Characteristic Magnetic Resonance Imaging Findings in Machado-Joseph Disease

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Objective: To clarify the characteristic magnetic resonance imaging (MRI) findings in patients with Machado-Joseph disease (MJD) diagnosed by genetic analysis.

Patients and Methods: Using MRI, we examined 31 patients genetically diagnosed as having MJD, 20 patients with sporadic olivopontocerebellar atrophy, and 26 control subjects.

Results: The MRIs of patients with MJD disclosed remarkably reduced width of the superior cerebellar peduncles, atrophy in the frontal and temporal lobes, diminished transverse diameter of the globus pallidus, and decreased anteroposterior and transverse diameters of the pons, which correlated with the width of the middle cerebellar peduncle. The width of the superior cerebellar peduncles also correlated with the diameter of the dentate or red nucleus in patients with MJD, but not in controls or in patients with sporadic olivopontocerebellar atrophy. On T2- and/or proton-weighted axial MR imaging, a high signal intensity in the transverse pontine fibers was observed in 14 (45.2%) of 31 patients with MJD and in all patients with sporadic olivopontocerebellar atrophy, but not in any controls.

Conclusion: Affected afferent and efferent cerebellar tracts and atrophy of the frontal and temporal lobes and globus pallidus are characteristics of MRI of patients with MJD.

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PATIENTS AND METHODS

We studied 31 patients with MJD (16 men and 15 women; mean±SD age, 50.3±13.7 years; mean±SD duration of illness, 12.9±6.6 years), 20 patients with sporadic olivo-pontocerebellar atrophy (sOPCA) (6 men and 14 women; mean±SD age, 55.1±11.6 years; mean±SD duration of illness, 3.2±3.1 years), and 26 age-matched control subjects without intracranial lesions (11 men and 15 women; mean±SD age, 49.6±17.2 years). The condition of patients with MJD was diagnosed by genetic analysis and by symptoms and signs, including cerebellar ataxia, pyramidal tract signs, extrapyramidal symptoms, and amyotrophy. The condition of patients with sOPCA was diagnosed by the clinical criteria proposed by Quinn, excluding familial spinocerebellar degeneration by genetic analysis. Informed consent for the genetic analysis was obtained from all patients.

Patients with sOPCA and normal volunteers were examined using 1.5-T MRI. T1-weighted axial images (repetition time [TR], 450 milliseconds; echo time [TE], 30 milliseconds), T2-weighted axial images (TR, 2000 milliseconds; TE, 80 milliseconds), and proton-weighted axial images (TR, 2000 milliseconds; TE, 30 milliseconds) were obtained in the transaxial plane (5-mm thickness and 2.5-mm gap). Patients with MJD were examined using 0.5- to 1.5-T MRI. T1-weighted axial images (TR, 300-600 milliseconds; TE, 15-30 milliseconds), T2-weighted axial images (TR, 2000-4000 milliseconds; TE, 80-102 milliseconds), and proton-weighted axial images (TR, 2000-4000 milliseconds; TE, 15-30 milliseconds) were obtained in the transaxial plane (5- to 8-mm thickness and 0- to 2.5-mm gap). Measurements were performed separately by 3 neuroradiologists (Y.M., S.Y., and Y.I.) who did not know the clinical or genetic status of the subjects.

Anteroposterior and transverse diameters of the pons, midbrain, medulla oblongata, and fourth ventricle were measured on T1-weighted axial images. The width of the middle cerebellar peduncle was also measured on T1-weighted axial images. It was difficult to measure the width of the superior cerebellar peduncle directly on the transaxial T1 MRI, so we evaluated the diameter of the midbrain at the level of the superior cerebellar peduncle, which would indirectly reflect the width of the superior cerebellar peduncles. The diameter of the dentate nucleus, red nucleus, and globus pallidus was determined on T2-weighted axial images. The area of the cerebellum was evaluated on T1-weighted axial images. We tried to exclude the sulcus indentations in the outline of the cerebellum at the edge shown in Figure 1 using a computer software package (MacSCOPE, Mitani Co, Fukui, Japan) on a Macintosh computer. The threshold was determined to represent the edge of the cerebellum accurately and the binary image was made. Thereafter, pixels in the cerebellar area were counted and the area of the cerebellum was measured. The degree of atrophy in the frontal, temporal, parietal, and occipital lobes was visually divided into 4 grades (0, none; 1, mild; 2, moderate; and 3, severe) by observers (Y.M., S.Y., and Y.I.) unaware of the subject status. The appearance of the abnormal signal intensity of transverse pontine fibers was assessed on T2- and/or proton-weighted axial images.

All data were analyzed using the computer software package JMP 3.0 (SAS Institute Inc, Cary, NC) on a Macintosh computer. Differences between the groups were examined by analysis of variance. Frontal, temporal, parietal, or occipital lobe atrophy was analyzed by the Wilcoxon rank sum test. Probability values less than 5% were accepted as significant.

