

Porencephaly and optic hypoplasia in neonatal isoimmune thrombocytopenia

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SUMMARY Five children with prenatal intracerebral damage associated with neonatal isoimmune thrombocytopenic purpura are described, and characteristic neurological features listed. These include optic hypoplasia which has not been previously documented in this condition.

Neonatal isoimmune thrombocytopenic purpura accounts for 20% of cases of thrombocytopenia in the newborn. Two per cent of women are platelet antibody A₁ negative and therefore at risk of an affected pregnancy.¹

The disease has a mortality of 10–14%¹ and haemorrhagic complications are common. Intracerebral lesions are the main cause of mortality and serious morbidity. Perinatal haemorrhage is well recognised. More recently the prenatal development of such lesions has been documented.^{2–6}

We describe five children with neonatal isoimmune thrombocytopenic purpura and porencephaly as a result of prenatal intracerebral damage.

Case reports

Details of the five cases are shown in tables 1 and 2. All infants developed skin purpura shortly after delivery and were found to be severely thrombocytopenic. All had proved neonatal isoimmune thrombocytopenic purpura, and other causes of thrombocytopenia were excluded.

CASE 1

This infant had an intracranial haemorrhage in the immediate prenatal period. After an atraumatic delivery she presented aged 2 hours with evidence of neurological abnormality. Cranial ultrasonography showed two haemorrhagic lesions in the right frontoparietal region. There was central resolution of these lesions, the appearances being consistent with haemorrhage several days previously. Apart from transient neonatal seizures she has had no other neurological or developmental problems.

CASES 2–5

Cases 2–5 present a different picture. Despite severe

thrombocytopenia, none had evidence of a perinatal intracranial bleed. All have subsequently presented with serious neurological problems, and a characteristic clinical picture. This consists of porencephaly with or without communicating hydrocephalus, visual impairment with optic hypoplasia, mental handicap, and a variable degree of cerebral palsy. All must have had a prenatal intracerebral vascular event.

Case 5 is of particular interest as the diagnosis of neonatal isoimmune thrombocytopenic purpura was made retrospectively when he was 10 years old. He had neonatal thrombocytopenia of unknown aetiology, and later presented with visual impairment. He had had the characteristic features described above, and we confirmed the diagnosis of neonatal isoimmune thrombocytopenic purpura serologically.

Discussion

The recognition that intracerebral lesions may occur prenatally in patients with neonatal isoimmune thrombocytopenic purpura has important implications for the further understanding of this condition and for the management of affected pregnancies. Though a number of such cases have now been reported there is no information regarding the incidence, mechanism, and neurological consequences of these lesions.

We have described five infants with neonatal isoimmune thrombocytopenic purpura and porencephaly resulting from prenatal damage. One had an intracranial haemorrhage in the immediate prenatal period. In the other four, severe neurological damage was the result of an intracerebral event that occurred earlier in pregnancy. These earlier lesions give rise to a characteristic pattern of neurological abnormality including optic hypoplasia, which has not previously been described in this disease. Interestingly, one previous case report of congenital porencephaly in two siblings with neonatal isoimmune thrombocytopenic purpura documents similar features, although they describe optic atrophy rather than optic hypoplasia.⁶ Examination of our patients clearly indicated that the optic nerves were hypoplastic rather than simply atrophic. The presence of optic hypoplasia is difficult to explain as the result of a

Table 1 *Neonatal data*

	<i>Case 1</i>	<i>Case 2</i>	<i>Case 3</i>	<i>Case 4</i>	<i>Case 5</i>
Maternal and family history	Aged 30, parity 1+0 Sibling well	Aged 27, parity 0+1	Aged 25, parity 1+0 Smoker Sibling well	Aged 25, parity 1+0 Sibling well	Aged 22, parity 1+0 Sibling died age 7 hours – hydrocephalus
Obstetric problems	Reduced fetal movements from 35 weeks High blood pressure	None	Intrauterine growth retardation from 32 weeks	None	None
Method of delivery	Elective caesarean section	Emergency caesarean section	Spontaneous vertex delivery	Spontaneous vertex delivery	Forcops delivery
Birth weight	3200 g	3100 g	2400 g	2900 g	3000 g
Resuscitation required	None	None	None	None	None
Neonatal problems	Petechiae, jittery, seizures	Petechiae	Petechiae, gastric bleeding	Petechiae	Petechiae
Initial platelet count	$<10 \times 10^9/l$	$10 \times 10^9/l$	$7 \times 10^9/l$	$10 \times 10^9/l$	$8 \times 10^9/l$
Platelet typing	Mother platelet antibody A ₁ negative Father platelet antibody A ₁ positive	Not done	Not done	Not done	Mother platelet antibody A ₁ negative Child platelet antibody A ₁ positive
Maternal platelet specific antibodies	Positive	Positive	Positive	Positive	Positive
Treatment	Exchange transfusion, washed maternal platelets infusion, intravenous immunoglobulin	Exchange transfusion, washed maternal platelets infusion	Donor platelets	None	None
Time taken for platelet count to become normal	24 Hours	5 Days	7 Days	7 Days	7 Days
Neonatal cranial ultrasound findings	Two haemorrhages in right frontoparietal regions	Not done	Large left occipital cyst	Not done	Not done

