Isoimmune neonatal thrombocytopenic purpura

P GALEA, M J PATRICK, AND K M GOEL

Royal Hospital for Sick Children, Glasgow

SUMMARY Ten cases of isoimmune neonatal thrombocytopenic purpura (4 pairs of siblings and 2 singletons) are described. The condition was diagnosed by excluding other causes of thrombocytopenia, and in 8 cases it was confirmed by detecting antiplatelet antibodies in the mother. Perhaps steroids should be given to affected infants as soon as the condition is diagnosed in order to stabilise the capillary membrane. Exchange transfusion, using platelet antigen-negative blood if available, helps to remove antibodies and should be followed by the infusion of antigen-negative platelets, easily obtained from the mother by platelet-phoresis. The use of random donor platelets (as in 3 of these cases) was ineffective because 98 % of the population are platelet antigen-positive. Nine of the infants recovered completely. The exception was an infant who developed hydrocephalus, possibly as a result of intracranial haemorrhage.

Isoimmune neonatal thrombocytopenic purpura (INTP) is rare; 98 % of the population are platelet antigen-(PI^{A1} or ZW^A) positive, the characteristic being autosomal dominant in inheritance. Only the remaining 2 % of the female population are thus capable of sensitisation. Manifestations of maternal incompatibility, with sensitisation of the PI^{A1}-negative mother and thrombocytopenia in the PI^{A1}-positive infant, occur once or twice in 10 000 births.^{1–2} Several platelet antigens have been implicated in INTP. Some are restricted to platelets, others are shared by leucocytes and may be identical with certain antigens of the HLA system. The platelet antigenic system most commonly associated with INTP has been designated PI^{A1} or ZW^A. Therefore the finding of reactivity for the PI^{A1} antigen in the mother of an infant with neonatal thrombocytopenia is strong presumptive evidence of isoimmunisation to this antigen.³

The first affected PI^{A1}-positive infant of a PI^{A1}-negative mother is generally born undiagnosed until thrombocytopenia is manifest by haemorrhage. Fatalities, often due to intracranial haemorrhage, have occurred in about 14 % of reported cases.⁴

The diagnosis of INTP is based on the exclusion of other causes of neonatal thrombocytopenia, the demonstration of antiplatelet antibodies in the maternal serum, and the response to the infusion of PI^{A1}-negative platelets. The clinical history of 10 infants with INTP, with special reference to treatment is described.

Clinical material

Ten infants (4 pairs of siblings and 2 singletons) were admitted to special care nurseries in Glasgow between October 1971 and October 1978, showing the prevalence of the disorder in Glasgow. None of these babies was referred from hospitals outside Glasgow. There were 7 boys and 3 girls. Details of the clinical and laboratory findings are given in Tables 1 and 2. Maternal platelet counts were normal and there was no history of drug ingestion during pregnancy. There was no clinical or laboratory evidence of bacterial or viral infection.

The platelet antibodies were detected using a simple immunofluorescence test developed at the Central Laboratory of the Netherlands Red Cross Blood Transfusion Service in Amsterdam.⁵

Discussion

INTP should be suspected in any purpuric, but otherwise healthy, infant of a mother whose platelet count is normal. The diagnosis can be confirmed by the demonstration in the maternal serum of antibody which reacts with the platelets of the infant or the father, but not with those of the mother. Laboratory confirmation of isoimmunisation is difficult. The maternal antibody in these cases is of the complement-fixing or blocking variety and generally is not detectable by usual tests for platelet agglutinins. Nevertheless by using paraformaldehyde

Table 1 Clinical findings in 10 cases of isoimmune neonatal thrombocytopenic purpura

Case	Sex	Birthweight (kg)	Gestation (weeks)	Mode of delivery	Apgar score	Clinical features
1	M	3.60	41	Forceps	6 at 1 min	Day 1, petechiae on trunk, bruising on forehead Day 2, 3, 4, irritable baby Day 11, haematuria and melaena Week 4, rapidly increasing head circumference Week 5, hydrocephalus confirmed by air ventriculography
2 (sister of Case 1)	F	3.53	40	Spontaneous	9 at 1 min	Day 1, petechiae on trunk and limbs
3	M	3.01	40	Spontaneous	9 at 1 min	Day 1, bruising and petechiae on trunk and limbs particularly in groin and axillae
4 (brother of Case 3)	M	3.28	41	Spontaneous	8 at 1 min	Day 1, petechiae on trunk rapidly extending to limbs
5	M	2.60	38	Spontaneous	8 at 1 min	Day 1, generalised petechiae on arms and trunk, mild jaundice Day 4, maximum serum bilirubin 360 $\mu\text{mol/l}$ (21 mg/100 ml)
6 (brother of Case 5)	M	3.30	40	Spontaneous	9 at 1 min	Day 1, facial petechiae rapidly extending to trunk and limbs. Blood in vomitus and urine Day 2, jaundiced, serum bilirubin 245 $\mu\text{mol/l}$ (14 mg/100 ml). Irritable
7	M	3.78	40	Spontaneous	10 at 1 min	Day 1, generalised petechiae and bruising
8 (sister of Case 7)	F	3.81	40	Spontaneous	10 at 2 min	Birth, extensive scalp bruising Day 1, fresh blood in gastric aspirate. Fine petechiae on trunk
9	M	3.56	40	Spontaneous	10 at 2 min	Birth, petechiae on face Day 1, petechiae on trunk and limbs
10	F	1.45	35	Spontaneous	9 at 1 min	Birth, subconjunctival haemorrhage Day 1, bruising on back, petechiae on trunk

