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Dyskinetic cerebral palsy in term asphyxiated neonates – clinical features and brain magnetic resonance imaging

Vlatka Mejaški Bošnjak[1], Ivana Đaković[1], Josip Marjanović[2], Tonći Grmoja[2]

Dyskinetic cerebral palsy is rare, occurring in about 14 per 100 000 live births and accounting for about 7% of all cerebral palsy cases, but represents one of the most disabling forms of cerebral palsy. Increasing use of magnetic resonance imaging offers an opportunity to visualize brain lesions in cerebral palsy, which are in dyskinetic cerebral palsy typically caused by hypoxic lesions of the thalami, basal ganglia and parasagittal region and hippocampus in term asphyxiated neonates. Moreover, degrees of magnetic resonance imaging lesion patterns can be defined, which correlate with the severity of motor impairment and accompanying neurodevelopmental disorders. The aim of this study was to describe the profile of motor disability and accompanying impairments in children with dyskinetic cerebral palsy in four term asphyxiated infants as well as their magnetic resonance imaging lesion patterns. All four term children had severe perinatal asphyxia according to data at birth, followed by moderate to severe hypoxic-ischemic encephalopathy in three of them. Subsequent magnetic resonance imaging showed hypoxic lesions of the thalami, basal ganglia and central regions or hippocampus, classified as mild (Patients 2 and 4) or severe (Patients 1 and 3). Neurodevelopmental outcome was poor in three of the four children. Three of them had severe dyskinetic cerebral palsy of choreoathetoid subtype, whereas the fourth patient had less severe dyskinetic cerebral palsy. Accompanying impairments were in all four patients related to severe speech disturbance, epilepsy in Patients 1 and 4, while cognitive development was normal or mildly affected. The severity of dyskinetic cerebral palsy and accompanying disorders correlated with the severity of hypoxic lesions in the strategic domain, i.e. thalamus, n. lenticularis, central regions and hippocampus.

Keywords: cerebral palsy; asphyxia; infant, newborn; thalamus; basal ganglia; hippocampus; magnetic resonance imaging

INTRODUCTION

Cerebral palsy (CP) is the most common cause of physical disability in early childhood, affecting 2-3 *per* 1000 live-births (1). The Surveillance of Cerebral Palsy in Europe (SCPE) is the largest international collaborative study among cerebral palsy registers and surveys in the world (1). According to the SCPE proposed classification of CP, there are three basic types: spastic, dyskinetic and ataxic, with subtypes of bilateral and unilateral spastic cerebral palsy, and dystonia or choreo-athetosis for dyskinetic cerebral palsy (1). For further functional assessment of CP, the Gross Motor Function Classification System (GMFCS) and Bilateral Fine Motor Function (BFMF) are used to assess the function of lower limbs and upper limbs, respectively, and accompanying neurodevelopmental disorders (visual, hearing, intellectual, epilepsy) are recorded as well (1-3).

Dyskinetic cerebral palsy is rare, occurring in about 14 *per* 100 000 live births, accounting for about 7% of total CP, but represents one of the most disabling forms of cerebral palsy (4-8).

[1] Department of Pediatrics, Children's Hospital Zagreb, Klaićeva 16, Zagreb
[2] Clinical Department of Children's Radiology, Children's Hospital Zagreb, Klaićeva 16, Zagreb

Correspondence to:
Vlatka Mejaški Bošnjak, MD, PhD, Children's Hospital Zagreb, Department of Pediatrics, Klaićeva 16, 10000 Zagreb,
e-mail: vlatka.mejaskibosnjak@gmail.com

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TABLE 1. Perinatal history

Patient no.	Gender	Gestational age	Birth weight/length	Clinical data
1	F	39	2920/?	Meconium aspiration, Apgar score 1/3, resuscitation, artificial ventilation, neonatal seizures day 1-4, HIE stage 3
2	M	39	2650/47	IUGR, ruptured uterus, placental abruption, emergency CS, meconium stained amniotic fluid, Apgar score 1/3, neonatal seizures day 1-3, HIE stage 2
3	F	39	4000/54	Dystocia, prolonged labor, abnormal CTG, vacuum extraction, Apgar score 1/2/4, resuscitated, seizures day 1-3, HIE stage 2
4	M	42	3750/52	Post term, meconium aspiration, Apgar score 3/5, resuscitated

