Recent advances in dyskinetic cerebral palsy

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Background: Dyskinetic cerebral palsy results from extrapyramidal damage, often with high handicap in movement and hard to treat. In this article, we discuss the classification of epidemiology and etiology, neuroimaging findings, treatment and prognosis of dyskinetic cerebral palsy in children.

Data sources: The literature about dyskinetic cerebral palsy was reviewed.

Results: Dyskinesia accounts for approximately 20 percent in all types of cerebral palsy. The primary semiological features of dyskinetic cerebral palsy are voluntary motion disorders with increased involuntary movements which may show various combined symptoms such as torsion spasm, dystonia, chorea, athetosis and so on. Dyskinesia due to hypoxic ischemic brain injury and bilirubin encephalopathy may have different clinical and pathophysiological basis. The magnetic resonance imaging (MRI) findings of dyskinesia are characteristic. In general, the handicaps relating to dystonia belong to moderate and severe disabilities, which are almost hard to ambulate, while pure athetosis are mild disabilities with good prognosis.

Conclusions: The symptoms and neuroimaging findings are dependent on the period, etiology, spot of brain lesions. MRI should be considered as the optimal selection for the diagnosis and etiological research of dyskinetic cerebral palsy.


Key words: dyskinetic cerebral palsy; semiology; etiology; neuroimaging findings; prognosis

Cerebral palsy as a chronic disease of the central nervous system is harmful to the physical and mental health of children, with a high prevalence rate and morbidity. Dyskinetic cerebral palsy, the commonest type resulting from extrapyramidal damage, is often associated with severe handicap in movement and hard to treat[1,2]. In recent years, studies have shown that dyskinetic cerebral palsy may display various syndromes corresponding with different etiologies and lesions[3-5]. The magnetic resonance imaging (MRI) findings of dyskinetic cerebral palsy are also correlated with the clinical situation.

Semiology and classification

Extrapyramidal primary lesions in the basal ganglia may result in voluntary motion disorders with increased involuntary movements, showing torsion spasm, dystonia, chorea, athetosis and others. How these symptoms are combined in children with dyskinetic cerebral palsy depends on the period, etiology, and spot of the brain lesions. Moreover, many signs including remnants of primitive reflects, hypotonia of the head and trunk, difficulty in keeping a posture[6] may occur too. Yokochi et al[6] examined motor function of 35 children with dyskinetic cerebral palsy retrospectively using videotape recordings made at 5 to 8 months of age. Many infants showed asymmetric tonic neck, Moro and Galant reflexes. Movements shown to be difficult included keeping a symmetric supine posture, isolated movements of the hips and knees, forward extension of the upper extremity, extension of the neck and trunk in prone position and in ventral suspension, flexion of the neck in traction response, and weight support by the upper extremities. Asymmetric or excessive opening of the mouth was present in all infants.

In the past decades in China, cerebral palsy caused by extrapyramidal lesions was defined as athetosis and was further divided into tense type and non-tense type[7]. These guidelines were controversial because of their restriction. According to the new classification...
Epidemiology and etiology

In recent years, epidemiological studies have shown that the prevalence of cerebral palsy was around 2‰ to 3‰, and that of dyskinesia about 11.4% to 15%. A sampling survey in 6 cities of China from May 1997 to October 1998 showed that the prevalence of cerebral palsy was 1.92‰, of which 4.63% went for athetosis, fewer than reported overseas. Similarly, the lower prevalence of dyskinetic cerebral palsy was reported in other areas of China too. This disparity is related to the diagnostic techniques used by investigators including pediatricians, neurologists and healthcarers, who only received short-term training. However, case analysis at our rehabilitation center showed that dyskinetic cerebral palsy held 19.1% to 21.2% in all types, close to 28.6% reported elsewhere.

Dyskinesia is mainly due to hypoxic ischemic brain injury and bilirubin encephalopathy, which cause selective injury to the basal ganglia in children. Near-total perinatal asphyxia causes selective lesions in the putamen and thalamus because in severe hypoxic-ischemic encephalopathy, the excitatory glutamatergic pathways into the putamen and thalamus are overactive, but the globus pallidus may be protected because its activity is silenced by inhibitory neuronal activity. In contrast, the relatively high resting neuronal activity in the globus pallidus might make it more vulnerable to less intense, subacute oxidative stresses from mitochondrial toxins such as bilirubin or from genetic mitochondrial disorders.

The pathogenesis of bilirubin encephalopathy is multifactorial, involving the transport of bilirubin or albumin/bilirubin across the blood-brain barrier and delivering bilirubin to target neurons. Also disruption or partial disruption of the blood-brain barrier by disease or hypoxic ischemic injury facilitates transport of bilirubin/albumin into the brain. The main target neurons are the basal ganglia, ocular movement nucleus, and acoustic nucleus of the brain stem. The mild disruption is left cognition impairment, while the severe one results in dyskinetic cerebral palsy, showing the involvement of dystonia, chorea, athetosis, which is often associated with upgaze paralysis and sensorineural deafness. In spite of the incidence of typical kernicterus that leads to cerebral palsy has been greatly reduced by effective monitoring and treatment for hyperbilirubinemia, the disease conditions especially bilirubin toxic reaction in preterm infants may have a high risk of brain damage, that even occurs at the safe level of bilirubin.

