IgG2 class red cell antibodies and autoimmune haemolysis

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Abstract—Aim. To examine the role of IgG2 red cell autoantibodies in autoimmune haemolysis. Methods. Study of immunohaematology case records. Results. Six patients had only IgG2 autoantibodies detected by direct antiglobulin testing and in red cell eluates; two individuals, whose red cells were also coated with complement, suffered from autoimmune haemolytic anaemia. Conclusions. IgG2 antibodies are found alone in <1% of patients with warm autoantibodies and even more rarely cause red cell destruction. Several factors are important for inducing haemolysis. They include allele differences in the FCRIIA genes encoding for the FcγRII receptors — an allele with high affinity for IgG2 is needed for haemolysis. Topography of red cell antigens may also be significant; IgG2 is a relatively inflexible molecule and access of effector cell Fc receptors to the recognition sites on the IgG2 might be impossible unless the antigens are on, or proud to, the red cell surface. On rare occasions, IgG2 activates complement (as in our patients with active haemolysis); the synergistic effect between red cell bound immunoglobulins and C3 in causing haemolysis is well recognised.

Keywords: Anaemia; haemolytic; autoimmune; autoantibodies; Fc receptors; IgG subclass; IgG2; immunoglobulins.

INTRODUCTION

The role of IgG2 antibodies in autoimmune haemolysis is unclear. They occur in association with other IgG subclasses in approximately 20% of patients with warm reacting autoantibodies [1, 2], but are found alone in <1% of cases [1, 3]; IgG2 mediated autoimmune haemolytic anaemia is even rarer [2, 4]. This paper describes the findings in a series of patients with red cell autoantibodies solely of IgG2 class.

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MATERIALS AND METHODS

The records of all patients referred to the Trent Centre Immunohaematology Department between 1st January 1986 and 31st January 2000 were reviewed. Cases with increased amounts of red cell bound IgG2 were selected for further study.

The investigations performed at this Centre have previously been reported in detail [1, 5–8]. They included direct antiglobulin testing for red cell bound IgG, IgM, IgA, C3c and C3d and for IgGl, IgG2, IgG3 and IgG4. In the case of IgG, the reagents would detect a minimum of 150 mol/rbc [8]. The immunoglobulin class and IgG subclass of autoantibodies in red cell eluates were determined by indirect antiglobulin techniques. Two methods of elution were used: chloroform/trichloroethylene or acid elution; full technical details have been published previously [8]. Both methods result in antibody concentration making them more sensitive than direct antiglobulin testing for IgG subclass determination; in the present study, this was important in excluding small increases in red cell bound IgGl, 3 and 4. The eluted autoantibodies were tested for specificity against the following antigens: Rh (C, D, E, c, e), Kk, MNSs, P1 Lea, Leb, Fya, Fyb, Jka and Jkb. Serum haptoglobins were measured by their haemoglobin binding capacity [9], our normal range being 0.4–2.0 g/l.

RESULTS AND DISCUSSION

Six patients were found where only IgG2 autoantibodies were detected by direct antiglobulin testing and in red cell eluates; their details are shown in Table 1. Chloroform/trichloroethylene eluates were prepared in patients 1–3, 5 and 6, and acid eluates in patient 4. The eluted IgG ranged in titre (where tested) from 1:4 to 1:64. It was important to examine eluates, both to confirm that the IgG2 was autoantibody by its ability to rebind to normal red cells after elution and also to show that the red cells were not additionally sensitized with small amounts of other IgG subclasses. Concentration of eluted antibody during production meant that testing eluates was a more sensitive way of determining the IgG subclass pattern than direct antiglobulin tests. During the course of the present work we saw several other patients (not included) where direct antiglobulin testing suggested IgG2 alone was on the red cells, but where additional IgG subclasses were detected in the eluates. In an earlier study, further subclasses were found in 82 out of 314 cases where eluates were tested [1]. Patient 1 had presented with autoimmune haemolytic anaemia approximately three and a half years previously when IgGl, IgG2 and IgM autoantibodies were identified in a red cell eluate. He apparently made a good recovery and only IgG2 was found on this occasion (Table 1). Similarly, non-Hodgkin’s lymphoma, a feature of the present episode, was not evident on the first occasion. Elution studies were particularly useful in patient 6 (Table 1): the absence of elutable IgA, taken with the raised serum IgA level, indicated that the IgA component of the positive direct antiglobulin test was due to non-specific adsorption and that IgG2 was the only red cell autoantibody present.