Legend: IUGR = intrauterine growth retardation; CS = cesarean section; CTG = cardiotocography; HIE = hypoxic-ischemic encephalopathy (Sarnat and Sarnat)

TABLE 2. Classification of motor impairment and associated disorders in children with dyskinetic choreoathetoid cerebral palsy at last assessment

Patient no.	Gender	Age at last assessment (yrs)	GMFCS level	BFMF level	Cognitive impairment	Communication (Viking speech scale)	Visual impairment	Epilepsy
1	F	4.5	5	5	Mild	4	Mild	Yes
2	M	15.5	5	5	No	3	No	No
3	F	14	5	5	Mild	4	No	No
4	M	16.5	2	3b	Mild	3	No	Yes

Legend: GMFCS = Gross Motor Function Classification System; BFMF = Bilateral Fine Motor Function

TABLE 3. Magnetic resonance imaging of the brain in children with dyskinetic-choreoathetoid cerebral palsy

Patient no.	Gender	Number of MRI studies	Lesion pattern	Affected brain region			
				Thalamus	N. lentiformis	Central region	Hippocampus
1	F	2	severe	Ventrolateral	+	+	+
2	M	1	mild	Ventrolateral	+	-	-
3	F	3	severe	Ventrolateral	+	+	+
4	M	5	mild	Ventrolateral	+/-	-	-

Increasing use of magnetic resonance imaging (MRI) offers an opportunity to visualize brain lesions in children with CP, which are in dyskinetic CP typically caused by hypoxic lesions of the thalami, basal ganglia, parasagittal region and hippocampus in term asphyxiated neonates (9-12). Moreover, degrees of MRI lesion patterns can be defined, which correlate with the severity of motor impairment and accompanying neurodevelopmental disorders (9-13).

Dyskinetic cerebral palsy is characterized by abnormal patterns of posture and/or movement or accompanied by involuntary, uncontrolled, recurring and occasionally stereotyped movements, thus dyskinetic CP may be either of dystonic subtype, dominated by hypokinesia and hypertonia, or of choreoathetoid subtype, dominated by hyperkinesia and hypotonia (5-8). Motor impairment is often, but not always, severe (5-8). Speech and language are disturbed, necessitating alternative and augmentative communication (5-8).

The aim of this study was to describe the profile of motor disability and accompanying impairments in children with dyskinetic CP in four term asphyxiated infants, as well as their MRI lesion patterns.

SUBJECTS AND METHODS

Perinatal history of the four children is shown in Table 1. All four children were born at term and experienced sentinel perinatal event, three of them fulfilled the criteria for moderate/severe hypoxic-ischemic encephalopathy according to Sarnat and Sarnat criteria (14). Patient 2 additionally had intrauterine growth retardation (IUGR).

All four children later developed CP, which was classified according to SCPE criteria, using GMFCS and BFMF scales for upper and lower limb functions, respectively, and accompanying impairments were noted: cognitive, sensory (visual, hearing) and epilepsy (1-3). Communication problems were considered as well. Speech disturbances were assessed using the so-called Viking scale (15).

All children underwent MRI examination using 1.5 T machine under general anesthesia to avoid artifacts caused by involuntary movements.

