The Brain Pathology in Fukuyama Type Congenital Muscular Dystrophy
—CT and Autopsy Findings—

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The findings of computed tomography on Fukuyama type congenital muscular dystrophy were presented. They included low density area in the cerebral white matter with cortical atrophy. The pathologic examination of autopsied brain, on the other hand, revealed agyria and microgyria of the cerebral and/or cerebellar cortices, and maldevelopment and poor formation of the myelin in the cerebral white matter and pyramidal tracts in the brain stem. These pathologic alterations were considered to indicate a dysgenetic or dysplastic process, occurring in early uterine life. Intimate correlation between CT findings and neuropathologic observations of the brain was mentioned. Repeated CT examination would be convenient for taking care of these patients.

Key Words: Fukuyama type congenital PMD, Muscular dystrophy, Computed tomography, Dysgenetic and or dysplastic process, Agyria, Micropolygyria.

Fukuyama type congenital muscular dystrophy (CMD) is considered to be a distinct subtype of muscular dystrophy, having dystrophic muscular change associated with severe involvement of the central nervous system1,2,3). Clinically, patients show hypotonia and weakness of the muscles of the whole body and mental retardation with joint contracture, on occasion, from soon after birth. The course is slowly progressive. Although autosomal recessive inheritance has been suspected in some cases, no precise cause has not yet been noted.

Recently, interesting pictures were found by computed tomography (CT) in the cerebral white matter of Fukuyama type CMD. In this paper, the figures of CT, obtained in the living cases are demonstrated. Then, these characteristic figures are compared with neuropathologic alterations, found in the brain of an autopsy case.

COMPUTED TOMOGRAPHY

Five cases (3 boys and 2 girls) of Fukuyama type CMD, investigated by CT, are shown on Table 1. Age at examination was between 8 months and 12 years. Three cases (case 1, 2 & 3) had no family history. Case 4 and 5 were siblings.

On CT, two cases (case 1 & 2) had Table 1. Clinical data and CT findings in the cerebral white matter.

<table>
<thead>
<tr>
<th>Age at examination</th>
<th>Sex</th>
<th>Family history</th>
<th>Course</th>
<th>Low density in cerebral white matter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1 1 y 5 m</td>
<td>M</td>
<td>-</td>
<td>Died at 1 y 6 n</td>
<td>+++</td>
</tr>
<tr>
<td>Case 2 8 m</td>
<td>F</td>
<td>-</td>
<td>Alive</td>
<td>++</td>
</tr>
<tr>
<td>Case 3 3 y 6 m</td>
<td>M</td>
<td>-</td>
<td>Alive</td>
<td>+</td>
</tr>
<tr>
<td>Case 4 12 y</td>
<td>M</td>
<td>+</td>
<td>Alive</td>
<td>+</td>
</tr>
<tr>
<td>Case 5 5 y 4 m</td>
<td>F</td>
<td>+</td>
<td>Alive</td>
<td>-</td>
</tr>
</tbody>
</table>

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localized areas of low density in the cerebral white matter, dominantly observed in that of bilateral frontal, temporal and parietal lobes (Fig. 1). EMI density value of these low-density areas was 5~10 in case 1 and 9~14 in case 2, respectively, whereas that of normal cerebral white matter should be 12~18. These areas of low density showed no change in figure or density on CT with enhancement by contrast medium.

In addition to the findings in the cerebral white matter, atrophy of the cerebral cortex was detected on CT as well as asymmetry of the skull itself.

Two other cases (case 3 & 4) had the same lesions of low density of a milder grade, in terms of nature and localization, in the cerebral white matter on CT. Case 5 did not show any abnormalities in the
cerebral white matter. Atrophy of the cerebral cortex and asymmetry of the skull were observed in case 3, 4 and 5, either.

The first two cases (case 1 & 2), which had prominent findings on CT had severer clinical features; Case 1 having died of pneumonia at the age of 18 months (without autopsy), case 2 being alive with recurrent infections of the respiratory system.

REPORT OF AN AUTOPSY CASE

This case has been briefly reported by one of us in Japanese several years ago\(^2\). The patient was delivered at term by aspiration, because lack of progress in delivery. His weight at birth was 3,100g. No family members were known to be mentally retarded or have muscle disorders.

He was mentally retarded and floppy with weakness and atrophy of all the muscles. He was always bed-ridden and could not sit up, stand or talk meaningfully. Serum CPK level was 860u. (normal 0~25u). EMG was of the myogenic pattern. EEG was not contributory. Biopsied quadriceps femoris muscle showed intensive proliferation of connective tissue with scattering of degenerated or necrotic muscle fibers, compatible changes of muscular dystrophy (Fig. 2).

His mental and physical development was poor and muscle involvement was not improved at all. He died of pneumonia at the age of 11 months.

Fig. 2. Biopsied quadriceps femoris muscle. Intensive proliferation of connective tissue is seen with scattering of degenerated or necrotic muscle fibers. H. & E., 600X.

