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Cerebellar MR in Fukuyama Congenital Muscular Dystrophy: Polymicrogyria with Cystic Lesions

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PURPOSE: To determine the MR appearance of cerebellar abnormalities in Fukuyama congenital muscular dystrophy. **METHODS:** We reviewed brain MR images of 25 patients with Fukuyama congenital muscular dystrophy and examined the autopsy specimens of a 23-month-old girl with the disease to determine the pathologic nature of the MR findings. **RESULTS:** MR studies revealed two characteristic cerebellar abnormalities: (*a*) disorganized cerebellar folia (16 cases) that were recognized as unusual distortions of the cortex; and (*b*) clusters of intraparenchymal cysts (23 cases). The two lesions were located close to each other, and milder lesions tended to affect only the superior semilunar lobule. The autopsy specimen revealed small cerebellar cysts, which consisted of dilated subarachnoid spaces buried beneath the malformed cortex. **CONCLUSION:** The disorganized folia represent cerebellar polymicrogyria, and the presence of cerebellar cysts is related to the polymicrogyria. These two MR changes are often present in Fukuyama congenital muscular dystrophy and are distinct enough to suggest the radiologic diagnosis.

Index terms: Muscular dystrophy; Cerebellum, abnormalities and anomalies; Cerebellum, magnetic resonance; Pediatric neuroradiology

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Fukuyama congenital muscular dystrophy (FCMD) is a genetic disease with an autosomal recessive mode of inheritance (1, 2). It produces a unique constellation of clinical and neuropathologic abnormalities and is common in Japan (2, 3). Recently, the location of a gene for FCMD was reported (4). FCMD causes severe mental retardation, seizures, muscular weakness soon after birth, and pathologic muscular changes that are consistent with muscular dystrophy (1). 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 on biopsy or an increased serum creatine kinase level in the appropriate clinical context.

The brains of patients with FCMD are characterized by abnormal cerebral migration, myelin pallor in the white matter, and cerebellar cortical dysplasia (2, 5, 6). Thus magnetic resonance (MR) can be useful in the diagnosis. However, previous neuroradiologic reports have been mainly concerned with abnormalities of the supratentorial structures. The present report describes the MR findings of cerebellar abnormalities in FCMD.

Patients and Methods

Neuroradiologic Examinations

We reviewed 32 MR studies performed in 25 patients with FCMD. At the time of imaging, the patients ranged from 2 months to 21 years of age. Four patients also had siblings with FCMD.

We performed MR studies with 1.5-T scanners in 13 patients (18 examinations) and with a 0.5-T scanner in 12 patients (14 examinations). The 1.5-T studies consisted of spin-echo T1-weighted images (400–450/15–20/2 [repetition time/echo time/excitations]) and T2-weighted images (2500–3000/80–100/1). The 0.5-T studies con-

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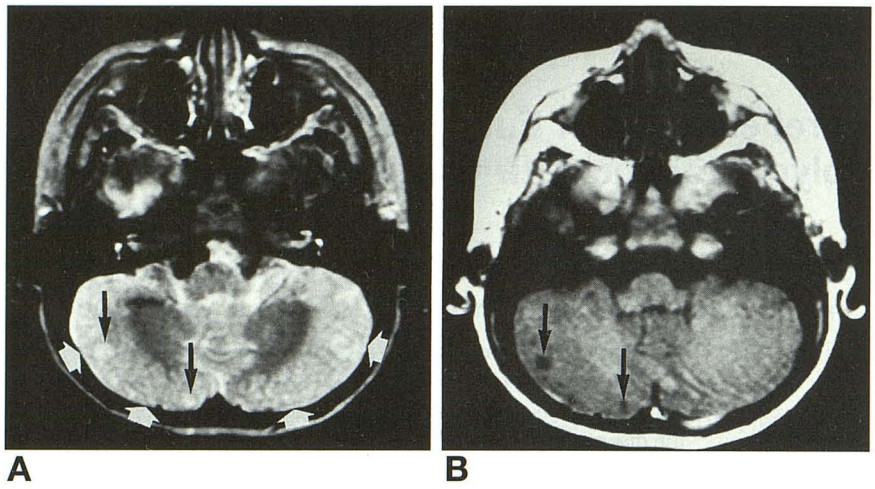

Fig 1. A girl 2 years 11 months of age.
A, Axial T2-weighted (2500/80/1) and *B*, T1-weighted (400/15/2) images of midportion of the cerebellum. The T2-weighted image shows diffuse cortical abnormalities (*white arrows*), with disorganized and irregularly distorted folia. Some intraparenchymal cysts (*black arrows*), of various sizes in the posterior aspect of the hemispheres, are seen in both images.