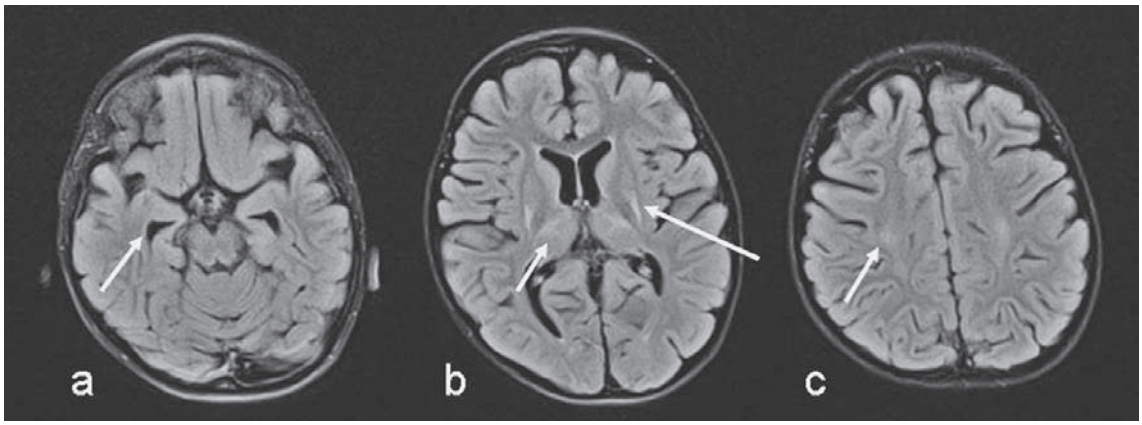

FIGURE 1. **Patient 1 magnetic resonance imaging, axial FLAIR sequence: a) enlarged temporal horns of lateral ventricles, indirectly pointing towards lesion of the hippocampus (arrow); b) basal ganglia and thalamus lesions with abnormally high signal; long arrow indicates pathology in the posterior putamen and short arrow in the ventrolateral thalamus; c) level of the central region and motor cortex: abnormally high signal subcortically (arrow) with white matter atrophy.**

RESULTS

Clinical data on neurodevelopmental outcome are shown in Table 2 and MRI findings in Table 3.

Classification of motor impairment (type and subtype of CP) was performed in all four children between age 4.5 and 16.5 years. All four children had dyskinetic cerebral palsy with choreoathetoid subtype. Three of them, i.e. Patients 1, 2 and 3, had severe CP (GMFCS level 5 and BFMF level 5), whereas Patient 4 had moderate motor impairment (GMFCS level 2, BFMF level 3b). Communication due to orofacial dyskinesia was hampered causing no understandable speech in Patients 1 and 3 (Viking speech scale level 4) and moderately disturbed speech, i.e. unclear speech and not usually understandable to unfamiliar listeners out of context (Viking speech scale level 3) in Patients 2 and 4. Three of four patients had active epilepsy, whereas Patient 3 was seizure-free at the last assessment at age 14 years.

Cognitive impairment was mild in Patients 1, 3 and 4, being difficult for objective assessment due to communication problems. Only Patient 2 was assessed to have normal cognitive functions. Mild visual impairment was only recorded in Patient 1, whereas the other three patients had normal vision and hearing. All four children underwent MRI of the brain: Patient 2 only once at the age of 14 years; Patient 1 twice at the age of 11 months and 4.5 years; Patient 3 three times, in neonatal age and subsequent MRIs at the age of 3 and 9 years; and Patient 4 had five MRIs, the last one at the age of 15 years under general anesthesia because all previous MRIs were inconclusive due to the artifacts caused by dyskinesias. This patient had mild lesion pattern, affecting only ventrolateral thalamus and *posterior putamen*. Patient 2 also had mild lesions of the ventrolateral thalami and putamen, although more expressed than in Patient 4.

Patients 1 and 3 had severe lesion patterns with affected thalamus, *n. lentiformis*, central cortical region and hippocampus (Figure 1 a, b, c).

DISCUSSION

Dyskinetic CP is a less common type of CP with the prevalence varying among different CP registers from 3% to 7% of all CP children (4-8).

These differences may be explained by varying diagnostic criteria (4-8). In some centers, coexistence of spastic and dyskinetic signs always leads to the diagnosis of spastic CP, whereas in others the dominant symptom provides the basis for diagnosis. That is true for cases of children with dyskinesia (in the form of choreo-athetosis and/or dystonia), as the disabling movement disorder, irrespective of added signs of spasticity, is diagnosed as dyskinetic CP (4-8).

The majority of children with dyskinetic CP are born as full term, have had experienced perinatal sentinel events and with neuroimaging findings supporting a perinatal etiology (9-12). This was the case in all four patients presented.

Three different degrees of MRI lesion patterns could be defined: mild pattern (involvement of *nucleus lentiformis* and ventrolateral thalamus only), intermediate pattern (involvement of *nucleus lentiformis*, ventrolateral thalamus and pericentral region), and severe pattern (involvement of *nucleus lentiformis*, entire thalamus, pericentral region and hippocampus). This grading of MRI findings correlates significantly with the severity of motor impairment and accompanying neurodevelopmental disorders (13, 16, 17).

Patient 1 suffered from severe hypoxic-ischemic encephalopathy (stage 3), which caused a severe pattern of the thalami, *n. lentiformis*, parasagittal and hippocampus hypoxic

lesions. Neurodevelopmental outcome was poor, with severe dyskinetic CP choreoathetoid subtype, active, intractable epilepsy, no understandable speech, and mild cognitive and visual problems.

