Athetoid cerebral palsy with cysts in the putamen after hypoxic-ischaemic encephalopathy

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Abstract

Three cases of athetoid cerebral palsy after hypoxic-ischaemic encephalopathy (HIE) are reported. All three neonates had haemorrhagic lesions in the basal ganglia and thalami on magnetic resonance imaging (MRI). Prior cranial ultrasound had detected the lesions in only two cases. In all three children athetoid movements began within the first year of life. Follow up MRI scans showed bilateral symmetrical cystic lesions in the posterior putamen. Although haemorrhagic lesions within the basal ganglia are a common MRI finding in neonates with HIE, few of these babies develop athetoid cerebral palsy. We believe this to be the first report of discrete cystic lesions found in the basal ganglia of children with athetoid cerebral palsy.

The relationship between neonatal asphyxia and lesions in the thalamus and basal ganglia has been recognised for many years. The appearance of status marmoratus was first described in 1911,¹ but it was not until 1950 that an association with this lesion and a history of birth asphyxia was suggested.² In recent years, lesions in the thalami have been described using ultrasound in neonates with severe hypoxic-ischaemic encephalopathy (HIE)³⁻⁵ and the more sensitive techniques of magnetic resonance imaging (MRI) have shown haemorrhagic lesions within thalami and basal ganglia in babies with even mild HIE (JM Pennock *et al*, personal observation). However, to date there have been no published reports of clinical or radiological follow up on infants with these thalamic lesions. In this paper we describe three infants with thalamic and basal ganglia lesions on neonatal MRI scans who have developed cystic lesions in the putamen on follow up images. All three infants now have athetoid cerebral palsy.

Patients and methods

These infants were part of our prospective study of babies with HIE and were assessed with the following techniques: regular neurological examination, using a standardised proforma,⁶ regular cranial ultrasound, cerebral Doppler blood flow studies, continuous electroencephalographic monitoring, computed tomography, and MRI. On follow up visits each baby had a neurological examination, cranial ultrasound until closure of the anterior fontanelle, and Griffiths's developmental assessment. Follow up MRI scans were performed when possible.

Cranial ultrasound was performed with an Advanced Technical Laboratories Ultramark III sector scanner using both 5 mHz and 7.5 mHz transducers. A Picker 0.15 Tesla magnet was used for MRI. Imaging was performed using both T1 weighted inversion recovery and T2 weighted partial saturation sequences. The parameters used during the neonatal period and infancy have been described elsewhere.⁷

All infants over 3 months of age were sedated with 80 mg/kg of chloral hydrate. Younger babies were imaged while asleep and after a feed. All patients were monitored with electrocardiography and an apnoea alarm.

Results

In our current series of 25 infants with HIE who have shown haemorrhagic lesions in the basal ganglia and thalamus on neonatal MRI scans only four have developed cerebral palsy with athetoid movements. In the three with appropriate follow up scans we have demonstrated bilateral cystic lesions within the posterior part of the putamen. The fourth child has not had repeat imaging using the same sequence. Clinical details of each infant with lesions in the putamen and details of their ultrasound, computed tomograms, and MRI scans are given below and in tables 1 and 2.

Table 1 Clinical details in neonatal period

Case No	Delivery	Apgar score (1,5 min)	EEG	Cranial ultrasound	Discharge examination
1	Spontaneous vaginal delivery	1,1	Discontinuous activity, low amplitude activity	7.5mHz only, periventricular densities	2 Weeks, jittery tremors, ↑ arm tone, feeding well
2	Emergency caesarean section	1,1	Discontinuous activity, low amplitude activity, seizures	Slit-like ventricles, thalamic densities	12 Days, irritable asymmetrical tone, feeding well
3	Emergency caesarean section	3,7	Low amplitude activity	Featureless, thalamic densities	12 Days, ↑ tone, adducted thumb feeding well

EEG=electroencephalogram.

