CASE REPORT

Autoimmune haemolytic anaemia in a newborn infant

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The case is reported of an infant with autoimmune haemo-
lytic anaemia of perinatal onset. Combined treatment with
steroids and cyclosporin was necessary to improve
haemolysis and reduce the high transfusion requirements.
Treatment was discontinued at 13 months of age. The child
was healthy at the follow up at 24 and 36 months of age.

Autoimmune haemolytic anaemia (AIHA) is a rare
disease; the annual incidence is about one case in
80 000 live births. It is more common than acquired
aplastic anaemia and less common than immune thrombocy-
topenic purpura. Infants of any age can be affected, although
neonatal occurrence is considered exceptional. We describe a
patient with severe haemolytic anaemia of perinatal onset.

CASE REPORT

The male infant was born by normal vaginal delivery at term
with a birth weight of 3120 g. Apgar scores were 9 at one and
two minutes. The direct antiglobulin test (DAT) on cord blood
was slightly positive (titre 1:64). Twelve hours after birth, he
was transfused with packed red cells because of severe ana-
emia. Two weeks later, he needed another blood transfusion,
and at 23 days of life he was transferred to our hospital
because of the persistence of anaemia. His family history
showed no significant disease; his parents were non-
consanguineous. The mother's blood type was A Rh positive,
and the infant's was O positive.

Physical examination showed pallor, hepatosplenomegaly,
and no lymphadenomegaly.

Haemoglobin concentration was 59 g/l (17% packed cell
volume; red blood cells 1870 × 10\(^9\)/l), reticulocytes were
absent, platelets were 314 × 10\(^9\)/l. Leucocyte count was 8.6 ×
10\(^9\)/l (neutrophils 54%, lymphocytes 36%, and monocytes 6%).
A blood smear showed anisopoikilocytosis and spherocytosis.

DAT was positive (titre 1:250). Serum lactate dehydroge-
nase concentration was 1314 U/l.

Clotting tests (prothrombin time, partial thromboplastin
time, fibrinogen) were normal, and the autoantibody assay
(anti-nuclear, anti-extractable nuclear antigens, anti-DNA,
anti-cardiolipin) was negative. Investigations for HIV, Epstein-
Barr virus, cytomegalovirus, herpes simplex virus 1-2, and
hepatitis A, B, and C viruses did not indicate a congenital
infection. Serology for parvovirus showed positivity of IgG and
negativity of IgM in both mother and infant.

A tibial bone marrow aspiration showed normal cellularity,
the presence of megakaryocytes, and normal granulocytic
and lymphocytic lineages. A paucity of erythroid precursors,
blocked at the stage of basophil erythroblast, was observed. No
abnormal blast cells or malignant cytological abnormalities
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Cultures of peripheral blood cells, obtained by separation of
mononuclear cells and stimulated with several cytokines
(granulocyte colony stimulating factor, erythropoietin, inter-
leukin 3), showed normal growth of haematopoietic progeni-
tor cells.\(^2\)

Lymphocyte phenotype was characterised by a reduction in
total T cells, with inversion of T4/T8 ratio and relative increase
in T activated lymphocytes and B cells: CD3, 33%; CD3’/DR’,
18%; CD4, 16%; CD8, 18%; CD5, 50%; HLA-DR, 58%; CD19,
24%; CD16, 30%; TCR\(\gamma\delta\)/CD4/CD8, 1%; CD95, 78%.

Serial measurements of polyspecific DAT showed a stable
positivity with titre 1:256 up to first 8 weeks of age. These
findings, along with a negative indirect Coombs test and
irregular antibody test in the mother, suggested AIHA.

A monospecific anti-human globulin test was positive for
anti-IgG, and negative for anti-IgA, anti-IgM, anti-C3c, and
anti-C3d.

Immunosuppressive treatment with methylprednisolone at
a dose of 2 mg/kg/day was started. After four weeks, because of the persistence of significant haemolysis (high transfusion

Figure 1 Number of transfusions (indicated by arrows) and
schedule of treatment related to packed cell volume and reticulocyte
counts, during the first 15 months of life in an infant with
autoimmune haemolytic anaemia.

