Acute haemolytic anaemia associated with polyagglutinability of red cells

T. BIRD AND J. STEPHENSON

From the Department of Haematology, Newcastle General Hospital

SYNOPSIS  A 7-week-old albino infant developed acute haemolytic anaemia following an operation for strangulated inguinal hernia. This was considered to be due to polyagglutinability of the red cells, the haemolysis subsiding as the cells returned to normal. The red cell changes were shown to be due to activation of T-antigen, reacting with anti-T in the adult blood transfused to the infant.

All human red cells contain hidden antigens in the surface membrane, and one of these, T antigen, can be activated by the action of bacteria or enzymes derived from them. When this occurs the cells are agglutinated by an agglutinin, anti-T, present in most sera, but very rare in newborn and very young infants. The original observations were made in cell suspensions infected in vitro by a wide variety of organisms (including V. cholerae, Pneumococcus, Streptococcus, and Corynebacteria), and was called the Hübener-Thomsen-Freidenreich phenomenon. Anti-T acts most strongly at low temperatures but can be distinguished from the common cold agglutinins and other antibodies by the fact that it can be absorbed from serum only by 'activated' cells.

Polyagglutinability in vivo is rare, usually associated with severe bacterial infections, but occasionally seen in normal people. It is usually a transient finding, lasting from days to weeks, and of importance only because of possible difficulties in grouping blood, but very occasionally it has been associated with acute haemolysis.

Case Report

A male albino infant, aged 7 weeks, was admitted with a history of intestinal obstruction for 36 hours. He had a strangulated inguinal hernia which was relieved and the hernia repaired. The haemoglobin on admission was 13 g/100 ml. During the operation he received 100 ml of whole blood, and next day the haemoglobin was 11 g/100 ml. Progress was satisfactory until the fourth day when he became slightly jaundiced. Haemoglobin was 10·4 g/100 ml, white cell count 10 000/cmm with neutrophilia, and tests showed no evidence of transfusion reaction. On the fifth day, haemoglobin was 9·1 g/100 ml, with 3% reticulocytes, and a second blood specimen showed polyagglutinability. On the ninth day he was very poorly, haemoglobin had fallen to 4·1 g/100 ml, haematocrit was 11%, white cell count was 9000/ cmm, and reticulocytes were 15%. The blood film showed anisocytosis, with many normal (transfused) cells, 8% normoblasts, occasional myelocytes, and abundant platelets. No fragmented cells were seen. The serum bilirubin was 10 mg/100 ml, with bilirubin and urobilin in the urine. Serum proteins were only 5 g/100 ml, with a decrease in gamma globulin, and other liver function tests were normal. The abdominal wound was infected, and E. coli and B. proteus were cultured. Eighty ml of blood was given, the haemoglobin rising to 9·8 g/100 ml, and a course of Tetracyclin was started. He began to improve, with a decrease in reticulocytes to 2% and a slow fall in haemoglobin to 8·1 g/100 ml, on the twentieth day. He was discharged on the twenty-fifth day. He was seen during the next year and appeared well. He was admitted again at 2½ years of age with febrile convulsions later thought to be due to epilepsy, with some EEG changes in the left parietal lobe. No blood abnormality was found in repeated examinations.

Serology

He was grouped as A Rh positive, with no difficulty at 20° and 37°C, and fully compatible blood of the same group was given. When jaundice was reported on the fourth day, the suspect bottle was checked against the original serum and all tests were normal.

On the fifth day a second specimen showed agglutination of the infant's red cells with several anti-B grouping sera at 4°C and 20°C, but not at 37°C, and the direct Coombs test was negative.
Acute haemolytic anaemia associated with polyagglutinability of red cells

On the ninth day, when the haemoglobin was 4.1 g/100 ml, a third specimen showed agglutination with anti-B sera at 4°C, 20°C, and 37°C. The infant’s serum contained no agglutinins. It was possible to crossmatch another bottle of A Rh-positive blood with a little difficulty while carrying out further tests to determine the abnormality.

The infant’s red cells were agglutinated strongly by 10 different anti-B grouping sera and four AB sera at all temperatures. They were also agglutinated by 10 random adult AB and anti-B sera but not by three cord blood sera. The direct Coombs test was positive with several different antihuman globulin sera. Polyagglutination, rather than acquisition of a B antigen (Marsh, 1960), now seemed probable.