Hypoxic ischemic brain injury has been the principal cause for dyskinetic cerebral palsy, often associated with pyramidal lesions. In 22 children with dyskinetic cerebral palsy reported by Yokochi et al, 16 had perinatal asphyxia, 4 had no association with predisposing conditions, and only 2 had neonatal jaundice. Guitet et al reported 20 full-term children with dyskinetic cerebral palsy; fetal distress was observed in 15 patients, of whom 10 had clinical manifestations of neonatal hypoxia ischemia, and only 1 had severe hyperbilirubinemia. Krageloh-Mann et al reported 17 patients, of whom 9 had birth asphyxia, and 4 had neonatal shock; no adverse event was identified in 4 patients.

Dyskinetic cerebral palsy has the risk of familial recurrence. Amor et al studied 22 patients with dyskinetic cerebral palsy and found that 16 patients in...
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a literature search had familial recurrence of athetoid cerebral palsy, which was typically associated with significant spasticity, microcephaly, intellectual disability, seizures, and lack of birth asphyxia. Most of these signs could be explained by either autosomal-recessive or X-linked-recessive inheritance. The risk of the recurrence in siblings being lower than 10% may suggest genetic contribution to dyskinesia.

**Neuroimaging findings**

It has been reported that the detection rate of cerebral palsy by MRI is 80%-100%[^19],[^29] and that MRI findings are related to the type, cause, and gestational age of the disease[^32,33]. Others reported a MRI detection rate of 54.5% for dyskinetic cerebral palsy[^19]. In premature babies with PVL, the MRI detection rate was 87%, whereas in term infants with derangements of the globus pallidus, putamen, and thalamus, which are related to asphyxia and jaundice, the MRI detection rate was 17%[^24,31,38]. The abnormal findings in patients with dyskinesia caused by bilirubin encephalopathy were in the globus pallidus, whereas those by hypoxia were in the putamen and thalamus.[^2,9]

Krageloh-Mann et al[^5] investigated 17 patients with cerebral palsy (aged from 1 year and 6 months to 17 years) who had bilateral lesions of the basal ganglia and thalamus. They divided MRI lesions into 3 patterns: mild (involving the nucleus lentiformis and ventro-lateral thalamus; n=7), moderate (involving the nucleus lentiformis, ventro-lateral thalamus, and pericentral region; n=3), and severe (involving the nucleus lentiformis, entire thalamus, pericentral region, and hippocampus; n=7). This grading correlated significantly with the severity of both cognitive and motor impairment and type of cerebral palsy. Pure dyskinetic cerebral palsy was only seen in the mild pattern, whereas dyskinetic-spastic or spastic cerebral palsy was seen in the 3 lesion patterns. Dyskinetic-spastic cerebral palsy was more related to the moderate pattern and pure spastic cerebral palsy more related to the severe pattern. Yamada et al[^5] divided 38 patients with severe cerebral palsy associated with motor delay and mental retardation into 5 types according to their MRI. Type 1: nine patients showed predominantly cyst-like ventricles and periventricular hyperintensity (PVH) on T2-weighted imaging and only scarred basal ganglia and thalamus were visible. All suffered from neonatal asphyxia and the clinical type was rigospastic tetraplegia (RST). Type 2: eleven patients showed predominantly PVH and hyperintensity on T2-weighted (HT2) in the basal ganglia and thalamus. All suffered from neonatal asphyxia and the clinical type was RST or rigospastic diplegia. Type 3: five patients showed PVH and three had cortical atrophy. All suffered from neonatal asphyxia and the clinical type was spastic diplegia. Type 4: four patients showed predominantly HT2 in the putamen and thalamus. Three had cortical atrophy. All suffered from neonatal asphyxia. The clinical type was athetotic CP (ATH). Type 5: nine patients showed predominantly HT2 in the globus pallidus. Four had cortical atrophy and two had hippocampal atrophy. All suffered from neonatal jaundice and the clinical type was ATH. All the patients who suffered from neonatal asphyxia and spastic cerebral palsy had MRI in PVH. All the patients who suffered from neonatal asphyxia and ATH showed HT2 in the putamen and thalamus. Almost all the patients who suffered from neonatal jaundice and ATH showed HT2 in the globus pallidus.