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Accepted 7 January 1992

Table 2 Clinical details on follow up

Case No	6 Weeks	1 Year	Diagnosis
1	Jittery, irritable, ↑ arm tone	Hypertonic, drooling, athetoid movements	Athetoid cerebral palsy
2	Irritable, ↑ tone	Dystonia, athetoid movements, mouth open++	Athetoid cerebral palsy
3	Irritable, tremors, fisting ↑ tone	Infantile spasms, athetoid movements, drooling, tight hip adductors	Athetoid cerebral palsy

CASE REPORTS

Case 1

A boy, weighing 4200 g, was born to healthy West Indian parents. A fetal bradycardia was recorded for 20 minutes before the delivery when the cord was found tightly around the neck. The baby was intubated but spontaneous respiration was not established for 20 minutes. A prolonged convulsion occurred at 6 hours of age, despite 35 mg phenobarbitone given prophylactically by the referring hospital. A further dose of phenobarbitone was

Figure 1 (A) Haemorrhagic lesions (arrows) in the basal ganglia and thalami on inversion recovery sequence. (B) Cystic lesions (arrows) in the posterior putamen on inversion recovery sequence.

Figure 2 (A) Haemorrhagic lesions (arrows) in the basal ganglia and thalami on inversion recovery sequence (some movement artefact). (B) Cystic lesions (arrows) in the posterior putamen on inversion recovery sequence.

given and a maintenance dose given for one week. There were no recorded episodes of hypoglycaemia, polycythaemia, acidosis, or hypocapnia. The maximum serum bilirubin concentration was 52 $\mu\text{mol/l}$. A computed tomogram on day 11 showed decreased attenuation in the periventricular areas but no lesions within the basal ganglia. MRI inversion recovery sequence on day 9 showed patchy areas of high signal intensity within the thalamus and basal ganglia, consistent with haemorrhage or haemorrhagic infarction (fig 1A).

A repeat MRI scan at 22 months showed bilateral symmetrical low signal intensity lesions in the putamen on inversion recovery sequence with a corresponding high signal intensity on partial saturation images (fig 1B). This is consistent with cyst formation. No other lesions were seen and myelination was within normal limits. At this stage head circumference was on the 10th centile and the weight <3rd centile.

Case 2

A girl, weighing 2600 g, was born to a white mother and African father. Labour was induced for maternal diabetes and delivery was by emergency caesarean section for fetal distress and meconium stained liquor. An initial umbilical arterial blood gas showed a mixed acidosis with a pH of 7.07. A chest radiograph was compatible with meconium aspiration. Convulsions were noted on day 3. These were treated with two doses of phenobarbitone and ceased after 24 hours. Early Doppler blood flow studies showed a pulsatility index of <0.55. Maximum serum bilirubin concentration was 42 $\mu\text{mol/l}$ and there were no episodes of hypoglycaemia, polycythaemia, or hypocapnia.

Inversion recovery sequences on MRI at 10 days showed high signal areas in the basal ganglia and thalami (fig 2A). Repeat MRI at 13 months showed bilateral symmetrical low signal areas in the putamen on inversion recovery sequences with a corresponding high signal on partial saturation images (fig 2B). No other lesions were seen and myelination was within normal limits. At the time of writing her head circumference has fallen to the 3rd centile but her weight has also fallen to below the 3rd.

Case 3

A boy, weighing 3400 g, was born to healthy Asian parents. Delivery was by emergency caesarean section for fetal distress after failed Kielland's forceps delivery and failed vacuum extraction. The baby was intubated after delivery and ventilated for 45 minutes. A capillary blood gas at 1 hour of age showed a pH of 7.1. Convulsions were noted at 5 hours of age and continued for 48 hours despite anti-convulsant treatment, necessitating a period of reventilation. There were no recorded episodes of hypoglycaemia or polycythaemia and there was no jaundice. A computed tomogram at 10 days showed generalised low attenuation of the white matter, but no lesions were seen within the thalami or basal ganglia. An MRI inversion recovery sequence showed bilateral high signal areas in the thalami and basal ganglia at 8 days (fig 3A). A repeat MRI scan at 17 months showed bilateral symmetrical low signal areas in the putamen on inversion recovery sequences with a corresponding high signal intensity on partial saturation images (fig 3B). No other lesions were seen and myelination was within normal limits. His head circumference was on the 10th centile and his weight was below the 3rd centile.

Figure 3(A) Haemorrhagic lesions (arrows) in the basal ganglia and thalami on inversion recovery sequence. (B) Cystic lesions (arrows) in the posterior putamen on inversion recovery sequence.

