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Clinical and MR Correlates in Children with Extrapyrarnidal Cerebral Palsy

John H. Menkes and John Curran

PURPOSE: To identify the characteristic MR findings in extrapyramidal cerebral palsy. **METHOD:** Six patients who had suffered intrapartum asphyxia and who subsequently developed extrapyramidal cerebral palsy were identified. Asphyxia was evidenced by severe neonatal systemic acidosis as documented by a venous cord pH of less than 7.0 whenever available, or acidosis in subsequent arterial blood gas samples, and clinical signs of an acute hypoxic-ischemic encephalopathy during the neonatal period. In addition, 1- and 5-minute Apgar scores were 3 or less, and there had been need for intubation or vigorous resuscitation in the delivery room. There were three boys and three girls, all born at term, with birth weight appropriate for gestational age, and without a history of bilirubin levels above 15 mg/dL. MR imaging at 1.5 T was performed between 1 and 19 years of age. **RESULTS:** In all subjects focal high signal abnormality was demonstrated in the posterior putamen and the anterior or posterior thalamus. There were no other findings in most cases. **CONCLUSION:** MR demonstrated lesions in the putamen and thalamus in all of our six patients with severe extrapyramidal cerebral palsy who had suffered intrapartum asphyxia.

Index terms: Cerebral palsy; Brain, magnetic resonance; Pediatric neuroradiology

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The term *extrapyramidal cerebral palsy* refers to a nonprogressive but evolving motor disorder developing in early life (1). The condition is marked by the presence of a variety of involuntary movements, abnormal motor patterns, and postural instability secondary to a defective regulation of muscle tone and coordination. As a rule, one observes a variety of transitions between pure athetosis without spasticity and spasticity with only slight choreoathetotic movements. In the experience of Crothers and Paine (2), the extrapyramidal and the mixed pyramidal and extrapyramidal forms of cerebral palsy constituted 35.1% of all patients with cerebral palsy. In a more recent series (3), extrapyramidal cerebral

palsy accounted for 13.0% of all term-born subjects with cerebral palsy.

Autopsy studies on patients who during life had extrapyramidal cerebral palsy and who had an antecedent history of abnormal birth, presumably with perinatal asphyxia, have disclosed extensive and unique changes within the basal ganglia, which are frequently referred to as *status marmoratus* (4).

Although neuroimaging studies have been used to study the anatomy of other forms of cerebral palsy (5-9), few such studies are currently available for the extrapyramidal type of cerebral palsy. Yokochi et al (10), who studied the magnetic resonance (MR) findings in 22 children with extrapyramidal cerebral palsy, found symmetrical high-intensity areas in both the thalamus and putamen in six of the cases, in the thalamus alone in five, and in the putamen alone in a single case. Symmetrical periventricular high-intensity areas were seen in six children. The MR imaging study was normal in seven. Clinical details were not provided in this study, and the diagnosis of perinatal asphyxia rested solely on low Apgar scores or an abnormal neonatal period. Because MR imaging is superior to computed tomographic

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TABLE 1: Clinical characteristics of six asphyxiated children with subsequent extrapyramidal cerebral palsy

Case	Prenatal Complications	EGA (Weeks)	BWt (g)	Apgar Scores	pH (Time)	Neo SZ	Sarnat Level	Age at MR (years)	Current Clinical Condition			
									XP	P	Int	SZ
1	Fetal bradycardia, vacuum extraction	40	3540	0,3,3	6.81 (20)	+	3	13/12	1+	3+	mild mental retardation	0
2	Prolonged CS, delayed resuscitation	38	2400	1,1,1	6.82 (cord)	+	3	5 6/12	3+	2+	prof mental retardation	+
3	Fetal bradycardia, midforceps delivery	39	3180	2,2	7.33 (35)	+	2-3	14	3+	1+	near normal	0 AC
4	Shoulder dystocia	40	4230	1,0	6.84 (21)	+	2-3	6 7/12	3+	1+	near normal	0 AC
5	Fetal bradycardia, vacuum extraction	40	3164	1,1,4	6.60 (9)	+	2	12/12	2+	2+	mild delay	0
6	Meconium staining	44	3830	3,5	ND	+	2-3	19	2+	2+	mod delay	+

Note.—EGA indicates estimated gestational age; BWt, birth weight; Apgar, Apgar scores at 1, 5, and 10 minutes; pH, initial arterial pH (time when drawn in minutes); the cord pH is venous pH; ND, not done; Neo SZ, neonatal seizures; XP, severity of extrapyramidal movement disorder; P, severity of associated pyramidal signs; Int, Intelligence; SZ, seizure disorder at last examination; prof, profound; CS, cesarean section; and AC, on anticonvulsant therapy. Sarnat Level was estimated from the clinical course and classified according to the scheme of Sarnat and Sarnat (13). The values presented are the lowest Sarnat level during the neonatal period.

