

MR Imaging of Fukuyama Congenital Muscular Dystrophy: A Case Report¹

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Fukuyama congenital muscular dystrophy is a genetic disease and common in Japan. The typical clinical features are hypotonia with an early infantile onset and severe developmental delay. The diagnosis is based on pathologic evidence of muscular dystrophy revealed by biopsy or an increased serum creatine kinase levels. Involvement of the brain is characterized by abnormal cerebral cortical dysplasia, cerebellar dysplasia, and white matter changes. We encountered a case of Fukuyama congenital muscular dystrophy in which brain MRI findings were typical, and present this case together with a review of the literature.

Index words : Infants, newborn, central nervous system

Infants, newborn, skeletal system

Brain, MR

Fukuyama congenital muscular dystrophy (FCMD) is a genetic disease with an autosomal recessive mode of inheritance (1, 2). It is most common in Japanese patients and is the second most common form of muscular dystrophy in Japan, after Duchenne muscular dystrophy (2). FCMD causes severe mental retardation, seizures, muscular weakness soon after birth, and pathologic muscular changes that are consistent with muscular dystrophy. The typical clinical features are hypotonia with early infantile onset, and severe developmental delay (1), and diagnosis is based on pathologic evidence of muscular dystrophy revealed by biopsy or increased serum creatine kinase levels. Since the neurologic assessment of young infants is not always straight-

forward, however, definite diagnosis is occasionally difficult, and in this respect, MRI may be helpful; the modality readily demonstrates various brain malformations occurring in FCMD, and may therefore facilitate diagnosis(3 - 6). The findings of MRI and neuropathology have four known categories: cerebral cortical malformations, cerebellar malformations, white matter changes, and miscellaneous abnormalities (7). We present the MRI findings of a typical case of FCMD.

Case Report

A 4-month-old male patient was admitted due to hypotonia, sucking difficulty and developmental delay, though initial crying was good. He was born at 40 weeks gestation by difficult vaginal delivery, and birth weight was 3.4Kg. Due to poor sucking power he was admitted to a local clinic during his third day of life and was treated under the impression of aspiration pneumonia.

He was the second baby, and his elder brother had also suffered from hypotonia and mental retardation since infancy, without any diagnostic study. With slowly progressing symptoms, this brother died from asphyxia

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when ten years old.

Other than motor weakness, physical and neurological examinations showed no significant abnormal findings. The serum creatine kinase (CK) level was 1,330 (normal range 5 - 130) IU/l, and lactic dehydrogenase (LDH) was 1,780 (normal range 58 - 170) IU/l. EMG showed a diffuse myopathic process in muscles of the upper and lower extremities, compatible with congenital muscular dystrophy. Muscle biopsy of the vastus rectus muscle was performed, revealing extensive degenerated myofibers, fibrosis, and distorted myofilaments, but preserved myofiber structures. These findings were consistent with congenital muscular dystrophy.

MR was performed on a 1.5-T imaging system (Siemens, Erlangen, Germany), and T1- and T2-weighted spin-echo images were obtained. Myelination was present in the internal capsule and corpus callosum, but

in other parts of the brain was absent. T2-weighted images revealed symmetric unmyelinated white-matter changes, with extensive high signal intensities (Fig. 1). Pachygyria were prominent in both occipitotemporal lobes, and in the frontoparietal region, some polymicrogyria were also present (Fig. 1). In addition, curvilinear bands with high signal intensity on T2-weighted images were noted in deep layers of the pachygyric cortices (Fig. 1). Cerebellar MRI showed diffuse cortical abnormalities with distorted folia, and multiple, small intraparenchymal cysts, about 1-2mm in diameter, in the posterior aspect of the hemispheres (Fig. 2).

