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Original article

A small pons as a characteristic finding in Down syndrome: A quantitative MRI study

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Abstract

Background: Down syndrome (DS) is the most common chromosomal aberration, but the characteristics of the brainstem component in this condition during childhood (from newborn to preteen stages) have not been clarified.

Objective: To evaluate the morphological features of the brainstem in DS on magnetic resonance imaging (MRI).

Materials and methods: MRIs for 32 children with DS (16 boys and girls each; age range, 0–11 years) without major brain insults, and 32 age-matched controls (16 boys and girls each) were retrospectively analyzed. Height, width, and area of the midbrain, pons, and medulla oblongata were measured on sagittal T1-weighted images; these were compared in children with DS and age-matched controls. The ratios of the brainstem to the size of the posterior fossa (BS/PF index) were calculated; these were also compared in the children with DS and the control group.

Results: The width and area of the midbrain; height, width, area of the pons; and area of the medulla oblongata were significantly smaller in children with DS than in control children ($P < 0.05$); the area of the pons, particularly for the ventral part, showed the largest differences in the mean relative differences. The BS/PF indices of the height, width, and area of the pons were significantly smaller in children with DS than in the control group ($P < 0.01$). However, the BS/PF indices for the midbrain and the medulla oblongata did not differ between these two groups.

Conclusions: Children with DS may have small brainstems, particularly in the pons; this may be a characteristic morphological feature of the brainstem on MRI in childhood including neonates.

Keywords: Down syndrome; Brainstem; Infants; Children; Magnetic resonance imaging; Posterior fossa

Abbreviations: DS, Down syndrome; MRI, magnetic resonance imaging; CT, computed tomography; TR, repetition time; TE, echo time; MP-RAGE, magnetization-prepared rapid acquisition gradient echo; ABR, auditory brainstem response; BS/PF index, ratios of the brainstem to the posterior fossa

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1. Introduction

Down syndrome (DS), or trisomy 21, is the most common chromosomal aberration and occurs at an estimated rate of 1/1000 live births [1]. The general features of DS include mental retardation and multiple congenital malformations in the cardiovascular, endocrine, and gastrointestinal systems [1]. DS has also been associated with neuroanatomical abnormalities such as reduced total brain volume, ventriculomegaly, and hypoplasia of the cerebellum, frontal lobe, temporal lobe, and brainstem; these findings have been identified during autopsy investigations [2,3]. The structural brain abnormalities associated with DS have also been shown by computed tomography (CT) and magnetic resonance imaging (MRI) studies, identifying small volumes in the entire brain or volume reduction in some areas such as the brainstem, cerebellum, and posterior fossa [4–9]. These tendencies were also found in children with DS in several studies such as one using CT and another using MRI in infants (2–4 years old) [4,10]. However, abnormalities of brainstem components (i.e., the midbrain, pons, and medulla oblongata) during childhood have not been well clarified.

Recently, the brain MRI has been commonly performed in children, and this is also the case with neonates. Routine MRI examinations should be performed not only in axial planes but also in sagittal planes, particularly in children, to assess the midline structures [11]. Therefore, it is necessary to be aware of the typical imaging findings of the brainstem of children with DS in a wide range of age groups to identify the correct radiological diagnosis in such patients, particularly with brainstem symptoms. Therefore, we aimed to evaluate the morphological features of the brainstem in neonates and pre-teens with DS using MRI.

2. Materials and methods

2.1. Patients

The radiology reporting database in our institution was searched for children with DS who underwent MRI between August 2004 and November 2014. We identified 80 children with DS. We included patients without major intracranial diseases and patients who were $\leqslant$15 years of age. We excluded patients with major intracranial insults such as intraparenchymal abnormal intensities ($n = 18$), intracranial space-occupying lesions ($n = 7$), history of chemotherapy ($n = 6$), and hydrocephalus ($n = 2$). Because this study focused on the quantitative analysis of the whole brainstem and the posterior fossa, cases with incomplete or unreadable MRI examinations such as those with motion artifacts or interruption of the MRI examination without sagittal images of the whole posterior fossa were also excluded ($n = 15$). In cases of repeated scans, only the first MRI was considered for image analysis. Finally, we included 32 children with DS (16 males and females each; age range, 2 days–11 years; mean age, 3.7 years) in this study. All patients had been diagnosed with DS by chromosomal tests [standard type ($n = 30$) and translocation type ($n = 2$)]. The included children with DS had the following clinical conditions for MRI examination: epilepsy ($n = 7$), leukemia ($n = 6$), atlantoaxial instability ($n = 6$), internal disease ($n = 5$), convulsions ($n = 3$), hemophagocytic syndrome ($n = 1$), gaze nystagmus ($n = 1$), vestibular aqueduct ectasia ($n = 1$), and mental disorders ($n = 2$). The MRIs for the patients with leukemia were examined before treatment, and no involvement in the central nervous system was found. We also selected 32 age-matched controls (16 males and females each; age range, 9 days–11 years; mean age, 3.7 years) who underwent brain MRI without abnormalities during the same period. They had following clinical conditions: convulsions ($n = 6$), leukemia ($n = 6$), epidermal nevus ($n = 4$), extracranial tumor ($n = 4$), mental disorders ($n = 3$), spinal lipoma ($n = 1$), ocular motility disorders ($n = 1$), muscle weakness ($n = 1$), cardiovascular malformation ($n = 1$), headache ($n = 1$), epilepsy ($n = 1$), fetal distress ($n = 1$), meningitis ($n = 1$), and hyperlacticacidemia ($n = 1$). The MRIs for the patients with leukemia were examined before treatment, and no involvement in the central nervous system was found. The MRIs for these children were retrospectively analyzed. The hospital's research ethics board approved the research protocol, and informed consent was waived.

2.2. MRI

MRI was performed in either a 1.5-T unit (Visart MRT-200, Toshiba Medical systems Inc., Tokyo, Japan; Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany) or a 3.0-T unit (Magnetom Verio, Siemens Medical Solutions) using a head coil for each. A routine brain MRI examination included axial T1- and T2-weighted imaging, diffusion-weighted imaging, coronal T2-weighted imaging, and sagittal T1-weighted imaging. The sagittal T1-weighted imaging was obtained differently among scanners; those included 2D spin-echo imaging and 3D gradient echo imaging. The parameters for sagittal T1-weighted imaging were as follows: spin-echo imaging, repetition time (TR)/echo time (TE): 300–631/9.4–20 ms; spin-echo inversion-recovery imaging, TR/TE: 1800–2000/10–11 ms, inversion time: 784–858 ms; 3D gradient-echo, TR/TE: 20/2.9–8 ms, flip angle: 90–170°; and magnetization-prepared rapid acquisition gradient echo (MPRAGE), TR/TE: 1400–1570/1.8–2.8 ms, inversion time: 800 ms, flip angle: 9–12°. The images were 1.0–5.0 mm thick slices, and the in-plane image resolution was 0.56–1.04 mm^2/pixel. The sagittal plane was