Acute Acquired Haemolytic Anaemia Associated with Polyagglutination

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Polyagglutination is an abnormality of red cells so that they are agglutinated by most normal sera, except that from very young infants. Polyagglutination occurs in red cells which have been infected in vitro. Rarely it occurs in vivo, when it has usually been associated with severe bacterial infection. There are very few reported cases where polyagglutinationability has led to increased red cell destruction. This report concerns such a case, in which a 14-month-old child developed a severe acute haemolytic anaemia associated with polyagglutination. It is reported because of the rarity of this variety of haemolytic anaemia and because of the intrinsic interest of its mechanism.

Case Report

The patient, a 14-month-old mongol boy, was admitted in March 1968. He had had no previous illnesses. A chromosome count performed at the age of 6 months showed trisomy 21. His accomplishments at 14 months were approximately those of a normal 9-month-old child.

Five days before admission he had developed an upper respiratory tract infection associated over the next few days with fever, increasing cough, and breathlessness, and finally cyanosis. On admission he was very ill with severe respiratory distress. His temperature was 40.8° C., pulse rate 140/minute, respiratory rate 60/minute, and blood pressure 100/50 mm. Hg. He was restless, cyanosed when breathing air, and had intercostal recession. There were rhonchi over the whole chest but no localized signs. Chest x-ray showed widespread bilateral consolidation, most marked in the right upper lobe. Hb 9.9 g./100 ml., WBC 6000 per cu.mm., with 5340 neutrophils per cu.mm., many of which showed toxic granulation. The other haematological findings on admission and the patient’s subsequent progress are shown in the figure. The culture of a cough swab which was the only culture material obtained before treatment grew no pathogens.

He was nursed in 60% oxygen which abolished the cyanosis, and treated with intramuscular penicillin and ampicillin. The breathlessness was greatly improved within 24 hours, but 3 days after admission he was noticed to be pale and slightly jaundiced and to have developed enlargement of the liver, its edge being palpable 4 cm. below the costal margin. The pallor increased, and 5 days after admission the Hb level had fallen to 5.6 g./100 ml., with 13% reticulocytes and 20 nucleated red cells per 100 white cells. Examination of the blood film showed marked polychromasia, some red cell fragments and spherocytes, and the total white cell count had risen to 33,000 per cu.mm. with 79% neutrophils. Serum bilirubin was 2.5 mg./100 ml. (indirect reacting 2.0 mg./100 ml.). Schumm’s test for methaemalbumin was positive.

A film of bone-marrow from the iliac crest 7 days after admission showed erythroid hyperplasia with megaloblastic features. Leucopoesis was active with occasional giant metamyelocytes. Megakaryocytes were plentiful and platelet numbers were normal. The myeloid: erythroid ratio was 1·5:1.

The results of the peripheral blood and bone-marrow aspiration were consistent with an acute haemolytic process. 7 days after admission (28.3.68) Hb had fallen further to 3.7 g./100 ml. and he was transfused with 120 ml. of packed cells which raised his Hb to 7.2 g./100 ml. Five days later a further transfusion of 190 ml. of washed packed red cells raised his Hb to 9.2 g./100 ml. From that time there was no further fall in Hb level nor evidence of haemolysis.

After the initial improvement his respiratory symptoms were very slow to resolve completely. He still had a respiratory rate of around 40 per minute and some intercostal recession until 3 weeks after admission. A chest x-ray showed that the consolidation was resolving slowly, some change still being apparent in the right upper lobe 5 weeks after admission. Cloxacillin was added to the original antibiotics 7 days after admission and antibiotic treatment was continued for a total of 3½ weeks. The Mantoux test was repeatedly negative.

Clinical summary. A previously healthy 14-month-old mongol child developed a severe bilateral bronchopneumonia. Pathogenic organisms were not isolated. About 1 week after the onset of respiratory symptoms he developed a severe haemolytic anaemia

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with fall in Hb from 9·9 g./100 ml. to 3·7 g./100 ml., and required 2 blood transfusions. Haemolysis apparently ceased about 1 week after it started and the pneumonia very slowly resolved. He is now well.

Haematological Investigations

These were performed according to the methods of Dacie and Lewis (1963). The Figure shows the changes in the child's haemoglobin, reticulocyte count, total white cell count, and neutrophil and lymphocyte counts.

Further serological and biochemical studies were made to investigate the cause of the haemolysis.

Serological studies. The occurrence of polyagglutination was first noticed during the acute haemolytic episode when grouping and compatibility tests were being done for the first transfusion 7 days after admission. At room temperature a 5% suspension of the patient's red cells in saline was agglutinated by anti-A, anti-B, and anti-A + B serum as well as by the serum from a group AB subject, but it was not agglutinated by three cord sera. The agglutination was most marked with fresh sera but all the adult sera used gave some reaction. The cells were also agglutinated to a variable degree by some rabbit antisera, including broad spectrum antihuman globulin serum and antisera to human IgG, IgA, IgM, and the third and fourth components of complement. The degree of agglutination, however, was independent of their content of antibody; in fact the strongest reaction was obtained with an absorbed normal rabbit serum containing no antibodies against human proteins. Finally, the patient's red cells were strongly agglutinated by a saline extract of peanuts (Arachis hypogea) known to contain a specific anti-T-like lectin (Bird, 1964).

Subsequent changes in the agglutinability of the patient's red cells by peanut anti-T are shown in the Figure. Four weeks after the polyagglutination was demonstrated his red cells were no longer agglutinated by the extract. Haemolysis had ceased, Hb level was slowly rising, and the reticulocyte count was normal (Figure).

The polyagglutination made ABO and Rh typing of the patient's cells impossible at room temperature. However, at 37° C. the polyagglutination was much less marked and the cells were shown to be group O Rh (D) positive. Serum grouping confirmed that the child was group O.

No free antibodies were detected in the patient's serum using enzyme treated red cells and the indirect antiglobulin test. The cold agglutinin titre at the time of maximal haemolysis was normal.

Biochemical studies. During the acute haemolytic episode Schumm's test for methaemalbumin was positive, indicating intravascular haemolysis.

After recovery from the haemolytic episode, further investigations were done to exclude an intrinsic abnormality of the red cells which might have produced haemolysis. The results of these tests were all negative. The osmotic fragility of the red cells was normal both before and after incubation. Autohaemolysis was also normal at 48 hours; 1·1% lysis without added glucose diminished to 0·4% in the presence of 0·5% glucose. A screening test (Jacob and Jandl, 1966) for detection of enzyme deficiencies in the pentose phosphate shunt gave a normal result. No Heinz bodies were seen, there was no haemosiderinuria, and Ham's acidified serum lysis test (Ham, 1939) on the patient's cells was negative and a 'cold-antibody haemolysis' test gave a

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**Figure:** Serial haematological and serological data on the patient. Anti-T was a saline extract of peanuts, and '4' refers to strongly positive agglutination, while '1' is weakly positive agglutination of the patient's red cells by this extract.
A 14-month-old mongol child developed acute haemolytic anaemia during the course of severe bronchopneumonia. The haemolysis was associated with polyagglutinability of the patient's red cells. Since no other cause for the haemolytic anaemia was shown, it was considered to be due to the polyagglutination. As the child recovered from the chest infection the polyagglutinability disappeared and the haemolysis subsided. He is now clinically well and haematologically normal.

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REFERENCES