Figure 1. Measurements on T1- and T2-weighted axial magnetic resonance images. 1 indicates anteroposterior diameter of the globus pallidus; 2, transverse diameter of the globus pallidus; 3, anteroposterior diameter of the midbrain; 4, transverse diameter of the midbrain; 5, width of the superior cerebellar peduncles; 6, width of the middle cerebellar peduncle; 7, diameter of the dentate nucleus; 8, diameter of the red nucleus; 9, anteroposterior diameter of the pons; 10, transverse diameter of the pons; 11, anteroposterior diameter of the fourth ventricle; 12, transverse diameter of the fourth ventricle; 13, anteroposterior diameter of the medulla oblongata; 14, transverse diameter of the medulla oblongata; and 15, area of the cerebellum.
Moderate cerebellar atrophy and marked brainstem atrophy, especially in the pontine tegmentum, were observed in the MJD group, which is consistent with previous MRI and pathologic studies. Our study also disclosed a moderate to severe atrophy in the frontal and temporal lobes, and remarkable atrophy in the superior and middle cerebellar peduncles and globus pallidus in patients with MJD. Marked dilatation of the fourth ventricle was also observed in patients in the MJD group, which probably could be attributed to the atrophy of the pontine tegmentum and dentate nucleus.

To evaluate the accuracy of measurement in the dentate nucleus, red nucleus, and globus pallidus on 0.5-T MRI, we investigated the size of the dentate nucleus, red nucleus, and globus pallidus on 0.5-T MRI, we investigated the size of the dentate nucleus, red nucleus, and globus pallidus in 23 healthy volunteers on 0.5-T MRI. Therefore, the size of the dentate nucleus, red nucleus, and globus pallidus would not be underestimated compared with that measured on the 1.5-T MRI. Therefore, the size of the dentate nucleus, red nucleus, or globus pallidus would not be influenced by variable magnetic fields, and would therefore be reliable.

The atrophy of the pons or midbrain is age-dependent, because significant reverse correlation was found between age and the transverse diameter of the pons (P<.05) or the anteroposterior diameter of the midbrain (P<.01) in patients in the MJD group. The duration of illness correlated with the decrease in the anteroposterior (r=0.40, P<.05) and transverse diameters (r=0.53, P<.01) of the globus pallidus in patients in the MJD group, and with the degree of temporal or occipital lobe atrophy in MJD (P<.05). These data indicate that changes disclosed by MRI are age-related and develop according to the disease process.

The width of the superior or middle cerebellar peduncle was significantly decreased in patients in the MJD group compared with controls (P<.05). There was a significant correlation between the anteroposterior or transverse diameter of the pons and the width of the middle cerebellar peduncle. The atrophy of the pons and the middle cerebellar peduncle suggests that the afferent cerebellar tract from the pontine nuclei to the cerebellum through the middle cerebellar peduncle is affected in MJD.

To characterize MRI features peculiar to MJD, we compared the MRI findings of 31 patients who had MJD with those of 20 patients who had sOPCA, although sOPCA might include miscellaneous disease entities. There was a significant difference in the duration of illness between the patients with MJD and sOPCA (P<.05), probably due to more rapid progress in patients with sOPCA. In patients with sOPCA, the superior cerebellar peduncle was preserved, but it was atrophied in patients with MJD. Moreover, the correlation was observed between the width of the superior cerebellar peduncles and the diameter of the dentate or red nucleus in patients with MJD, but not in controls or in patients with sOPCA. Although there was no significant difference in the diameter of the dentate or red nucleus among the 3 groups by analysis of variance, the atrophy of the superior cerebellar peduncle seems to proceed in parallel with the atrophy of the dentate and red nucleus in patients with MJD. The dentate or red nucleus and the superior cerebellar peduncle are spared in patients with sOPCA and in controls. Therefore, no close relationship exists between the width of the superior cerebellar peduncles and the diameter of the dentate or red nucleus in patients with sOPCA and in control subjects.
dition, sOPCA progresses more rapidly than MJD, so disproportionate atrophy may be present in sOPCA. Furthermore, the atrophy of the dentate nucleus seems to be related to the pontocerebellar tract, but not to the dentatorubrothalamic tract. These findings indicate intact efferent fiber systems in sOPCA, which has been indicated by previous reports in contrast to MJD. The involvement of the efferent dentatorubral system, which runs through the superior cerebellar peduncle in MJD shown by autopsy studies, seems to characterize the MRI of patients with MJD.

A high signal intensity in the transverse pontine fibers on T2-weighted axial image was previously reported to be characteristic in sOPCA. In the present study, almost half (14 of 31) of patients with MJD had the pontine high signal intensity, which presum-
ably reflects the gliosis and myelin sheath loss along the degenerated pontocerebellar fibers elucidated by morphological studies on MJD. Age-related pathological changes in pontocerebellar fibers may contribute to the appearance of a high signal intensity in the transverse pontine fibers on T2 and/or proton-weighted MRIs, which can be detected in various cerebellar diseases. Moreover, the pons or midbrain decreases its size and is packed according to aging. Consequently, an abnormal high signal intensity in the pons could be observed in older patients with MJD and is not specific to sOPCA.

Frontal or temporal lobe atrophy or decrease in the transverse diameter of the globus pallidus and the aforementioned findings may fortify the neuroradiological diagnosis of MJD. These MRI findings and the clinical features characteristic of MJD may prompt us to identify the gene responsible for MJD. These results also seem to help the differentiation of MJD from sOPCA.

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