Menkes and Curran[^6] identified the characteristic MR findings in 6 patients with intrapartum asphyxia who subsequently developed extrapyramidal cerebral palsy. In all these patients focal high signal abnormality was found in the posterior putamen and the anterior or posterior thalamus. In 20 patients with dyskinetic cerebral palsy studied by Guitet et al retrospectively,[^27] abnormal MR findings included high intensity areas on T2 weighted images in the nucleus thalamus (6 patients), putamen (4), thalamus and putamen (1), thalamus and pallidus (2), thalamus and lenticular nucleus (3), and lenticular nucleus (1). In 5 patients, high intensity areas were identified on T1 weighted images at the same sites. Their findings suggested that dyskinetic cerebral palsy had characteristic focal MR abnormalities in the basal ganglia, especially in the putamen and thalamus.

Govaert et al[^31] studied 8 infants (preterms or terms) with jaundice prospectively. Among them, 5 preterm infants of 25-29-week gestational age presented with the levels of total serum bilirubin (TSB) below the exchange transfusion thresholds. One infant died on day 150, and the rest had dyskinesia and hearing loss. Hyperintense on T1 was observed in the globus pallidus in the early period but hyperintense on T2-weighted MR images in the late. Two patients showed MRI abnormalities in the hypothalamus, and 3 full-term infants with typical kernicterus with MRI images similar to those of the preterms.

[^1]: World J Pediatr, Vol 2 No 1 · February 15, 2006 ·
Other scholars reported that bilateral symmetric hyperintense signal changes in the globus pallidus on MRI should be considered as severe neonatal indirect hyperbilirubinemia. These studies indicated that brain MR imaging should be selected to identify the causes of dyskinesia patients.

**Treatment and prognosis**

Dyskinesia and dystonia as moderate or severe handicap in children with cerebral palsy could be evaluated according to the International Classification of Impairments, Disabilities and Handicap (ICID) and the Gross Motor Function Classification System (GMFCS). The handicap involves the voluntary movements of shifting, hand function, language, and skills of social communication. Current treatments of the disease include exercise rehabilitation for neuroauxology in consideration of all handicaps and the relevant lesioned areas. They should concentrate on early physical and occupational recovery, as well as early correction of mouth movement, eating skills, speech and language function. The therapist should recognize (1) primary impairments of muscle tone/movement patterns, distribution of involvement, balance, and sensory impairment; (2) secondary impairments of range of motion/joint alignment, force production, health, and endurance; (3) personality characteristics or motivation; and (4) family factors including support to children, family expectations, and support to the family. Besides, personal training program is needed, emphasizing the importance of family training. Most importantly, posture control keeping the head, neck, trunk, extremities in a centralized and stable position in any time is helpful to carry out relaxation therapy and avoid any stimulations aggravating the symptoms, for instance, changing posture frequently, resistant motion, and clapping with strong pressure. Hence, children with cerebral palsy can be trained to control posture, to decrease involuntary movements, and to make voluntary movements accurately and effectively.

Treatment options in the management of spasticity in children with cerebral palsy included chemodenervation with botulinum toxin or phenol, rhizotomy, intrathecal baclofen, and orthopedic surgery. Those methods usually did not work in dyskinesia. In several studies, intrathecal baclofen was proved effective in the treatment of dystonia in patients with cerebral palsy. Dachy et al evaluated the effect of intrathecal baclofen in a group of dystonic children by electrophysiological procedures previously validated in spastic children. They found that H reflex and area of flexor reflex significantly decreased after baclofen, though no significant clinical improvement of the Barry-Albright Dystonia Scale (BADS) was observed.

Few studies focused on the prognosis of dyskinesia. Nordmark et al studied 167 patients with cerebral palsy who were born in the period of 1990-1993. They found that independent ambulation occurred in 86% of patients with hemiplegias, 63% of patients with pure ataxia, 61% of patients with diplegia, 21% of patients with dyskinesia, and none of patients with tetraplegia. This finding suggested the poor prognosis in patients with dyskinesia and tetraplegia. In 18 children with lesions in the thalamus and putamen reported by Yokochi et al, two thirds suffered from pure athetosis and mild disabilities or moderate mental retardation and could walk alone. Ten children had the lesion in the thalamus, putamen, and peri-Rolandic area. Their symptoms of dyskinesia were characterized by severe disabilities such as severe mental retardation and inability to sit, speak words or grasp an object. We conclude that the prognosis of dyskinesia is related to the region of lesion and the cognition level of the patient.

In conclusion, dyskinesia as the main type of cerebral palsy that results from extrapyramidal lesion accounts for 10%-30% of all types of the disease. Its clinical symptoms can be subdivided into different types according to the etiology of the lesion. Further classification of the symptoms is necessary. The MRI findings of dyskinesia are characteristic. The lesion in the thalamus and putamen was due to hypoxic ischemia, whereas in the globus pallidus and hypothalamus it was due to kernicterus. The handicaps is related to the types of symptoms of the disease. When dystonia belongs to moderate and severe disabilities, patients are almost hard to ambulate, but those with pure athetosis of mild disabilities with eusemia may show a good prognosis.

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