Discussion

The development of athetoid cerebral palsy has been associated with two particular neonatal conditions, kernicterus and HIE.⁸ Pathological lesions in the basal ganglia and thalamus were first documented over 40 years ago both in children with a history of kernicterus⁹ and in those with birth asphyxia.^{10 11} With improvements in perinatal care kernicterus has become an unusual cause of athetoid cerebral palsy in the developed world,¹² and in children presenting with athetoid cerebral palsy there is often now a history of HIE. In contrast to the detailed descriptions of kernicterus the literature relating to the development of athetoid cerebral palsy after HIE is limited. In children with HIE who then develop athetoid cerebral palsy most studies are retrospective with poor documentation of clinical state and investigations in the neonatal period.^{8 13 14}

We are unsure whether the neonatal course of our infants is typical of babies who go on to develop athetoid cerebral palsy after HIE. We are, however, able to show that the neonatal findings in our babies were very different from babies who develop athetoid cerebral palsy following kernicterus. Since the term kernicterus was coined by Schmorl in 1903¹⁵ there have been many descriptions of the early and later clinical course of infants with this disorder.^{8 16 17} After an initial period of hypertonia with opisthotonus the infant becomes hypotonic. This lasts for a variable time but athetoid movements may not appear for several years. In contrast our three babies all showed some hypotonia in the first few days but once anticonvulsants had been discontinued the babies all showed varying forms of hypertonia and were excessively irritable with persistent tremulous and jittery movements. Despite these neurological findings all three babies were ready for discharge home by the end of the second week of life. Of interest is that although severely asphyxiated babies often have prolonged problems in establishing normal feeding, all our babies were feeding well by day 10.

After the neonatal period infants with HIE are reported as being hypotonic for a variable period of time, with persistence of primitive reflexes.^{13 18} The onset of athetoid movements is usually after the first year of life. Once the condition is established the tone may be hypotonic, hypertonic, or fluctuating in nature. Children who develop athetoid movements before the age of 1 year are thought to be less severely affected.¹⁸ Our babies do not appear to have followed this 'classical' clinical course. After the neonatal period they were hypertonic with jittery and tremulous movements for several months. Persistent mouth opening and/or dribbling was noted early on and all had developed abnormal movements by the end of the first year. However, in contrast to previous reports none could be described as having only mild cerebral palsy.¹⁸ In all three children the head circumference remained proportional to the weight and there was no evidence of cortical atrophy on MRI.

Myelination was also described as within normal limits in all three children. Maintenance of good head growth may provide an early clue that an infant with abnormal tone pattern will develop athetoid cerebral palsy as opposed to a spastic quadriplegia.

It is well recognised that the basal ganglia and thalamus are particularly vulnerable to hypoxic-ischaemic damage,¹⁹ but we have been unable to find any reports of athetoid cerebral palsy occurring in an infant with a thalamic/basal ganglia lesion documented in the neonatal period. To date most reports of these lesions have used cranial ultrasound or computed tomography.^{3 4 20 21} Two of our patients had computed tomography performed and no lesions were seen in this area. However, the scans were not performed during the first week of life and any haemorrhage may have become isodense with the surrounding tissue. When the lesions were identified using cranial ultrasound a 5 mHz scanning head was needed. It may be that when haemorrhage in these areas is documented with an imaging technique that is less sensitive than MRI it is so severe and/or extensive that the clinical outcome has often been death.^{4 20 21} It is of interest that in our current series of 25 infants with lesions seen at this time only four have developed athetoid movements. In the three of these who have had appropriate follow up images we have shown very isolated and apparently identical lesions. In addition to our three reported babies, two out of the 12 children who had follow up scans had cysts in the lentiform nucleus. One of these had small bilateral cysts in the medial putamen, but an otherwise normal scan, and is now developmentally normal. The second child has widespread damage throughout the basal ganglia and thalami with bilateral cysts in the globus pallidum and has developed a severe spastic quadriplegia. From these cases it would appear that damage to a very specific area of the putamen may be responsible for the development of athetosis. However, as all three children had more extensive lesions within this area in the neonatal period these may be contributing to the development of the athetosis.

Athetoid cerebral palsy has been reported in children with a wide variety and combination of lesions within the basal ganglia and thalamus.⁸ It is not known whether a specific site of damage, or combination of sites, is responsible for the disorder. In addition the disturbance or neurotransmitter imbalance that leads to athetosis is still not understood.²² Information on the site of damage and the neurotransmitter imbalance in athetoid cerebral palsy can only be established by further research. Studies using techniques such as MRI, magnetic resonance and spectroscopy, and positron emission tomography in children with established athetosis may provide the answers.

We would like to thank Professor Graeme Bydder, department of magnetic resonance imaging, for his help in interpreting the images. Dr Mary Rutherford is supported by The Spastics Society.

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