(CT) scans in demonstrating the proliferation of glial elements and the abnormalities of myelination characteristic of status marmoratus (11), we undertook examining a group of children whose extrapyramidal cerebral palsy was known to result from well-documented perinatal asphyxia, and relate neuroimaging findings to the clinical status.

Subjects and Methods

MR imaging was performed between the ages of 7 months and 23 years on 8 term-born patients (five male and three female) with extrapyramidal cerebral palsy. In six subjects, an element of spasticity also could be demonstrated. The extrapyramidal movements and the pyramidal component were rated as mild (1+), moderate (2+), or severe (3+) by one of us (J.H.M.) independent of the MR imaging studies.

In all cases there was a clear history of intrapartum asphyxia. The diagnosis of intrapartum asphyxia rested on evidence for severe neonatal systemic acidosis as documented by a venous cord pH of less than 7.0 whenever available, or acidosis in subsequent arterial blood gas samples, and clinical signs of an acute hypoxic-ischemic encephalopathy during the neonatal period (12). The latter was expressed in terms of the lowest Sarnat score (13). In addition, 1- and 5-minute Apgar scores were 3 or less, and there had been need for intubation or vigorous resuscitation in the delivery room.

Clinical characteristics of the subjects are summarized in Table 1.

All MR studies included sagittal, axial T1-weighted (450–600/11–16/2 [repetition time/echo time/excitations]), and T2-weighted images (2000–3000/80–150/2) obtained at 1.5 T. The presence or absence of hippocampal atrophy could not be consistently assessed on the films available and therefore was not included in the evaluation. Coronal images, which are the most satisfactory method of assessing hippocampal volume, were not in general obtained. These studies were performed over a number of years, some before the recognition of the potential for macroscopic hippocampal injury in cases of perinatal asphyxia. On axial images it is possible to recognize severe hippocampal atrophy. Although assessment of mild to moderate atrophy on occasion has been based on axial images we felt that in the present study such an approach would require too subjective a judgment.

In two subjects the MR scan was inadequate to provide details of basal ganglia structure. These subjects were excluded from further analysis. The MR studies were reviewed retrospectively by one of the authors (J.C.) who had knowledge of the diagnosis of extrapyramidal cerebral palsy but not its severity or any associated clinical findings.

Results

The appearance of the MR was remarkably uniform in all six subjects. They demonstrated focal high signal abnormalities on T2-weighted

images in the posterior putamen and anterolateral thalamus, probably the ventrolateral nucleus, or the posterior thalamus (Figs 1 and 2). In two cases prolongation of T1 at the same sites was identified (Fig 3). Otherwise the T1-weighted images were unremarkable. Apart from mild ventriculomegaly and sulcal enlargement no other

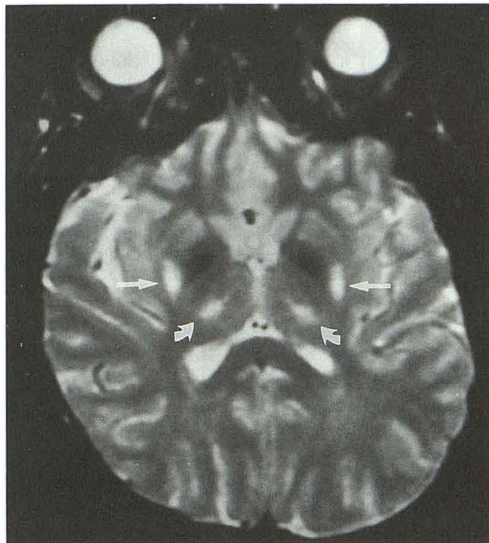


Fig. 1. Axial T2-weighted image (3000/150/1) illustrating bilateral focal hyperintensities in the posterior putamen (*straight arrows*) and the ventrolateral nucleus of the thalamus (*curved arrows*) (case 2).



