The clinical outcomes of deep gray matter injury in children with cerebral palsy in relation with brain magnetic resonance imaging

Ja Young Choi [a], Yoon Seong Choi [b], Dong-wook Rha [a], Eun Sook Park [a],*

[a] Department of Rehabilitation Medicine, Severance Hospital, Research Institute of Rehabilitation Medicine, Yonsei University College of Medicine, Seodaemun-gu, Seoul 03722, Republic of Korea
[b] Department of Radiology, Severance Hospital, Yonsei University College of Medicine, Seodaemun-gu, Seoul 03722, Republic of Korea

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ABSTRACT

In the present study we investigated the nature and extent of clinical outcomes using various classifications and analyzed the relationship between brain magnetic resonance imaging (MRI) findings and the extent of clinical outcomes in children with cerebral palsy (CP) with deep gray matter injury. The deep gray matter injuries of 69 children were classified into hypoxic ischemic encephalopathy (HIE) and kernicterus patterns. HIE patterns were divided into four groups (I–IV) based on severity. Functional classification was investigated using the gross motor function classification system-expanded and revised, manual ability classification system, communication function classification system, and tests of cognitive function, and other associated problems. The severity of HIE pattern on brain MRI was strongly correlated with the severity of clinical outcomes in these various domains. Children with a kernicterus pattern showed a wide range of clinical outcomes in these areas. Children with severe HIE are at high risk of intellectual disability (ID) or epilepsy and children with a kernicterus pattern are at risk of hearing impairment and/or ID. Grading severity of HIE pattern on brain MRI is useful for predicting overall outcomes. The clinical outcomes of children with a kernicterus pattern range widely from mild to severe.

What this paper adds: Delineation of the clinical outcomes of children with deep gray matter injury, which are a common abnormal brain MRI finding in children with CP, is necessary. The present study provides clinical outcomes for various domains in children with deep gray matter injury on brain MRI. The deep gray matter injuries were divided into two major groups; HIE and kernicterus patterns. Our study showed that severity of HIE pattern on brain MRI was strongly associated with the severity of impairments in gross motor function, manual ability, communication function, and cognition. These findings suggest that severity of HIE pattern can be useful for predicting the severity of impairments. Conversely, children with a kernicterus pattern showed a wide range of clinical outcomes in various domains. Children with severe HIE pattern are at high risk of ID or epilepsy and children with kernicterus pattern are at risk of hearing impairment or ID. The strength of our study was the assessment of clinical outcomes after 3 years of age using standardized classification systems in various domains in children with deep gray matter injury.

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* Corresponding author at: Department of Rehabilitation Medicine, Severance Hospital, Research Institute of Rehabilitation Medicine, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 03722, Republic of Korea.
E-mail addresses: 0275502@yuhs.ac (J.Y. Choi), COSMOSPLANT@yuhs.ac (Y.S. Choi), MEDICUS@yuhs.ac (D.-w. Rha), pes1234@yuhs.ac (E.S. Park).

1. Introduction

Brain magnetic resonance imaging (MRI) is the optimal modality for early evaluation of the site and severity of brain injury. Therefore, visualizing the brain lesion and obtaining an insight into the outcome prediction is recommended in children with cerebral palsy (CP). Overall, 70–90% of children with CP have abnormal brain MRI findings that can be categorized into brain malformation, white matter damage and focal infarct, cortical-subcortical lesion and deep gray matter injury involving basal ganglia and thalamus. Previous population-based studies reported that deep gray matter injury, were found in 12.8–36.3% of children with CP (Bax, Tydeman, & Flodmark, 2006; Himmelmann, Hagberg, Beckung, Hagberg, & Uvebrant, 2005; Himmelmann, Hagberg, & Uvebrant, 2010; Reid, Dagia, Ditchfield, Carlin, Meehan, 2014; Towsley, Shevell, Dagenais, & Consortium, 2011).

The two distinguishable causes of deep gray mater injury on neuroimaging are neonatal hypoxic ischemic encephalopathy (HIE) and kernicterus (Hoon, 2005). In neonates with HIE, deep gray matter is the most prevalent site of injury (Rutherford et al., 2010), and thus brain MRI findings in neonates affected by HIE are characterized by abnormal signal intensity in the basal ganglia, thalamus and posterior limb of the internal capsule (Rutherford et al., 2006; Rutherford et al., 2010).