Abbreviations: AIHA, autoimmune haemolytic anaemia; DAT, direct
antiglobulin test
One baby died as a consequence of refractory AIHA. One child remained dependent on steroids, and underwent splenectomy. One child was also affected by autoimmune enteropathy, died at 6 months from severe diarrhoea. One of these, who improvement of anaemia, although for only two could so far been reported (table 1). Six responded to treatment with steroid and cyclosporin, and persistence of anaemia was achieved in all with a significant reduction in the transfusion requirement after two weeks (fig 1).

No appreciable side effects of cyclosporin were recorded. The last transfusion was at the age of 6 months; cortisone tapering was started two months later. Cyclosporin treatment was suspended at the age of 11 months, and treatment was finally discontinued at 13 months of age, when the DAT gave a negative result for the first time.

As a consequence of steroid treatment, the child initially showed hypoplasia (length < 3rd centile). However, clinical evaluation at 24 and 36 months of age showed that length and growth had been regained (> 25th centile), and there was no recurrence of haemolysis.

<table>
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<tr>
<th>Reference</th>
<th>Age at onset (weeks)</th>
<th>Diagnosis</th>
<th>Treatment</th>
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<td>12</td>
<td>AIHA</td>
<td>Not reported</td>
<td>Favourable</td>
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<td>Satake et al</td>
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<td>AIHA</td>
<td>Steroids</td>
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<td>Satake et al</td>
<td>4</td>
<td>AIHA</td>
<td>Immunoglobulin cyclosporin A</td>
<td>Improvement of anaemia; died at 6 months from severe diarrhoea</td>
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<td>Ritz &amp; Haber</td>
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<td>Steroids, ACTH</td>
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<td>Hadnagy 6</td>
<td>At birth</td>
<td>AIHA</td>
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<td>Lasky et al 4</td>
<td>10</td>
<td>AIHA</td>
<td>–</td>
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<tr>
<td>Gasser &amp; Hollander 7</td>
<td>7</td>
<td>AIHA</td>
<td>Steroids, splenectomy</td>
<td>Died at 4 months</td>
</tr>
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ACTH, Adrenocorticotropic hormone; AI, autoimmune.

DISCUSSION
To our knowledge, only seven young infants with AIHA have so far been reported (table 1). Six responded to treatment with improvement of anaemia, although for only two could treatment be discontinued without relapse. One of these, who was also affected by autoimmune enteropathy, died at 6 months of age with severe watery diarrhoea. One child remained dependent on steroids, and underwent splenectomy. One baby died as a consequence of refractory AIHA.

During the first 6 weeks of life, an infant’s ability to form antibodies is limited by an immature immune and reticuloendothelial system. Early immunological stimulation usually results in the production of low titre IgM specific antibodies, with a delayed switch from the IgM to the IgG class. However, the impaired responsiveness of the neonate is variable and the possibility of synthesis of autoimmune antibodies cannot be excluded.

Neonatal occurrence of AIHA is very rare. In only one of the reported patients* was the diagnosis made at birth as in our case. As AIHA is so rare, few data on clinical management and treatment strategies are available. The use of steroids is widely accepted, although long term treatment during infancy is associated with appreciable side effects, such as neurological and somatic growth retardation, hypertension, and hypertrophic cardiomyopathy. Tapering of steroid treatment should be considered when DAT becomes negative and the patient’s haemoglobin concentration and reticulocyte count remain satisfactory. Other immunosuppressive drugs such as cyclosporin, azathioprine, and cyclophosphamide are not often used in children, although they can be useful for refractory forms because the long term use of high dose steroids is undesirable.7

Splenectomy is sometimes considered for children with chronic AIHA, although it should be avoided in young infants because of the high risk of sepsis and mortality.

Transfusion may be complicated by the high requirement and the difficulty of obtaining compatible blood.18 When the antigenic specificity is panreactive, the cross match may well not identify any compatible blood units. In such cases, the blood bank designates certain units that are considered the “least incompatible” with the patient’s serum.

In our case the use of high dose steroid and intravenous immunoglobulin successfully treated the hypoplastic phase, and the use of cyclosporin controlled the disease (fig 1).

References