Anti-B sera were absorbed with a number of B and AB cells. Following this, they were negative against B and AB cells but still agglutinated, with mixed fields, the infant’s cells. Similar results were seen with anti-A sera absorbed with A cells, and agglutination was negative only when the sera were absorbed with the infant’s own cells. Absorption with AB-specific substance produced the same results. Activation of T-antigen now seemed most likely. This was confirmed when normal adult sera, known to contain anti-T, were absorbed with adult red cells ‘activated’ by V. cholerae, and did then not agglutinate the infant’s cells.

The mother was A2Rh positive (CDe CDe), the father was A1Rh positive (CDe CDe) and the infant was A1Rh positive (CDe CDe). The first donor was A1 and the second A2. Maternal serum showed no agglutination, at 20°C and 37°C, against the red cells of the father, the two donors, and known A1 and A2 cells, though cold agglutinins were found at 4°C. It was positive against the polyagglutinable cells of the infant at all temperatures, but not against his cells at a later date. No irregular agglutinins or haemolysins were found in the two donors. The infant’s cells were thought to be Coombs positive, but this was shown to be due to anti-T in the antihuman globulin sera. The Donath-Landsteiner and acid-haemolysin tests were negative.

All tests were repeated on the twenty-fourth day and were normal. No evidence of blood disorder was found in the parents.

Discussion

Polyagglutinability was described, as an almost incidental occurrence, in a 7-week-old infant with autoimmune haemolytic anaemia by Gasser and Hollander (1951). The positive Coombs test could have been due to anti-T, which may be present in both broad-spectrum and specific antiglobulin, as in our case. The first well documented case with haemolysis is that of van Loghem, van der Hart, and Land (1955). They described an infant of 4 weeks, with an infected thoracic angioma, who developed polyagglutination and acute haemolysis two days after receiving a transfusion from the father and died in renal failure a few days later. The case reported by Dausset, Moulec, and Bernard (1959) in a male of 65 years with chronic haemolytic anaemia lasting nine years was due to activation of Tn antigen, a less common cryptantigen which can be separated from T antigen by absorption tests. Six cases were described briefly by van Loghem (1965), including four due to T, and two due to Tn, activation. None appeared to be in infants and severe bacterial infection was associated in three patients. The most recent case is that of Rickard, Robinson, and Worlledge (1969) in a 14-month-old mongol boy with a respiratory infection.

T antigen can be exposed by neuraminidase, synthesized by many bacteria, which removes neuraminyl groups from the red cell surface. Anti-T, an IgM antibody, which is widespread in normal mammalian sera, is specific for the antigen, and an identical agglutinin can be isolated from peanuts (Arachis hypogaea). Polyagglutinability due to T antigen can thus be specifically demonstrated by the action of this extract on the red cells, or by the ability of T-activated cells to remove the corresponding antibody without affecting others closely related such as Tn. Details of surface antigens and polyagglutinability have been well reviewed recently by Pardoe and Uhlenbruck (1972).

The polyagglutination and haemolysis in our case appear to be clearly related, with the haemolysis at its height when the polyagglutinability was most marked at 37°C and subsiding as the latter disappeared. As in van Loghem’s first case, anti-T was almost certainly introduced into the infant’s blood by the transfusion and then adsorbed onto the red cells.

It is tempting to suggest that the red cell changes were due to the organisms in the infected abdominal wound but unfortunately tests were not done to prove this. Reepmaker (1952) demonstrated such an association when organisms isolated from the urinary tract were shown to produce polyagglutination in the red cells of the affected patient and others.

There seems to be no reason to suggest a relationship with albinism as this has not been described in any other case.

We wish to thank Miss S. Humphries for secretarial assistance.

References

anemia with polyagglutinability of red blood cells due to a new factor present in normal human serum Anti-Tn. Blood, 14, 1079-1093.


Acute haemolytic anaemia associated with polyagglutinability of red cells
T. Bird and J. Stephenson

doi: 10.1136/jcp.26.11.868

Updated information and services can be found at:
http://jcp.bmj.com/content/26/11/868

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/