Fig. 2. Axial T2-weighted image (2570/80/1) with similar focal bilateral abnormality in the putamen (*long arrows*) and thalamus (*short thick arrows*). In the thalamus the hyperintensity extends medially (*short thin arrows*) in addition to involving the ventrolateral nucleus (case 4).

abnormalities were identified in these scans. (Table 2).

Although in a few cases there was a slight increase of signal in the perirolandic white matter and/or decreased volume of the median temporal lobes, the latter suggesting hippocampal atrophy, these findings were subjective and in no case clear-cut. In addition, there was no correlation between the presence of increased signal in the perirolandic white matter and the presence or severity of spasticity.

Discussion

MR imaging is more sensitive than CT for the detection of white matter abnormalities and various minor malformations of the brain (14). In subjects with cerebral palsy MR is abnormal in the overwhelming majority of cases. Thus in the series of Truwit et al (15), 93% of 40 patients had an abnormal MR. A spectrum of findings has been reported (8, 9, 16, 17). Although the number of subjects studied is still small, and identification of the injury responsible is difficult, MR changes in cerebral palsy seem linked to the gestational age of the infant at the time of the insult. Truwit et al (15) distinguish three patterns: gyral abnormalities, isolated periventricular white matter damage, and watershed cortical or deep gray nuclear damage.

In the preterm infant who has suffered an insult during the intrapartum period or after delivery there is evidence of periventricular white matter damage, as manifested by a reduction in the normal depth of white matter, without abnormal signal hyperintensity (15). These changes are largely located adjacent to the trigone or additionally extend backward to the occipital region. They correspond to the neuropathologic picture of periventricular leukomalacia (18). Occasionally there are more extensive changes with involvement of the frontal white matter. With the loss of brain tissue, there is corresponding ventricular dilation (17). Similar white matter abnormalities have been recognized in term infants and are believed to reflect intrauterine late second- or early third-trimester injury.

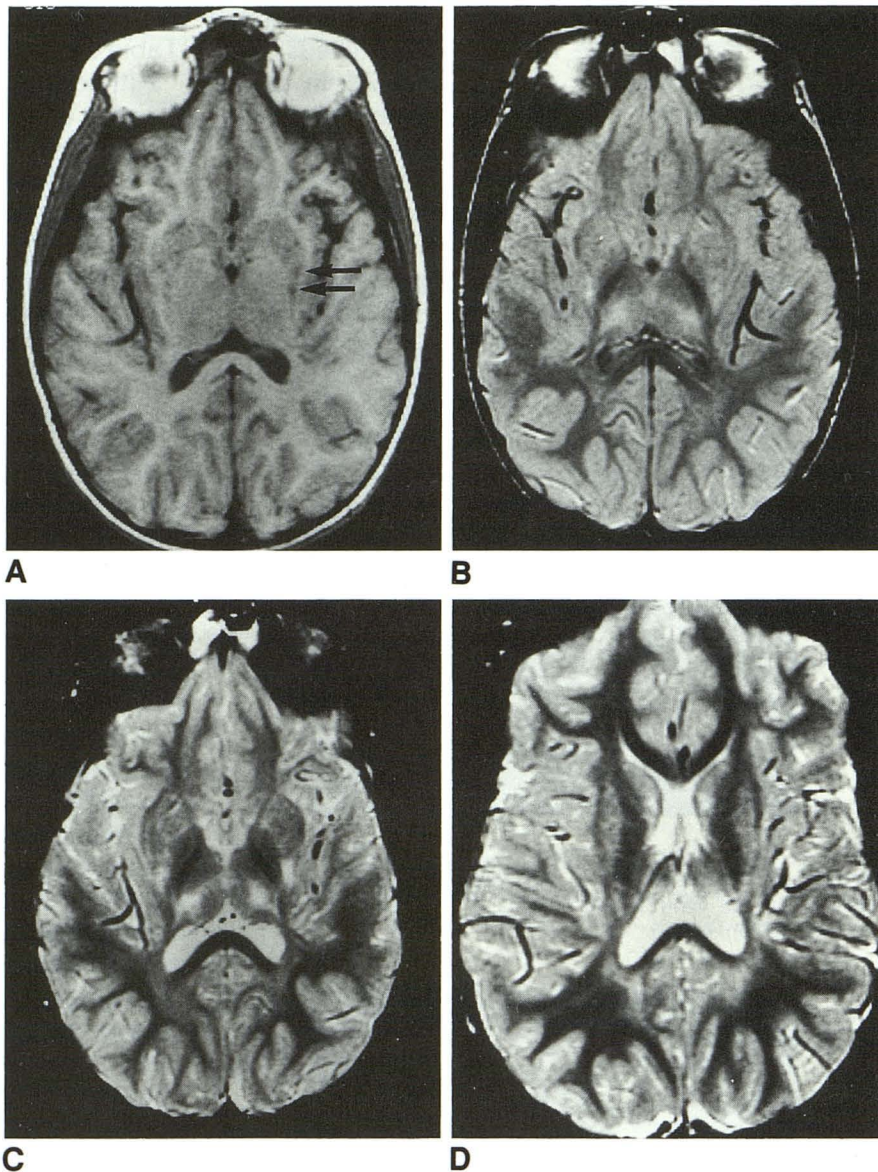
In term babies who go on to develop cerebral palsy, MR changes are more mixed. Most commonly one observes gyral abnormalities consistent with a mid-second-trimester insult, white matter abnormalities similar to those seen in premature infants, or watershed cortical or deep gray nuclear damage consistent with late-trimester,

