease, and development of common variable immunodeficiency.

Diagnosis of IgA-deficiency: Different methods with different sensitivity-levels are in use for the measurement of IgA. Immunology and biochemistry laboratories in Scotland employ different methods of testing and ways of reporting. Many cases are inadvertently discovered in the course of investigations for Coeliac Disease.
Currently most laboratories in Scotland use a cut-off of <0.05g/l IgA for the diagnosis of IgAD, and individuals with absolute or very severe IgAD cannot be identified within this group.

Frequency of detection of antibodies against IgA: Antibodies can be class-specific (anti-alpha) or of limited specificity (subclass-specific anti-IgA1 or –IgA2). In about 20-40% of patients with IgAD, antibodies against IgA can be found. However, anti-IgA antibodies can also be detected in normal human sera (ranging from 2-59% depending on method and cut-off level used; usually antibodies of limited specificity in this situation) (3, 4). The predictive value for increased likelihood of transfusion reactions in those with detectable anti-IgA antibodies are poorly evidenced.

Transfusion reactions in IgA-deficient individuals: Reactions to IgA are typically allergic/anaphylactic in nature. The incidence of severe transfusion reactions in this context is extremely rare and appears to be confined to individuals with very low levels of IgA (4, and HT, verbal communication). The incidence of IgA anaphylactic transfusion reactions is estimated at 1:20000 – 1:47000 transfusions (5).

Only 1 case of IgAD in the context of an acute transfusion reaction (ATR) was reported to SHOT in the period of 2004-2009. In the 2010 SHOT report two cases of low IgA-levels were reported in the investigation of 62 ATRs: One with an allergic reaction and one with a febrile reaction (6).

Patients with a past history of severe reactions are at greatest risk of further reactions.

Investigation of transfusion reactions in the context of suspected IgAD

If IgAD is suspected as a possible cause of an acute transfusion reaction, the IgA-level should be determined by an appropriate local hospital-laboratory. If IgA deficiency is confirmed, consideration should be made to testing for anti-IgA antibodies, though *the predictive value of the anti-IgA antibody level assessing the likelihood of reaction is poor. This test is not offered by SNBTS but can be performed by arrangement with NHSBT.*

Blood Components for IgA-deficient patients

Most IgA-deficient patients with or without anti-IgA-antibodies will not experience severe reactions with standard components.
Any requests for special components should always be discussed with SNBTS-Medical Staff. Specifically, information on the patient's transfusion history and general history of allergic reactions, reasons for measuring IgA-level, urgency of transfusion and likely future transfusion needs should be assessed.

General information on special components

All requests for special components such as plasma-reduced components or components from IgA-deficient donors must be discussed with and authorised by SNBTS-medical staff.

Plasma-reduced components are recommended not only in many patients with known IgAD, but also for some other indications, esp. patients suffering with recurrent severe allergic/anaphylactic transfusion reactions due to other reasons (see SNBTS-policy on the use of plasma-reduced red cells and platelets, 8).

SNBTS: SNBTS can provide platelets in platelet additive solution (PAS). Production of this component takes 3-4 hours, and the component has a shelf-life of 24 hours. The protein content is usually less than 0.5 g per unit.

Washed Red cells (automated, closed system method) can usually be provided within 3 hours and have a shelf-life of 14 days. They will require crossmatching at the local hospital blood-bank.

Of note, transport times from JCC to local hospitals must be added to the times mentioned above for the production of plasma-reduced components, to give a practical supply time.

SNBTS hold a very small stock of group A and group O IgA-deficient FFP which is derived from UK-donors, not Methylene Blue treated and imported from NHSBT.

IgA-deficient cryoprecipitate is not available.

NHSBT: NHSBT keep a small stock of IgA-deficient red cells, and are able to contact a small number of IgA-deficient platelet and plasma donors. Any request to / contact with NHSBT must be mediated by SNBTS.

NB: For choice of immunoglobulin-products and other plasma derivatives it is advised to discuss patients with an immunologist and check information on IgA-content provided by the manufacturer.

Specific transfusion advice

Patients with a past history of severe transfusion reactions are at greatest risk of further reactions.