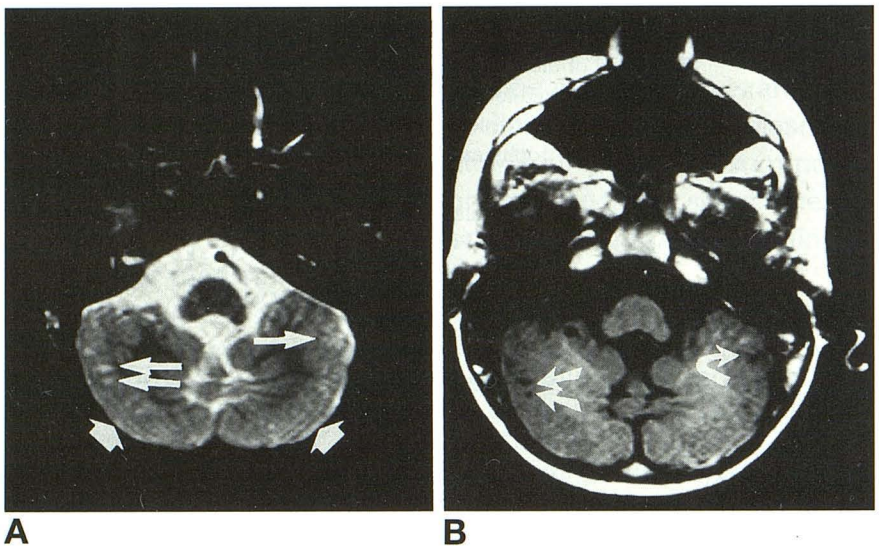

Fig 2. A 6-year-old boy.
A, Axial T2-weighted (2500/80/1) and *B*, T1-weighted (400/15/2) images of the midportion of the cerebellum. The peripheral halves of the hemispheres reveal disorganized folia (*thick white arrows*), whereas the central halves are relatively spared. There are some oval and round cystic lesions (*thin white arrows*).

sisted of spin-echo T1-weighted (500–600/26–30/2), T2-weighted (2000/100/2), and inversion-recovery images (2000–2200/500 [inversion time]/30/2).

Neuropathologic Examinations

We examined photographs and histologic sections of the cerebellums from the patients with FCMD, who were previously reported (5). Because the cerebellums were cut in the sagittal planes in most cases, horizontal sections were available from only one patient, a 23-month-old girl (patient 1 in reference 5). No MR study was performed in this patient.

Results

Neuroradiologic Findings

MR studies demonstrated two peculiar cerebellar abnormalities. We observed disorderly alignment of the cerebellar folia in 16 cases (Figs 1 and 2), and we found a cluster of intraparenchymal cysts in the posterior cerebellums in 23 cases (Figs 1–3). The former finding was seen on 5 of 13 T1-weighted images and 9 of 13 T2-weighted images at high field strength, whereas they were seen in 1 of 12 cases on T1-weighted images and 7 of 12 cases on T2-weighted images at low field strength. The latter was detected on 12 of 13 T1- and T2-weighted images with the 1.5-T scanners and 11 of 12 T1- and T2-weighted images with the 0.5-T scanner.

The disorganized folia were recognized by a distorted pattern of cerebellar foliation on T2-weighted images but were difficult to see on T1-weighted images. The 0.5-T scanner was less sensitive to this finding than were the 1.5-T scanners.