Fig. 3. A, Axial T1-weighted image (600/15/2) demonstrating mild hypointensity in the left putamen (arrows). Changes on the right are present but minimal (case 5).

B, Proton density-weighted image (2200/30/2) at approximately the same as A demonstrating bilateral focal hyperintensity in the posterior putamen (curved arrows) and the anterolateral thalamus (straight arrows) (case 5).

C, Axial T2-weighted image (2200/80/2) at the same level as B demonstrating bilateral focal hyperintensity in the posterior putamen (short arrows) and the thalamus (long arrows) (case 5).

D, Axial T2-weighted image (2200/80/2) at the next level above A, B, and C demonstrating bilateral focal hyperintensity in the caudate nuclei (arrows), the only patient with this finding (case 5).



perinatal, or postnatal injury. Of 29 term infants with cerebral palsy, 16 revealed developmental abnormalities suggesting an intrauterine pathogenesis, in most instances consistent with mid-second-trimester injury (15).

The subset of patients with cerebral palsy who manifest an extrapyramidal movement disorder has not been extensively studied (10, 19). The causes of extrapyramidal cerebral palsy are not completely understood. In the main, the condition is associated with presumed perinatal asphyxia, with severe neonatal jaundice, or with a combination of the two. In the series compiled by Friede (20), 70% of cases were associated with complications of delivery, including severe cyanosis, the need for resuscitation, neonatal seizures, and

other neurologic signs developing soon after birth. In other series of cases, such as those reported by Brun and Kyllerman (21) and Kyllerman et al (22), the neonatal period was complicated by severe perinatal asphyxia, hyperbilirubinemia, prematurity, or reduced birth weight for gestational age. In some severely asphyxiated term infants severe deep nuclear damage may be the main manifestation. These basal ganglia changes were noted by Anton (23) and subsequently termed *status marmoratus* by Vogt (24). They are evident on gross inspection of the brain in the form of irregular white streaks in the striatum. On microscopic examination, the picture is one of glial scarring corresponding to the areas of tissue destruction. In some cases myeli-

TABLE 2: MR findings in six patients with extrapyramidal cerebral palsy

Case	Caudate	Thalamus	Putamen	Globus Pallidus	Internal Capsule
1	Faint high signal posterior bilateral	High T2 signal anterior bilateral	Faint high T2 signal posterior bilateral	N	N
2	N	High T2 signal posterior bilateral	High signal posterior bilateral	N	N
3	N	High signal posterior bilateral	High signal posterior bilateral	N	N
4	N	High signal anterior bilateral	High signal posterior bilateral	N	N
5	High signal posterior bilateral	High signal posterior bilateral	High signal posterior bilateral	N	N
6	N	High T2 signal anterior lateral bilateral	High T2 signal posterior bilateral	N	N

nated nerve fibers, probably of astrocytic origin, are found in coarse networks; in others there is symmetric demyelination. These changes are seen within the putamen, the head of the caudate nucleus, the globus pallidus, and the thalamus (11, 20). Within the thalamus, the nucleus ventralis posterolateralis, the nucleus ventralis lateralis, and the nucleus medialis are the most severely involved (25). Status marmoratus is sometimes associated with lesions elsewhere in the brain, notably with severe fibrillary gliosis in the central gray matter of the midbrain (25), cerebral hemiatrophy, microgyria, cysts in the centrum semiovale, and focal laminar necrosis of the cortex (26).