Discussion

Congenital muscular dystrophy comprises a heterogeneous group of disorders characterized by muscular hy-

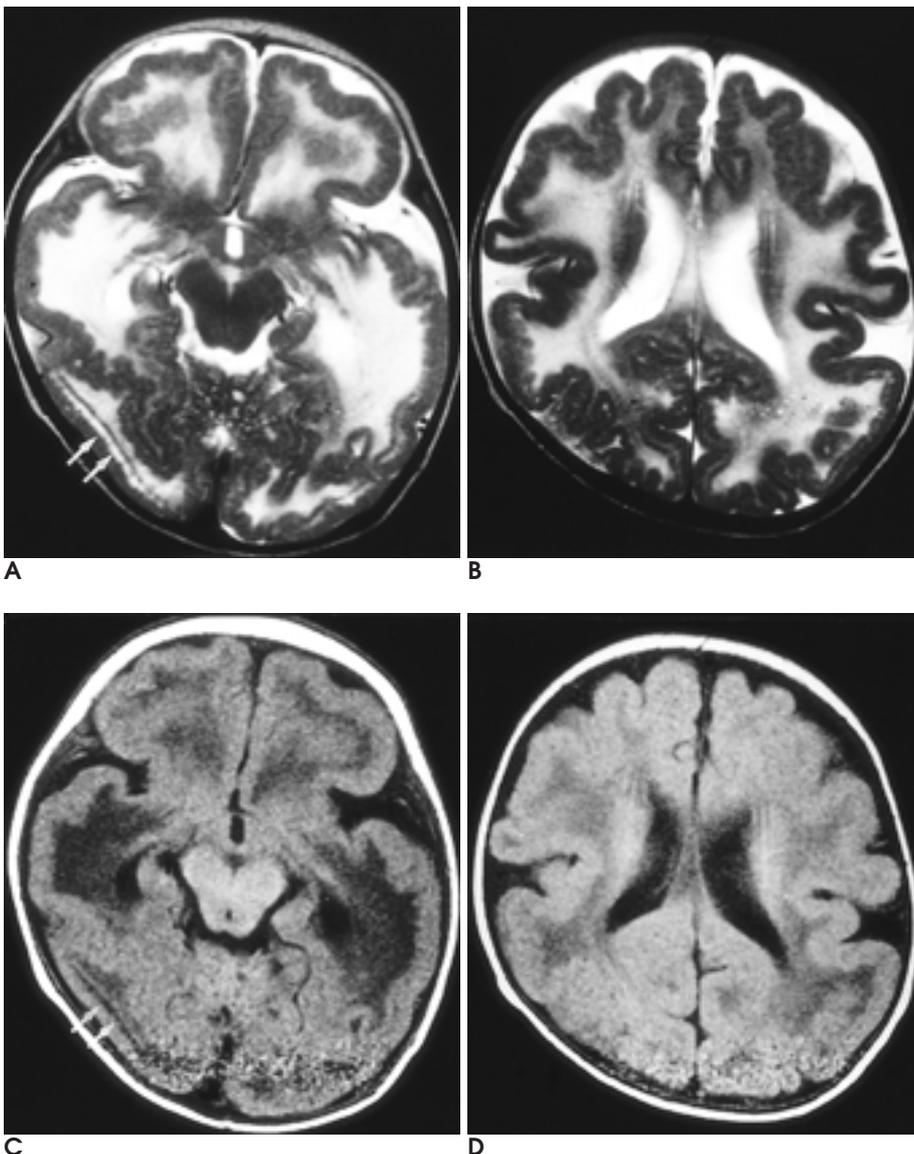


Fig. 1. Axial T2-weighted (A), (B) and T1-weighted (C),(D) MR images. The temporo-occipital lobes show thick cortices with smooth surface (pachygyria) and some frontoparietal lobes show slightly thick cortices with shallow sulci (polymicrogyria). The white matter changes are symmetric and extensive with low signal intensity on T1-weighted image and high signal intensity on T2-weighted image. And curvilinear bands presented deep within the pachygyric cortices (arrows) are also noted with low signal intensities on T1-weighted image and high signal intensities on T2-weighted image which may represent unmyelinated fibers in the third layer of pachygyria.

potonia and histologic features of muscular dystrophy (1, 2). On the basis of clinical features, pathologic findings, and pattern of inheritance, four distinct phenotypes are currently recognised : classic congenital muscular dystrophy, FCMD, muscle-eye-brain disease (MEBD), and Walker-Warburg syndrome(WWS) (8).

