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The Treatment of Neonatal Isoimmune Thrombocytopenia with Intravenous Immunoglobin (IgG i.v.)

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Summary. We present a report of the use of IgG i.v. to treat clinically manifest neonatal immune thrombocytopenia. The IgG i.v. was administered at a daily dosage of 0.4 g/kg body weight for 5 days. Treatment was started when the child was 3 days old and had a platelet count of 2×10^9/l. Four days later the platelet count had risen to 200×10^9/l. The diagnosis of immune thrombocytopenia was confirmed by platelet typing of the mother's and child's platelets and identification of anti-platelet antibodies in maternal serum.

Key words: Neonatal isoimmune thrombocytopenia – Anti Pl A^1 antibody – Immunoglobulin therapy

Isoimmune thrombocytopenia due to incompatibility of maternal and foetal blood is a rare but often severe disease in neonates.

The incidence of this condition is given in the literature as approximately 1 in 5000 newborn children [2, 6]. Complications such as intracranial and intestinal haemorrhages are not uncommon. The mortality is 10–15% in affected children [6]. The condition is caused by maternal IgG isoantibodies, which are transmitted to the foetus through the placenta [5].

The underlying pathogenesis of this condition is the same as that involved in haemolytic disease of the newborn. As in ABO incompatibility, even the first baby may be affected. As a first priority treatment is aimed at preventing bleeding, particularly into the central nervous system. Efforts to transfuse heterologous platelets often come to nothing, since donor platelets in most cases possess antigens similar to those which the child has inherited from its father. Thus transfusion of heterologous platelets provides only a short-term increase in platelet count, after which the donor platelets are destroyed by the maternal antibodies in the child's plasma.

Besides administration of platelet concentrates, exchange transfusions and steroids have been proposed for the treatment of this condition [5]. More recently, transfusion of maternal platelets has been described as the treatment of choice [2, 6]. In the last

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few years intravenous immunoglobulin has been used successfully to treat idiopathic thrombocytopenia [1]. On the basis of these results immunoglobulin therapy has also been employed in isoimmune thrombocytopenia. Originally, a preparation of immunoglobulin treated with β-propiolactone was used, later immunoglobulin prepared with the pH 4 procedure was used [3]. The therapeutic value of immunoglobulin remained unclear, since in these studies the type of preparation could have played a role [3]. We report on the first case of neonatal isoimmune thrombocytopenia successfully treated with IgG i.v. alone.

Case History

Medical History

The patient was the second child in the family. The parents and the first child were all healthy. The pregnancy was uneventful and the mother did not take any drugs. Birth occurred spontaneously in week 36, Apgar score after 1 min 8 and after 5 min 9. Birth weight: 2400 g (10–15 percentile), length 45 cm (10–50 percentile), head circumference 34 cm (50–90 percentile). Initial adaptation was uneventful. Subsequently, on the third day of life the baby developed rapidly progressive jaundice, petechial haemorrhages over the whole body surface and extravasation into the face and hands. The liver was normally palpable, about 1 cm below the costal arch and the spleen was not enlarged.

Laboratory Findings

Mother and child were of blood group B, rhesus positive, with negative Coombs test. On the third day of life blood indices were as follows: Hb 14.1 g%, reticulocytes 7.6%, WBC 6.8×10^9/l, platelets 2×10^9/l (maternal platelet count 325×10^9/l), prothrombin 100% (Quick's method), bleeding time and coagulation time normal. Total bilirubin was 314 μmol/l, direct bilirubin 5.1 μmol/l. Blood and urine cultures were bacteriologically and virologically negative. Serological tests carried out at the same time ruled out toxoplasmosis, cytomegalovirus infection, rubella or herpes virus infection.

Treatment

After blood sampling for diagnostic investigations, the child was given intensive blue light phototherapy for treatment of hyperbilirubinaemia, with concomitant intravenous immunoglobulin 0.4 g/kg body weight per day for treatment of the thrombocytopenia. The freeze-dried preparation of immunoglobulin employed was administered as a 3% solution given by infusion over a 3-hour period each day.