Deep gray matter injury resulting from acute perinatal hypoxia-ischemia has been recognized as an important cause of death and CP (Martinez-Biarge et al., 2011). Basal ganglia and thalamus play a key role in motor and postural control, locomotion and cognition (Utter & Basso, 2008) and thus the overall outcomes of children with deep gray matter injury resulting from HIE are unfavorable (Arnfield, Guzzetta, & Boyd, 2013; Himmelmann & Uvebrant, 2011; Himmelmann et al., 2005; Krageloh-Mann et al., 2002; Reid, Dagia, Ditchfield, Carlin, & Reddihough, 2014). On the other hand, other studies demonstrated the wide ranges of motor impairments of the children with deep gray matter injury according to the involvement of deep gray matter injury in the survivors of neonatal HIE (Krageloh-Mann et al., 2002; Martinez-Biarge et al., 2011; Martinez-Biarge, Diez-Sebastian, Rutherford, & Cowan, 2010).

Kernicterus is a pathologist's term describing the yellow deposits and brain cell death caused by very high levels of bilirubin (Maimburg, Bech, Bjerre, Olsen, & Moller-Madsen, 2009). The brain MRI of kernicterus is characterized by abnormally high bilateral signal intensity in the globus pallidus on T2-weighted images and hypointensity on T1-weighted images in the globus pallidus, especially on the posteromedial border (Manchanda, Prasad, & Baruah, 2013; Sugama, Soeda, & Eto, 2001). To the best of our knowledge, the clinical outcomes of children with kernicterus pattern on brain MRI have rarely been investigated.

An increasing trend in clinical practice is to classify CP based on functional independence including gross motor function and manual ability in daily life using the gross motor function classification system-expanded and revised (GMFCS-E&R) and the manual ability classification system (MACS). Recently, the communication function classification system (CFCS) has been used to characterize the daily communication abilities of children with CP. Combining the CFCS with the GMFCS-E&R and the MACS contributes to better delineation of the functional profile of children with CP (Hidecker et al., 2011). In addition, cognition plays an important role in functional independence and academic achievement. However, to our best knowledge, the clinical outcomes in various domains in relation with the degree of gray matter injury have rarely been investigated in children with CP.

Therefore, the aim of this study is to investigate the relationship between clinical outcomes in various domains such as gross motor, manual ability, cognitive and communication functions and the degree of gray matter injury of the children with CP.

2. Participants and methods

2.1. Participants

The present study was retrospective in design. This study was conducted in a university-affiliated, tertiary-care teaching hospital that includes pediatric rehabilitation department. The medical records of children with CP or developmental delay were reviewed between January 2006 and December 2014. As a result, the medical records of 7516 children were reviewed. Of those, 2843 children had brain MRIs which were entered into a picture achieving and communication system (PACS). Among them, 1633 children with a final diagnosis of CP were followed until at least 3 years of age and 81 children with deep gray matter injury without other combined brain lesions such as periventricular leukomalacia, cerebellar involvement, multicystic encephalomalacia, congenital malformation or focal cortical infarcts were selected (YS Choi). Eight children were excluded because brain MRI was performed before 6 months of age, and 4 were excluded due to incomplete functional level classification or cognitive function evaluation. Consequently, 69 children who had deep gray matter injury were selected for this study.

The characteristics of the subjects are described in Table 1. All children were born at term or near term except in two cases. One subject was born at 26 weeks' gestational age and experienced hypoxic brain injury at a corrected age of 6 weeks and the other subject had a history of urgent cesarean section due to fetal heart beat deterioration at 34 weeks' gestational age.

Nine children were younger than 4 years of age at the last follow-up visit. Of those, six were at GMFCS-E&R level V with severe intellectual disability (ID). The remaining 3 children were at GMFCS-E&R level I or II (level I/II = 2/1) with normal cognition. All children with kernicterus had a perinatal history of neonatal hyperbilirubinemia.