Patients with classic congenital muscular dystrophy exhibit normal intelligence, while those with FCMD, MEBD, and WWS have CNS malformations. In all three entities the clinical phenotypes are severe, and include severe mental retardation. WWS is the phenotype in which the more severe disorders occur, and is associated with type-II lissencephaly and ocular abnormalities(5, 8, 9). Brain malformations in WWS usually include agyral malformation, hypomyelination of white matter, and hydrocephalus, and these conditions are more severe and diffuse than in FCMD. In addition, cerebellar hypoplasia, cephalocele, and absence of the corpus callosum occasionally occur in WWS but not in FCMD(7-9). The pachygyria seen in MEBD is less pronounced than in FCMD, and agyria, seen in approximately half of FCMD cases, has not been reported(6 - 8). The distribution of gyral malformations seen in MEBD , which differ from those found in FCMD, include pachygyria over the frontal, temporal, and parietal regions, and polymicrogyria over the occipital region. Additionally, dysplasia of the septum pellucidum and corpus callosum are frequently seen in MEBD, but are rare in FCMD (7, 8).

Our patient showed delayed development, indicating associated CNS malformations in addition to muscle weakness. Brain MRI showed pachygyria in the occipi-

totemporal lobe and polymicrogyria in the frontoparietal lobe, findings distinct from those seen in MEBD. There was no dysplasia of the septum pellucidum and/or corpus callosum, a condition seen in MEBD and WWS.

The characteristic brain MR findings in FCMD include four abnormalities : cerebral cortical malformations, cerebellar malformations, white matter changes, and miscellaneous abnormalities (7). The histologic features of cerebral cortical malformations of FCMD have been divided by Takada et al.(3, 4) into three types : verrucose dysplasia (type 1), unlayered polymicrogyria (type 2), and the most severe type of cortical dysplasia (type 3), which is identical to type-II lissencephaly. For each type of cortical dysplasia, a characteristic regional distribution is also described: a predilection for the medial surface of the occipital lobe in type 1, for the frontal and parietal lobes in type 2, and for the lateral surface of the occipital and temporal lobes in type 3. MRI can demonstrate type-2 and -3 cortical dysplasia , but is unable to detect type-1 (6). Type-2 cortical dysplasia, unlayered polymicrogyria, is depicted as a slightly thick cortex with shallow sulci, and a gray-white matter interface which has a bumpy appearance. These radiologic findings are typical. Type-3 cortical dysplasia presents as a thick cortex with a smooth surface, typical radiographic findings of pachygyria. Aida et al. (5) reported that type-2 dysplasia involved the frontal lobe in all the cases they studied, and that type-3 involved the temporooccipital lobe in one-half. An increased number of curvilinear signal bands deep within abnormal cortices are detected in half of type-3 cases (7), appearing in the

