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Brain & Development xxx (2017) xxx–xxx

BRAIN & DEVELOPMENT
Official Journal of the Japanese Society of Child Neurology

www.elsevier.com/locate/braindev

Original article

Neuroimaging and neuropathological characteristics of cerebellar injury in extremely low birth weight infants

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Received 7 March 2016; received in revised form 14 April 2017; accepted 14 April 2017

Abstract

Objective: To determine the morphological characteristics and pathogenic factors of cerebellar injury in extremely low birth weight infants (ELBWI).

Subjects and methods: Neuroimaging examination was performed on 17 eligible surviving ELBWI. Their MR images were assessed and classified its pattern of cerebellar injuries. Brain pathology was examined on 15 patients, who isolated this neuroimaging subjects. The trend of brain pathologies was revealed.

Results: Four types of morphological pattern were recognized: (i) the absence of major portions in the cerebellum (6/17 cases); (ii) focal cerebellar tissue loss (2/17); (iii) unilateral cerebellar atrophy/hypoplasia (3/17); (iv) small cerebellum with entrapped fourth ventricle (6/17). In cerebellar pathology, the most common findings were focal or widespread cerebellar subarachnoid hemorrhage (12/15) and olivocerebellar degeneration (12/15). In addition, one-third of the cases indicated remote cerebellar parenchymal hemorrhage.

Conclusion: In MRI-defined lesions, the absence of major portions or focal tissue loss was associated with cerebellar parenchymal hemorrhage and/or hemorrhagic infarction, that is destructive lesion. On the other hand, small cerebellum or unilateral atrophy/hypoplasia, that is impaired development, may be related to the cerebellar neuron loss due to hemosiderin deposits in the surface of the cerebellum. The cerebellar injury in ELBWI is probably caused by not only environmental factors such as hemorrhage, hypoxia-ischemia, or other deleterious effect, but also immaturity of the rapidly growing cerebellum in particular gestational age.

Keywords: Cerebellar injury; Neuroimaging; Neuropathology; Premature infant; Vulnerability

1. Introduction

The survival rate of an extremely low birth weight infants (ELBWI) is increasing with the development of perinatal care, but clinical aspect such as cerebral palsy, intellectual disabilities and developmental disorders are also often found. Recently, cerebellar injury as well as white matter injury is important in clinical outcome. Cerebellar injury has been recognized in 9 (2.4%) of 381 patients with cerebral palsy who were born preterm [1]. The prevalence of cerebellar injury in preterm children with cerebral palsy after intraventricular hemorrhage (58%) is reported to be almost the same as that

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http://dx.doi.org/10.1016/j.braindev.2017.04.011
0387-7604/

of post-hemorrhagic hydrocephalus. Cerebellar injury is one of the most significant complications in preterm infants, affecting motor and verbal functions and being associated with epilepsy more than post-hemorrhagic hydrocephalus [2].

In the brain pathology, the widespread type of periventricular leukomalacia (PVL), intraventricular hemorrhage (IVH), periventricular white matter hemorrhage, olivocerebellar degeneration (OCD), and widespread distribution of neuronal karyorrhexis over pontosubicular necrosis have been found with significantly high incidence in ELBWI [3].

The neurodevelopmental disability is manifested by cerebral palsy, delayed motor development, epilepsy, neurosensory impairment, or subsequently cognitive, behavioral, attentional, and socialization deficits in ELBWI.

The purpose of this study is to clarify the characteristics of neuroimaging and neuropathological findings and then to discuss the relationship between the cerebellar injury and pathogenic potential for extremely premature brain.

2. Subjects and methods

2.1. Neuroimaging study

The sixty-eight patients of ELBWI have visited for therapies to two children's rehabilitation institutes, Yanagawa Institute for Developmental Disabilities (31 cases) and Minami-kyuushu National Hospital (37 cases) from 2000–2014. Yanagawa Institute for Developmental Disabilities and Minami-kyuushu National Hospital are one of the center hospitals for neurodevelopmental disability in Fukuoka and Kagoshima Prefecture, respectively. On brain magnetic resonance imaging (MRI), the 17 patients (25%) were selected apparent structural cerebellar injury and examined their MR images concerning the severity and distribution of the cerebellar lesion, the morphology of adjacent brain structure, and cerebral findings. MRI examination age ranged from term-equivalent ages to 3 years. Mean gestational age was 24 ± 1.5 weeks and mean birthweight was 635 ± 136 gm.

Their neuroimaging were evaluated independently by two child neurologists who were trained in the Division of Neuroradiology.

2.2. Neuropathological study

Thirty-nine patients with extremely low birthweight (<1000 gm) and extremely preterm (<28 weeks' gestation) were examined at the age of 3 weeks to 5 years, and 15 patients (38%) had cerebellar injury. Mean gestational age was 24.8 ± 1.6 weeks and mean birthweight was 766.4 ± 130 gm. Their main clinical diagnosis included coagulation or hemorrhagic diseases in 6 cases, sepsis or other infections in 5 cases, pneumothorax in one case, profound asphyxia in one case, and one of the twin in 2 families (Table 2).

The brain pathology was evaluated by a neuropathologist (S.T) in National Center for Neurology and Psychiatry and International University of Health and Welfare. The brain cuttings were requested from several hospitals in Japan. The brain was fixed in formalin for more than 2 weeks and examined macroscopically. Sections were selected, embedded in paraffin and cut at 6 μm. The specimens were then stained with hematoxylin and eosin (H & E) and luxol fast blue.

These neuroimaging and neuropathological studies were approved by the Research Ethics Committee in International University of Health and Welfare (No13-Io-90, No11-63②).

3. Results

3.1. Neuroimaging study

Several distinctive features were seen in all 17 patients (Table 1). The neuroimaging findings varied widely, as various parts of the cerebellum were involved. These was remarkable finding that fourteen of 17 patients had various grades of IVH, and 12 showed ventricular dilatation. On the other hand, the rate of IVH patients who did not have cerebellar injuries was 30 percent in our study. On the basis of the morphologic patterns, we characterized four types of cerebellar injuries. Type I was characterized by marked reduction in cerebellar volume. The overall shape of the cerebellum was not preserved, and part of the cerebellum was virtually absent (Fig. 1a). Type II presented focal tissue loss in cerebellar hemisphere and/or widening of cerebellar fissures (Fig. 1b). Type III had unilateral cerebellar atrophy or hypoplasia (Fig. 1c). Type IV was small cerebellum with large ventricle which was characterized by an enlarged balloon-shaped fourth ventricle. On midline sagittal images, the fourth ventricle lacked its characteristic outline. The cerebellar vermis was markedly reduced in size and had lost its shape, remaining as a small longitudinal structure. The cerebellar peduncles appeared elongated. The small hemispheres were pushed aside in the posterior fossa (Fig. 1d).

Type I included six patients (6/17 cases), Most (5/6) patients showed absence of the lower portion in the cerebellar hemisphere, and one of them had complete disappearance of the lower vermis. Another patient showed extensive cerebellar wasting with multicystic supratentorial lesions considered as severe brain destruction. Three patients had IVH, and the hemosiderin deposits of the lateral ventricles were seen in one of them (Table 1 patient No. 3). The fourth ventricle had a normal configuration in two patients. Type II included two patients

Please cite this article in press as: Matsufuji M et al. Neuroimaging and neuropathological characteristics of cerebellar injury in extremely low birth weight infants. Brain Dev (2017), http://dx.doi.org/10.1016/j.braindev.2017.04.011