On clinical examination, a majority of these children demonstrate involuntary movements which are frequently accompanied by spasticity, and by the persistence of primitive reflex patterns (1). Neuroimaging studies have disclosed a variety of abnormalities. On CT one may see such non-specific abnormalities as ventricular dilatation and cortical atrophy (27, 28). MR imaging in a series of children whose extrapyramidal cerebral palsy was presumed to have been caused by asphyxia or jaundice demonstrated high-intensity lesions on T2-weighted images in the thalamus, putamen, or white matter (10). Severe symmetric bilateral thalamic hemorrhage or necrosis was seen on ultrasound and CT in four term infants who had suffered from postnatal hypoxemia and fatal cardiorespiratory depression (19). In one of these infants there was decreased signal intensity in the thalamus on MR, presumably reflecting destructive changes. When the injury is less severe, gliosis, leading to an increased signal intensity, would be anticipated. On ultrasound the so-called bright thalamus has been correlated with the neuropathologic lesions of status marmoratus (29). However, on follow-up of six infants with ultrasound findings of bright thalamus none de-

veloped extrapyramidal cerebral palsy; rather, spastic quadriplegia or spastic diplegia were the usual findings (30).

The exact MR substrate of status marmoratus has not yet been defined. The single patient in the series of Truwit et al (15) who had extrapyramidal cerebral palsy had a normal MR. In the five dystonic patients with an antecedent history of perinatal ischemia, reported by Rutledge et al (31), three showed a mildly diminished neostriatal signal on MR, and two others had a normal MR examination.

In older children or in adults, extrapyramidal movement disorders are often associated with MR abnormalities in the deep nuclei (31). Apart from the signal loss accompanying iron deposition observed in the Hallervorden-Spatz syndrome (32), increased signal is often seen in the caudate and putamen in subjects suffering from secondary dystonia such as occurs after a cerebrovascular infarction or infectious illness (31, 33).

On the basis of their clinical picture and the known neuroanatomic lesions, we might anticipate MR abnormalities within the basal ganglia in children with the clinical picture of extrapyramidal cerebral palsy. This indeed proved to be the case, and a uniform picture of bilateral high-intensity signals in the anterior lateral thalamus, the posterior thalamus, and the posterior putamen was observed in all seven of our patients with documented perinatal asphyxia. This being a retrospective study, we were unable to determine from clinical data whether the infants had been subjected to a bout of acute, profound asphyxia, recurrent less severe asphyxia, or a combination of the two types of events. The location of the changes appears to correspond to the location of glial scarring seen by Hayashi et al (25) in autopsied subjects who had suffered from perinatal asphyxia. Although we have seen

these lesions in preterm infants in conjunction with other abnormalities, in particular with loss of white matter, and in children with other forms of cerebral palsy (8), the unique feature in our cases is the virtual absence of any of the other MR imaging lesions associated with cerebral palsy (8, 15).

The reasons for the predilection of these areas to perinatal asphyxia are still unknown but in part could be related to higher metabolic demands made by early myelination (8). In addition, damage may be induced by excitotoxins such as glutamate (34). Silverstein et al (35) have found that perinatal asphyxia damages high-affinity glutamate uptake in the striatum. Using autoradiography, Greenamyre et al (36) found marked, transient increases in high-affinity glutamate binding in human brain after birth. Because these transient increases were limited to the globus pallidus, it is not clear why the putamen and thalamus rather than the globus pallidus bore the brunt of focal asphyxial damage in our patients. Cherubini et al (37) suggest that in early postnatal life γ -aminobutyric acid functions as an excitatory rather than an inhibitory neurotransmitter, with a receptor distribution which is totally different from that to glutamate. Obviously much more needs to be learned before we unravel the complex mosaic of neurotransmission in this area, its ontogeny, and the peculiar vulnerability of the striatum to asphyxia (8).

Our observations thus support those of earlier reports (8, 10) that in severe extrapyramidal cerebral palsy resulting from perinatal asphyxia the MR scan shows characteristic focal abnormalities in the putamen and thalamus. In one additional child whose extrapyramidal movements were caused by kernicterus the scan was normal. This is consistent with the experience of Yokochi et al. (10).

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