Patient 2 had moderate hypoxic-ischemic encephalopathy (stage 2), mild pattern of ventrolateral thalamic and putamen lesions. He had severe dyskinetic (choreoathetoid) CP with severely affected speech but normal cognitive development, no epilepsy and sensory deficit.

Patient 3 had moderate hypoxic-ischemic encephalopathy (stage 2), with a severe pattern of hypoxic thalamic, *n. lentiformis*, parasagittal region and hippocampus lesions. She also had severe dyskinetic (choreoathetoid) CP, no understandable speech, mild cognitive impairment, but no epilepsy and sensory deficit.

Patient 4 had sustained severe perinatal asphyxia without hypoxic-ischemic encephalopathy. Four brain MRIs were performed from the age of 3 years onwards, being interpreted as normal findings although obtained on a lower resolution MRI machine or technically disturbed by the child's dyskinesias. The last MRI obtained under general anesthesia on a higher resolution MRI machine demonstrated a mild pattern of ventrolateral thalami and *posterior putamen* lesions. He had mild dyskinetic CP. Communication problems occurred due to orofacial dyskinesias, which together with athetotic hand movements aggravated his school performance. His epilepsy was well controlled and he had no sensorial problems.

Thus, the severity of dyskinetic CP in all four our patients corresponded with the extent of thalamus and basal ganglia, parasagittal and hippocampal lesions. All four patients had severe communication problems, two of them active epilepsy, but cognitive functions were normal or mildly affected.

In cases of asphyxiated neonates who are later developing dyskinetic CP, MRI of good quality is an important diagnostic step (13, 16, 17). Lesions, although small but in strategic domains, can cause severe motor and accompanying neurodevelopmental disorders (visual, hearing, intellectual, communication, epilepsy, etc.), but may be overlooked, therefore indicating unnecessary further diagnostic procedures (13, 16, 17).

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SAŽETAK

Diskinetska cerebralna paraliza u terminske asfiktične novorođenčadi – klinička obilježja i prikaz magnetske rezonancije mozga

Vlatka Mejaški Bošnjak, Ivana Đaković, Josip Marjanović, Tonći Grmoja

Diskinetska cerebralna paraliza je rijetka, javlja se u oko 14 na 100 000 živorođenih, s udjelom od oko 7% ukupnih slučajeva cerebralne paralize, ali je ujedno i njen oblik koji najviše narušava kakvoću života. Sve veća uporaba magnetske rezonancije poboljšava mogućnosti prikazivanja lezija vezanih za cerebralnu paralizu, a koje su u diskinetske cerebralne paralize tipično uzrokovane hipoksičnom lezijom talamusa, bazalnih ganglija i parasagitalne regije te hipokampusa u donošene djece koja su pretrpjela perinatalnu asfiksiju. Štoviše, pomoću magnetske rezonancije moguće je stupnjevati uzorke lezija koji koreliraju sa stupnjem motoričkog oštećenja i pridruženih odstupanja. Cilj ove studije je opisati karakteristike motoričkog oštećenja i pridruženih odstupanja u djece s diskinetskom cerebralnom paralizom prikazom četvero terminske djece koja su imala perinatalnu asfiksiju kao i slikovne prikaze uzoraka lezija mozga učinjene magnetskom rezonancijom. Sve četvero djece imalo je tešku perinatalnu asfiksiju, prema podatcima vezanim za porođaj, praćenu umjerenom do teškom hipoksično-ishemičnom encefalopatijom u troje od njih. Naknadni prikaz magnetskom rezonancijom pokazao je hipoksične lezije talamusa, bazalnih ganglija i centralne regije te hipokampusa, koje su klasificirane kao blage (bolesnici 2 i 4) ili teške (bolesnici 1 i 3). Neurorazvojni ishod je loš u troje od četvero djece. Troje ima tešku diskinetsku cerebralnu paralizu koreo-atetotskog podtipa, dok četvrti bolesnik ima blažu diskinetsku cerebralnu paralizu. Pridružena odstupanja se u sve četvero djece odnose na teški poremećaj govora, epilepsiju u bolesnika 1 i 4, dok je kognitivni razvoj uredan ili blago poremećen. Težina diskinetske cerebralne paralize i pridruženih odstupanja odgovara težini hipoksičnih lezija u strateški važnim područjima, tj. talamusu, n. lenticularisu, centralnim regijama i hipokampusu.

Ključne riječi: cerebralna paraliza; asfikcija; novorođenče; talamus; bazalne ganglije; hipokampus; magnetska rezonancija