Clinical Course

The rapid rise in the platelet count during the 5-day course of treatment with IgG i.v. is shown in Fig. 1. At the same time over the next ten days there was a rapid fall in bilirubin levels to below 170 μmol/l, and the petechial haemorrhages and extravasation resolved. During this period, the haemoglobin count remained stable at between 12 and 14 g/%. Regular check-ups in the outpatient department over the following

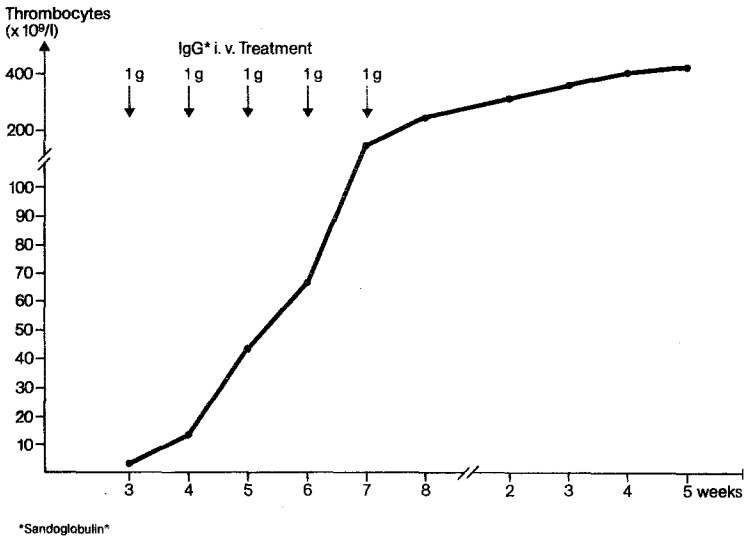

Fig. 1. Neonatal isoimmune thrombocytopenia due to maternal P1 A^1 antibodies. The figure demonstrates the course of the newborn's platelet counts after initiation of immunoglobulin therapy

4 months failed to reveal any abnormalities in development or in neurological status, and the platelet count remained normal at betwen 200 and 400×10^9/l.

Diagnosis of Immune Thrombocytopenia

The maternal platelets were P1 A^1 negative type. The platelet immunofluorescence test on the maternal serum was strongly positive for anti-P1 A^1 positive type. No evidence of free platelet auto- or alloantibodies was found in the child's serum.

Discussion

The presence of platelet imcompatibility between the P1 A^1 positive platelets of the father and child and the P1 A^1 negative platelets of the mother was confirmed by the demonstration of anti-P1 A^1 antibodies in the maternal serum.

After the start of treatment with IgG i.v. the platelet count normalized within 4 days. On the basis of these findings, the costly replacement of maternal platelets, described as the treatment of choice [6], may be dispensed with. The use of immunoglobulin also avoids administration of steroids, which is not without risk, and exchange transfusion [5] with its still greater attendant hazards.

However, the manufacturing procedure used to produce the immunoglobulin preparation employed seems to play a role. Thus an initial trial with immunoglobulin prepared by treatment with β-propiolactone was unsuccessful in the treatment of neonatal isoimmune thrombocytopenia [3]. A trial of pH 4 treated immunoglobulin in a subsequent phase afforded a rapid rise in the platelet count, but it was not entirely

clear whether the improvement was due to the immunoglobulin or to a spontaneous remission [3]. Our patient was treated without delay with IgG i.v., prepared by treatment at pH 4. Administration of IgG i.v. afforded an immediate, rapid and sustained increase in the platelet count to normal levels.

Hitherto, response to replacement therapy with maternal platelets has also been seen as a diagnostic criterion [4].

Treatment with IgG i.v. may be expected to afford a rapid rise in the platelet count and this too may be used as an additional aid to diagnosis. However, the diagnosis should be confirmed by assay of anti-platelet antibodies in a specially equipped laboratory.

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