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Original article

Outcome of hemiplegic cerebral palsy born at term depends on its etiology

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Abstract

Objectives: To elucidate the etiology and its relationship to the outcomes of hemiplegic cerebral palsy (HCP).

Participants and methods: MR images and outcomes of 156 children with HCP born at term and older than three years were investigated in two major centers for cerebral palsy in Japan. Etiologies were classified into perinatal ischemic stroke (PIS), cerebral dysgenesis (CD), and others. PIS was divided into periventricular venous infarction (PVI) and two types of arterial infarction; middle cerebral artery infarction (MCAI) and deep gray matter infarction (DGMI). Initial signs and the time of presentation were investigated among the three types of PIS. As functional outcomes, laterality of paresis, age at initial walk, affected hand's function, intellectual development, and occurrence of epilepsy were compared among all the four types.

Results: Etiology: PIS was found in 106 children (68%), while CD accounted for 28 (18%). Among PIS, venous infarction was more common than arterial infarction (62:44). Outcomes: PVI revealed later presentation of motor asymmetry and more involvement of lower extremity as the initial sign among PIS groups. Only MCAI showed right-side predominance in laterality of paresis. DGMI related to better intellectual development and PVI showed lower occurrence of epilepsy, while there was no significant difference in affected hand's function among the four groups. PIS groups showed significantly earlier attainment of independent walk, better intellectual development, and lower occurrence of epilepsy than CD.

Conclusions: PVI was the most common cause of HCP born at term, and the etiology closely related to the initial signs of hemiplegia and overall outcomes.

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Keywords: Hemiplegic cerebral palsy; Presumed perinatal ischemic stroke; Periventricular venous infarction; Arterial infarction; Etiology; Outcome

1. Introduction

Hemiplegic cerebral palsy (HCP) is a heterogeneous disease with various developmental outcomes, caused

by factors such as perinatal infarction, cerebral malformation, and infection. The most common cause of HCP is perinatal ischemic stroke (PIS), which is classified by the time of insult into fetal, neonatal, and 'presumed perinatal' [1,2]. Presumed perinatal ischemic stroke (PPIS) defines term-born children older than 28 days with normal neonatal neurological history, presenting with neurologic deficit or seizure referable to focal,

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chronic infarction. Its diagnosis is made by CT or MRI performed after the neonatal period, revealing a lesion consistent with remote ischemic or hemorrhagic stroke [3]. It is presumed (but not certain) that the ischemic event occurs sometime between the 20th week of fetal life and the 28th postnatal day [2]. According to recent studies, not only arterial but also venous infarction of the periventricular region may cause HCP in termborn children [4,5] and PPIS [3]. The objectives of this study are to investigate the ratio of arterial and venous infarction in a population of HCP and to compare functional outcomes between them and with those of children with cerebral dysgenesis (CD).

2. Participants and methods

2.1. Participants

Participants were HCP children recruited from outpatients of Morinomiya Hospital and Takuto Rehabilitation Center for Children, both of which are regional center hospitals for children with cerebral palsy in Japan. Inclusion criteria were (a) born at term (>36 weeks of gestational age), (b) older than three years at the time of investigation, and (c) with precise perinatal information on chart and brain MRI after the neonatal period (>28 postnatal days). All participants were Japanese. We excluded those who were diagnosed with asymmetrical diplegia or triplegia, and those who had hemiplegia caused by insults after the neonatal period. Finally, we selected 156 children, 97 boys and 59 girls, out of 251 children with HCP. A complete description of the selection of participants at each hospital is provided in Fig. 1. Most of them received weekly or monthly rehabilitation according to the severity of paresis, but none of them received constraint-induced movement therapy, hand-arm bimanual intensive training, or botulinum-A toxin injection to the affected hand. This study was approved by the ethical committees of



Fig. 1. Selection of participants.

Morinomiya Hospital and Takuto Rehabilitation Center for Children.

2.2. Neuroimaging analysis

MR images of participants were assessed by two experienced pediatric neurologists, one per each hospital, unblinded to functional outcomes. They classified abnormality on MRI into PIS, CD, and others. PIS was divided into periventricular venous infarction (PVI) and arterial infarction, which consists of middle cerebral arterial infarction (MCAI) and localized ischemic lesions in deep gray matter (DGMI). Typical MR images of arterial and venous infarction are shown in Fig. 2. The diagnosis of PVI was based on Kirton's criteria [3].

2.3. Initial signs and functional outcomes

We surveyed the patient characteristics (the number, sex, perinatal history, and laterality of paresis) of each group. Among PIS (PVI, MCAI, and DGMI), the detailed information about initial signs of HCP and the time of presentation were also investigated. Initial signs included apparent symptoms or signs of stroke during the perinatal period, motor asymmetry of extremities, and seizures. Dominant extremities of initial signs of PPIS (upper, lower, and both) were classified based on the topography of motor asymmetry their parents had first noticed. As to functional outcomes, we compared the age at initial walk, the affected hand's function, intellectual development at the time of investigation, and occurrence of epilepsy among the four groups (PVI, MCAI, DGMI, and CD). We classified the affected hand's function into four grades according to its best performance: pinch, grasp-release, press (e.g. press a sheet of paper to stop it from moving when writing), and disuse (totally neglected). We evaluated intellectual development by three grades: normal or mildly retarded (DQ or IQ above 70), moderately retarded (DQ or IQ between 30 and 70), and severely retarded (DQ or IQ below 30). DQ was evaluated by the Kyoto Scale of Psychological Development, and IQ was assessed by the third edition of Wechsler intelligence scale for children.

2.4. Statistical analysis

The mean ages at initial walk were analyzed using the Kaplan–Meier estimator and compared among groups by log-rank test. The ages of first clinical symptoms were compared by Kruskal–Wallis and Mann–Whitney non-parametric test. Difference in laterality, initial symptoms, degree of the affected hand's function, intellectual development, and occurrence of epilepsy were analyzed by chi-squared test. P < 0.05 was considered significant.

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