Table 2 Management of 10 cases of isoimmune neonatal thrombocytopenic purpura

Case	First platelet count ($\times 10^9/l$)	First normal platelet count	Maternal antibody	Treatment	Final outcome
1	29	Week 4	Not done	Prednisolone 10 mg a day for 6 weeks. Random donor platelet infusion $\times 6$	Hydrocephalus with Spitz-Holter valve
2	15	Day 6	Not done	Prednisolone 15 mg a day for 10 days. Maternal platelet infusion $\times 2$	Recovered
3	25	Week 5	Present (new undiagnosed specificity)	Prednisolone 15 mg a day for 6 weeks. Exchange transfusion. Random donor platelet infusion.	Recovered
4	10	Day 17	Present	Exchange transfusion. Random donor platelet infusion $\times 1$. Maternal platelet infusion $\times 1$	Recovered
5	126 20	Week 2	Present anti Zw ^A	Nil	Recovered
6	69	Day 4	Present	Prednisolone 20 mg a day for 10 days	Recovered
7	10	Week 4	Present HLA A ₁ + A ₃	Nil	Recovered
8	44	Week 4	Present	Prednisolone 10 mg a day for 3 weeks	Recovered
9	3	Day 5	Present anti Zw ^A	Nil	Recovered
10	24	Day 7	Anti Zw ^A	Random donor platelets $\times 1$	Recovered

hyde-fixed platelets, a simple method for detecting platelet antibodies, the platelet suspension immuno-fluorescence test has recently been developed.⁵ A petechial rash, with or without bruising, is evident within minutes or a few hours of delivery. The platelet count is usually low by the time the bleeding manifestations occur, as in 9 of our 10 infants. The

presence of an initially normal platelet count, as in Case 5, does not exclude INTP. It may be that in a few cases the platelets are inactivated by the antibodies but remain in circulation for some time before being removed.

A logical way of treating an infant with INTP would be to remove as much platelet antibody as

Fig. 1 (Case 3.) Serial platelet counts showing rapid sequestration of random donor platelets even after exchange transfusion.

possible by exchange transfusion, and then to replenish the infant's platelets with a transfusion of PI^{A1} -negative platelets. As in Cases 3 and 4, random donor platelets were rapidly sequestrated when infused, even after exchange transfusion, suggesting that a significant quantity of antibody remained and that the random donor platelets were PI^{A1} -positive (Fig. 1). There is a 98% risk of random donor platelets being PI^{A1} -positive and, as in Cases 1, 3, 4, and 10, the infused platelets were removed within a few hours. This has also been the experience of other workers.⁶ The most readily available source of PI^{A1} -negative platelets is the mother herself. Cases 2 and 4 clearly indicate the efficacy of using platelets from the mother (Fig. 2).

The action of prednisolone in this condition is difficult to assess and it is unlikely that it reduces the duration of the thrombocytopenia. The capillary membrane-stabilising action of steroids may help to reduce the risk of haemorrhage. In Cases 1, 2, 3, and 8, steroids had no effect on the platelet counts. Although in Case 6 the platelet count rose sharply within 36 hours of starting prednisolone, if the antibody titre is not excessively high, the platelet count

Fig. 2 (Case 2.) Serial platelet counts showing the efficacy of using maternal platelets.

could spontaneously rise to normal levels within a few days, as in Cases 5, 7, and 9.

Generally INTP follows a mild course and there is complete recovery between one and five weeks later without any sequelae. The period of greatest danger from haemorrhage is during the first 24 hours of life and is probably related to birth trauma and asphyxia. In our series all infants, except the one delivered by forceps (Case 1), recovered without sequelae.

When a pregnant mother of previously affected children is about to be delivered, one has to consider the safest way of delivering the baby with the least trauma. If an easy spontaneous delivery is not possible, the dangers of an instrumental or breech delivery have to be weighed against the relative safety of caesarean section.

In conclusion, the management of an affected infant should ideally start before birth, although it is not possible to diagnose the condition in a primigravida prenatally in the absence of an easy screening test. The administration of antepartum steroids to the mother has been suggested.⁷ This is not without risks and remains to be assessed. Steroids should

perhaps be given to all affected infants as soon as the condition is confirmed. Exchange transfusion, using PIA^1 -negative blood if available, may help to remove antibody and lessen the severity of the condition. However the best way of treating a severely affected infant is by the administration of antigen-negative platelets, easily obtained from the mother by platelet-phoresis.

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Correspondence to Dr K M Goel, Royal Hospital for Sick Children, Yorkhill, Glasgow G3 8SJ.

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