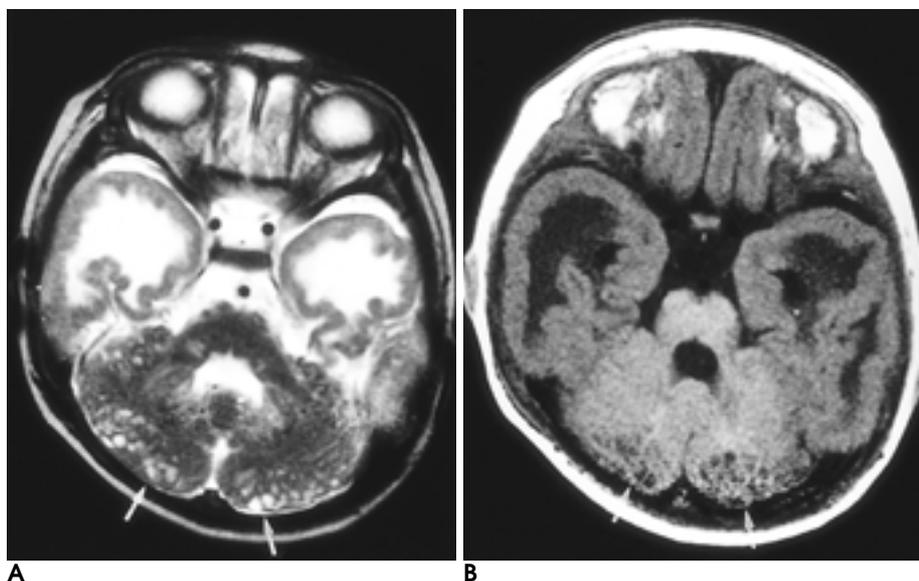


Fig. 2. Axial T2-weighted (A) and T1-weighted MR images (B) of the cerebellum. The T2-weighted image shows diffuse cortical abnormalities with disorganized and distorted folia. Multiple, various sized intraparenchymal cysts (arrows) are seen in the posterior aspect of the hemispheres with low signal intensities on T1-weighted image and bright signal intensities on T2-weighted image.

third layer of such cases as unmyelinated fibers (6). The pathogenesis of cortical malformations in FCMD remains speculative. Takada et al. (4) suggested that the pial-glial barrier might be disrupted in FCMD, leading to the development of neuroglial heterotopias within the extracortical glial layer.

Two hallmarks of cerebellar malformations in FCMD are cerebellar polymicrogyria and intraparenchymal cyst (3, 5). In most cases, cerebellar malformation is restricted to the superior semilunar lobules, but it is occasionally more diffuse (3, 5). The sulci are often obliterated by the fusion of malformed cerebellar folia, and small cystic lesions are usually located beneath the malformed cerebellar cortex, in areas of polymicrogyria. The cystic lumina contain leptomeningeal tissue, and the walls are lined by a parenchymal tissue composed of a histologically-nearly-normal molecular layer (7). The process by which cerebellar cysts develop in FCMD is unknown. The assumption is that the cysts may represent dilated subarachnoid spaces engulfed within the cerebellar parenchyma by fusion of the folia of the malformed cortex (5, 6). These cysts can be observed more easily than the cerebral cortical dysplasia present in FCMD, though they are not specific to FCMD and can arise in other types of congenital muscular dysplasia.

T2-weighted MR imaging of white-matter changes demonstrates diffusely increased signal intensities (7, 8, 10), though the cause of white-matter abnormality in FCMD has not been clearly explained. Myelin pallor and mild gliosis have been mentioned as possible causes (1-3), though on account of the way in which white-matter changes spontaneously regress, the neuroradiologic literature on FCMD has attributed them to delayed myelination (10). In the report by Aida et al. (5), however, the progressive myelination of white matter occurring in FCMD is described as centripetal rather than centrifugal, as in normal myelination, and this contradicts the hypothesis that delayed myelination is the cause of white matter abnormalities in FCMD (7).

In cases of FCMD, miscellaneous abnormalities such as enlarged subarachnoid space, ventriculomegaly due to hypoplasia, and a flattened ventral portion of the pons have been reported (6).

Differential diagnosis shows that WWS is more severe

than FCMD, with the occurrence of type-II lissencephaly, cerebellar anomalies, and associated ocular abnormalities (5, 8, 9). Gyral abnormalities are more severe and more diffuse, and white-matter involvement is more widespread than in FCMD. This latter, however, is associated with less severe cerebellar anomalies, and ocular involvement is less constant. The symptoms of MEBD are less pronounced than those of FCMD (5, 7, 9). Dysplasia of the septum pellucidum and corpus callosum, frequently seen in MEBD and WWS, are rare findings in FCMD (7).

Traditionally, the diagnosis of FCMD has depended on the clinical findings and a muscle biopsy. Nevertheless, it is difficult to assess the neurologic status of a young infant, and a muscle biopsy does not provide specific evidence of FCMD beyond the mere diagnosis of muscular dystrophy. The MR findings are thus useful for the early diagnosis of FCMD and may permit a correct diagnosis.

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