Fig. 3. Coronal section of autopsied brain. Agyria in the temporal lobes and micropolygyria in the parietal lobes are demonstrated. The cerebral white matter shows low stainability. A cavity (X) is noted in the right temporal white matter. Kluever-Barrera, 0.5X.

Fig. 4. Horizontal section of cerebellum and medulla. There are micropolygyria in the cerebellar cortex and poor formation of the pyramidal tracts in the medulla. Kluever-Barrera, 0.7X.

Fig. 5. Large magnification of cerebral white matter. Slight proliferation of astrocytes is observed among a sparse ground substance. There was no macrophage infiltration. H. & E., 800X.

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At autopsy, bronchopneumonia and dystrophic alteration of skeletal muscles were detected.

On neuropathologic examination (Fig. 3 & 4), the brain was a little smaller than normal. There were agyria in the temporal lobes and micropolygyria in the frontal and parietal lobes and cerebellar cortex, bilaterally. A cavity formation was noted in the right temporal white matter (Fig. 3).

Microscopic examination showed thickening of the meninges and their adhesion to the cerebral cortex. Although each neuron in the cerebral cortex had a normal appearance, distorted arrangement of the cortical neurons and poor development of the cerebral gyri were prominent in almost the whole brain, besides agyria and/or micropolygyria in the cerebral and cerebellar cortices.

In the myelin staining preparations (Fig. 3), the cerebral white matter, mainly in bilateral frontal and temporal lobes, showed low stainability. On large magnification of these areas in the cerebral white matter in H. & E. staining preparations (Fig. 5), a sparse ground substance with only slight proliferation of astroglia was observed.

The myelin formation of the pyramidal tracts were poor in the midbrain, pons and medulla (Fig. 4). The pyramidal tracts were partly observed as small, myelinated bundles in proper portion in each section. No marked gliosis or phagocytosis were observed in these areas.

The thalami, basal ganglia and tegmental structures of the brain stem showed no apparent abnormalities.

No inflammatory cell infiltration, phagocytic proliferation or inclusion bodies in neurons or glia cells were found in any parts of the brain.

The spinal cord could not be examined.

**DISCUSSION**

The CT findings in this study, including areas of low density in the cerebral white matter with cortical atrophy, were characteristic.

These findings were observed in 4 out of 5 living cases in this study; two cases were most prominent. There have been a few studies on CT of Fukuyama type CMD in Japan recently. Osawa et al. found the same kinds of alterations on CT as described in this study, and reported that the CT findings of cortical atrophy and asymmetry of the skull were rather frequently observed, but those of low-density areas in the cerebral white matter were not detected in high percentage.

The precise incidence of these CT abnormalities should be studied more in future.

The abnormalities, appeared on CT, would be compatible with the lesions, demonstrated in the present autopsy case, although the autopsy case was not one of those examined by CT scanning.

Neuropathologic examination of the present case showed dysgenetic and/or dysplastic changes of the cerebral and cerebellar cortices with maldevelopment and poor formation of the myelin in the cerebral white matter and pyramidal tracts of the brain stem. No destructive or dystrophic lesions, such as vascular diseases, metachromatic leucodystrophy, lipidosis or demyelinating diseases, were detected.

Several autopsy cases of Fukuyama type CMD have been reported in Japan and Australia. The brains of these cases were shown to have agyria, micropolygyria and cavity formation in the cerebrum and cerebellum as demonstrated in the present autopsy case.

Although some cases have definite evidence of heredity, exact cause of this disease has not yet been known.

Cytomegalovirus infection in uterine life has been reported to induce dysplastic changes in the fetal brain. No evidence, however, of cytomegalovirus infection could be found either in the serological studies, performed in the present living cases, or in the neuropathologic investiga-
tion, done in the present autopsy case. Neither description of cytomegalic inclusion has been found in the reported cases\(^2,^3,^5\).

The pathologic findings, detected in the cerebral white matter of the present autopsy case, are characteristic. They, however, have not been specifically described in the reported cases\(^2,^3,^5\). These features are considered to indicate a dysgenetic or dysplastic process, either associated with, or secondary to, the pathologic alterations, appearing in the cerebral and cerebellar cortices.

Maldevelopment of the myelin in the cerebral white matter has been noted in the case of phenylketonuria and maple syrup urine disease\(^7,^8\). The present living cases did not show any abnormalities in the analysis of urine amino acids.

Further studies should be done for elucidating the cause of the pathologic changes, appeared in the brain of CMD, in clinical and experimental aspects. The question why the pathologic alterations coexist in the muscles and central nervous system should be dissolved, either.

In this study an intimate correlation between CT findings and neuropathologic observations of the brain on Fukuyama type CMD was discussed.

Recognition of the grade, size and localization of the pathologic changes in the brain by repeated CT examination would be convenient for taking care of these patients.

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