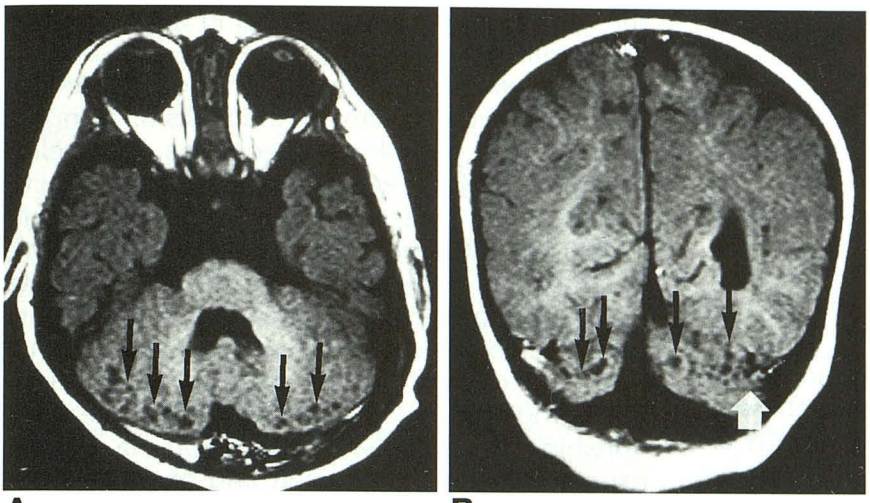

Fig 3. A 5-month-old boy.

A, Axial (400/15/2) and *B*, coronal (400/15) T1-weighted images of the cerebellum. The cerebellar hemispheres contain many peripheral cystic lesions (*black arrows*). The lesions are localized in the semilunar lobule just above the horizontal fissure (*B, white arrow*).

The cystic lesions varied in size, number, and extent, but were seen on both T1- and T2-weighted images, regardless of age, sequence, and the equipment used. Both types of abnormalities were located near each other. The lesions tended to be localized, particularly to the midportions and the dorsal halves of the cerebellar hemispheres, when they were few and less prominent.

Neuropathologic Findings

As reported previously, cerebellar polymicrogyria was present in all cases. In most of the patients, only the superior semilunar lobules showed malformations, but the lesions were more diffuse in a few cases. Cerebellar polymicrogyria consists of clusters of intermingled islands of the molecular and granular layers. In such areas, the sulci are often obliterated by the fusion of malformed cerebellar folia with each other.

Histologic sections from a 23-month-old girl revealed the presence of several small cysts in the cerebellar parenchyma. The lumens of the cysts contained leptomeningeal tissue, and a molecular layer of nearly normal cerebellar cortex lined the walls (Fig 4). These cysts were

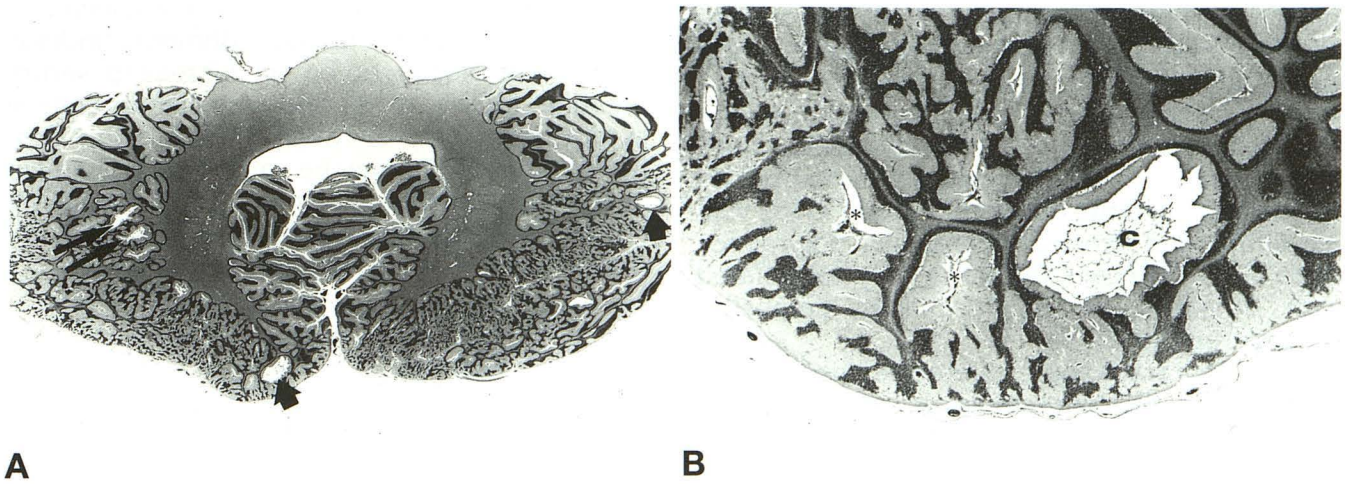

Fig 4. *A*, Histologic section of the cerebellum in a 23-month-old girl with FCMD. Malformed cerebellar cortex, or polymicrogyria, extends in the posterior portion of the cerebellar hemispheres (superior semilunar lobules). Several small cysts (*arrows*) are located beneath the polymicrogyria (hematoxylin and eosin, magnification ×2).