Table 2 *Follow up data*

	<i>Case 1</i>	<i>Case 2</i>	<i>Case 3</i>	<i>Case 4</i>	<i>Case 5</i>
Presentation	Routine follow up	Age 2 months	Age 2 months	Age 6 weeks	Age 5 months
Neurological features	Normal	Visually unresponsive Visual handicap, spastic diparesis, mental handicap, seizures	Visually unresponsive Visual handicap, spastic diparesis, mental handicap feeding problems	Hydrocephalus Visual handicap, spastic quadriplegia, mental handicap, seizures	Visually unresponsive Visual handicap, spastic diparesis, mental handicap, language delay
Ophthalmological features	Normal	Optic hypoplasia, visual evoked responses delayed, electroretinogram normal	Optic hypoplasia, visual evoked responses absent, electroretinogram normal	Optic hypoplasia, visual evoked responses delayed, electroretinogram normal	Optic hypoplasia, visual evoked responses absent, electroretinogram normal
Cranial ultrasound findings	Right frontoparietal porencephalic cysts	Left temporal and right occipital porencephalic cysts	Left temporal and cerebellar porencephalic cysts	Massive hydrocephalus and left parietal porencephalic cyst	Not done
Computed tomographic findings	Not done	Above with communicating hydrocephalus	Above with communicating hydrocephalus	Not done	Right occipital porencephalic cyst

haemorrhagic lesion, and the possibility that the primary event may have been ischaemic or thromboembolic requires investigation.

We suggest that intracerebral damage in neonatal isoimmune thrombocytopenic purpura may arise in three different ways. Perinatal haemorrhage may occur as a result of birth trauma. Spontaneous haemorrhage may occur prenatally secondary to severe thrombocytopenia (as in case 1). Finally, earlier prenatal lesions may occur giving rise to the neurological features we have described.

The relative incidence of these lesions is unknown; our experience with five cases suggests that prenatal lesions may be more common than previously thought. Further investigation of the mechanism of the earlier prenatal lesions is required as there are important implications for obstetric management. Regular antenatal ultrasound screening in pregnancies thought to be affected may give further information about the nature and timing of events.

Because the purpura is transient, neonatal isoimmune thrombocytopenic purpura may remain undiagnosed in the neonatal period. Some unexplained cases of porencephaly may therefore be the result of prenatal damage in neonatal isoimmune thrombocytopenic purpura (case 5). We looked at a further five children with unexplained porencephaly and carried out platelet typing of mother and child; in no case was there evidence of platelet incompatibility. Nevertheless, neonatal isoimmune thrombocytopenic purpura should be considered as a possible

diagnosis in unexplained porencephaly, particularly if it is associated with optic hypoplasia.

In conclusion, prenatal intracerebral lesions occur in association with neonatal isoimmune thrombocytopenic purpura and give rise to a characteristic pattern of neurological abnormality, including optic hypoplasia. Further clarification of the mechanism of these lesions is required.

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Flecainide toxicity

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SUMMARY Flecainide toxicity occurred in an infant being treated for refractory atrioventricular re-entry tachycardia. Ventricular tachycardia developed when dextrose was substituted for milk feeds. We believe that milk was interfering with the absorption of flecainide, and so a high serum concentration developed when milk feeds were stopped.

Flecainide acetate is a comparatively new drug for the treatment of supraventricular and ventricular arrhythmias. Early clinical experience in infants and children has shown that it is effective and well tolerated.^{1 2}

Case report

A baby boy was born at 34 weeks' gestation after an apparently uncomplicated pregnancy. He was hydropic at birth, weighing 3100 g (>90th centile). Resuscitation with endotracheal intubation was required, and mechanical ventilation was continued for three days. After extubation he remained cyanosed and a hyperoxic test confirmed the presence of an appreciable right to left shunt. Standard investigations did not identify a cause for the hydrops fetalis, and he was referred for cardiological assessment.

On transfer to our hospital at 6 days of age he weighed 2100 g and was no longer hydropic. He