The consequences of a delay of transfusion incurred by seeking special components should always be balanced against the risk of a reaction. In an emergency, *standard* red cells in SAG-M and *standard* platelets should be used.

The clinical team looking after a patient with IgAD should confirm the diagnosis and discuss the indication for the transfusion and its urgency with their local Haematologist.
Patients with confirmed IgAD and previous transfusion reaction should be flagged up on the hospital laboratory computer system and notified to other blood banks in Scotland where systems are in place to do so.

Any requests for special components will then require a discussion between the clinical team, local Haematologist and BTS medical staff. BTS-medical staff must authorize any special components and point out practical issues such as their preparation time and shelf-life. BTS-medical staff must also inform relevant BTS-processing staff of the outcome of discussions.

Transfusions for IgA-deficient patients should be closely monitored in an area where severe allergic and anaphylactic reactions can be managed appropriately.
Depending on the circumstances, premedication with or early use of hydrocortisone and chlorpheniramine may be considered.

RBC TRANSFUSION

1. Transfuse with red cells from an IgA deficient donor if time permits.

2. If not, then transfuse with washed red cells.

3. In emergencies use standard SAGM RBC (10).

FFP/PLATELET TRANSFUSION

Where time permits use FFP / Platelets from IgA deficient donors or use washed platelets if in the emergency situation.

The management of **patients with IgAD but *no* history of acute transfusion reactions** is far less clear (9, 10). They rarely suffer serious transfusion reactions.

However, especially if they have suffered other allergic reactions or if they are likely to require repeated transfusions in the future, provision of plasma-reduced components should be considered as far as the urgency of the transfusion allows.

Decisions in these situations should be made on a case by case basis.

Future introduction of a highly sensitive assay for the identification of individuals with *severe* IgAD would help to focus support with special components to those patients at highest risk of transfusion reactions.

Literature

1. European Society for Immunodeficiencies: Definition of IgA deficiency, 2005.

2. Latiff AHA, Kerr MA. The clinical significance of immunoglobulin A deficiency. Ann Clin Biochem 2007; 44: 131-139

3. Lillic C, Sewell WAC. IgA-deficiency: what we should –or should not-be doing. J Clin Pathol 2001; 54: 337-338

4. Sandler SG. How I manage patients suspected of having had an IgA anaphylactic transfusion reaction. Transfusion 2006; 46: 10-13

5. Pineda AA, Taswell HF. Transfusion reactions associated with anti IgA-antibodies: Report of four cases and review of the literature. Transfusion 1975; 15: 10-15

6. SHOT Annual Reports 2009/2010. Website: www.shotuk.org/shot-reports

7. Munks R, Booth JR, Sokal RJ. A Comprehensive IgA Service provided by a Blood Transfusion Centre. Immunohaematology 1998; 14: 155-160

8. Latif A, Paulus U. The use of plasma-reduced red cells and platelets. SNBTS Clinical Policy Guidelines 2012

9. Tinegate H. Investigation and Clinical Management of suspected Reactions to immunoglobulin A (IgA). NHSBT Information 2012; INF 486/1

10. BSH guideline on the investigation and management of acute transfusion reactions, 2012. Website: www.bcshguidelines.com

NATF 003 05

(Relates to SOP NATS QAD 081 and NATS TRN 003)

TRAINING REQUIREMENTS SHEET

Document Number: NATP CLIN 034 02

Document Title: THE TRANSFUSION MANAGEMENT OF PATIENTS FOUND TO BE IgA DEFICIENT

Departmental Manager must consider staff training and re-training requirements associated with the introduction of this document; and initial as appropriate the statements below for its application within their department:

A	**New Procedure – Training and competency assessment required for all staff who will need to carry out this procedure.**
B	**Significant Changes – Training and competency assessment required for all staff who need to carry out this procedure.**
C	**Minor Changes Only – Existing trained and competent staff to read and sign. No additional formal training required.**
D	**Information – Read and acknowledge understanding of this document.**
E	**Document not applicable to staff member.**

Staff Group	Training Requirements	Agreed By

Staff Names	A	B	C	D	E	Staff Signature	Date

Please use additional pages as required.