B, A higher magnification of the cerebellar cortex. The lumen of the cyst (C) is lined with the molecular layer and contains the leptmeningeal tissue. A few subarachnoid spaces (*asterisks*) are also buried beneath the malformed cortex, but not enlarged as cysts (hematoxylin and eosin, magnification ×14).

mostly located beneath the malformed cerebellar cortex or areas of polymicrogyria, near the boundary between the normal and polymicrogyric cortices. Although the three-dimensional structure was unclear, these cysts seemed to represent dilated subarachnoid spaces buried within the cerebellar parenchyma by the fusion of overlying malformed folia.

Discussion

FCMD is a severe form of congenital muscular dystrophy. In Japan, this disease is the second most frequent type muscular dystrophy after Duchenne muscular dystrophy, although it is rare in other countries (1). Walker-Warburg syndrome, which is variable in expression and not uncommon in the United States and Europe, is an allied disorder. Congenital muscular dystrophy, retinal and cerebellar dysplasia, and type II lissencephaly characterize Walker-Warburg syndrome (7). It remains controversial whether Walker-Warburg syndrome and FCMD represent phenotypic variants of the same disorder or are different diseases.

Some authors have pointed out various similarities between FCMD and Walker-Warburg syndrome (8–11); including the presence of diffuse cortical dysplasia, congenital muscular dystrophy, white matter hypoplasia, and ocular abnormalities. However, FCMD is associated with less-severe gyral malformations and cerebellar anomalies than Walker-Warburg syndrome, and ocular involvement is less constant in FCMD (7, 11). Cerebellar anomalies seem to be different in the two conditions; Walker-Warburg syndrome is associated with severe dysplasias comprising the Dandy-Walker malformation, vermian hypoplasia, hemispheric hypoplasia, and the absence of folia (7), as well as diffuse and extensive cerebellar polymicrogyria (11), whereas FCMD is only associated with localized or much milder cerebellar polymicrogyria (5, 6).

The neuroradiologic literature has documented all the supratentorial anomalies in Walker-Warburg syndrome (7, 12–14) and FCMD (2, 3, 15), as well as major cerebellar anomalies in Walker-Warburg syndrome (7, 12–14). In the present study, we demonstrated two distinct MR findings of the cerebellum in FCMD: disorganized cerebellar folia and intraparenchymal cysts. Both lesions tended to be located in the midportion and dorsal surface of the hemisphere, particularly in the superior semilunar lobule (Fig 3).

The former finding seems to reflect cerebellar polymicrogyria directly on the basis of comparison with the pathologic specimens. Cerebellar polymicrogyria were previously reported to preferentially affect the semilunar lobules in FCMD (5), although the reason is not known. Postmortem data show that the latter exists within or near the disorganized folia and is partially lined by leptomeningeal tissue. Although it is not clear how these cerebellar cysts develop, the pathologic study revealed their close relationship to cerebellar polymicrogyria, which usually show mutual fusion and obstruction of sulci in their upper parts. Therefore **we speculate that the cysts are likely to have formed from subarachnoid spaces that were engulfed by fusion of the folia of the malformed cortex, particularly in the boundary between the normal and polymicrogyric cortices.** Previous pathologic investigations of FCMD have indicated that a similar mechanism produces leptomeninges and medium-sized vessels extending deeply into the cerebellar parenchyma (5, 6). We believe that the subarachnoid spaces buried beneath the polymicrogyria, although not enlarged, may be seen as cysts in the MR examination, because they are filled with cerebrospinal fluid during life and are possibly larger than they are after death.

The diagnosis of FCMD is essential for adequate patient care and genetic counseling. It traditionally depends on the pathologic findings on muscle biopsy or on an increased serum creatine kinase level and consistent clinical symptoms. However, even the histologic features occasionally may be vague, particularly in very young infants. Thus the MR findings we report here may be useful for making an early diagnosis.

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