The Utility of Cerebral Blood Flow Imaging in Patients with the Unique Syndrome of Progressive Dementia with Motor Neuron Disease

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Two patients presenting with progressive dementia coupled with motor neuron disease underwent brain SPECT using N-isopropyl-p iodine-123-iodoamphetamine ([^{123}I]IMP). The characteristic clinical features of progressive dementia and motor neuron disease were noted. IMP SPECT also revealed reduced uptake in the bilateral frontal and temporal regions, with no reduction of uptake in the parietal, parietal-occipital regions. We conclude that IMP SPECT has potential for the evaluation of progressive dementia with motor neuron disease.

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Progressive dementia with motor neuron disease (MND) has been reported in ~30 cases in Japan (*1*). The symptoms associated with this finding are: global intellectual impairment; a loss of memory; personality change; emotional disorder; and the loss of spontaneous speech (*1,2*). These symptoms are usually interpreted as unclassified pre-senile dementia. Mituyama et al., however, have suggested that this disorder might be classified as a new form of dementia (*1-3*). The use of regional cerebral blood flow (rCBF) studies in this unique syndrome has not been previously reported. In this paper, we evaluate the usefulness of IMP SPECT in two cases with progressive dementia with MND.

CASE REPORTS

Case 1

A 52-yr-old woman was admitted to our institution presenting with slowly progressive dysarthria, dementia, and reduction of spontaneous speech, which was noted 9 mo prior to her admission. She had no past history of neurologic or psychiatric disease. On admission, her neurologic and psychologic findings were:

1. Mild dementia with a 21 score on Mini-Mental State examination.
2. Tongue atrophy with fibrillation.
3. Weakness of upper extremities.
4. Moderate atrophy with fibrillation of thenar muscle and triceps.
5. Hyperactive muscle stretch reflexes in the extremities and the jaw jerk.
6. Absence of sensory deficits.

Routine laboratory studies, roentgenogram of cervical spine, and an examination of spinal fluid were normal. An electroencephalography (EEG) was mildly abnormal: there was slow α-wave with some excess Q-wave activities in the background, but there was no paroxysmal pattern. An electromyography (EMG) showed neurogenic pattern. Computed tomography (CT) of the brain showed mild cortical atrophy in the frontal-temporal lobe without evidence of cerebrovascular attack (Fig. 1). This finding was suggestive of Pick's disease, but neurologic findings suggested a diagnosis of pre-senile dementia with MND.

An iodine-123-iodoamphetamine ([^{123}I]IMP) SPECT scan was performed using 111 MBq of [^{123}I]IMP with a ring-type gamma camera (SET-020, Shimadzu Co., Japan) consisting of a gantry assembly with 64 scanning detectors. This system has two rings and simultaneously acquires two parallel slices with a center-to-center interslice distance of 3.5 cm. A high-resolution collimator was used. The raw data were reconstructed by filtered backprojection, using a Romachan-Butterworth filter. The filter order was 8 and the cutoff frequency 28 mm. Reconstruction was performed by a Data General ECLIPSE S-120 processor for a 64 × 64 matrix image. Slice thickness was 16 mm. A total of 600,000 counts were collected beginning 30 min after intravenous injection of 3 mCi (111 MBq) of [^{123}I]IMP. The tomographic images were obtained at 3 cm and 6.5 cm above the orbital-meatal plane. IMP SPECT showed reduced uptake in the bilateral frontal and temporal regions with no reduction of IMP uptake in the temporal-occipital and parietal-occipital regions (Fig. 2).

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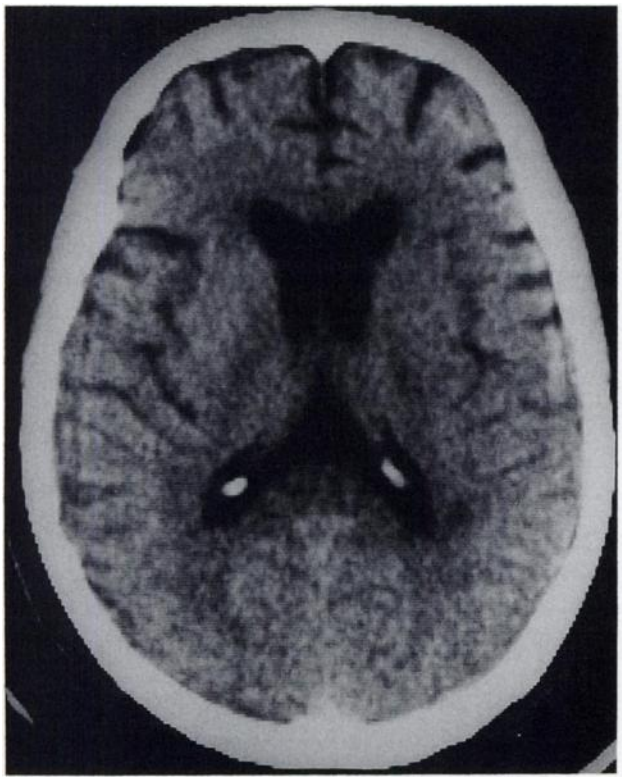

FIGURE 1
A brain CT scan showed mild cortical atrophy.

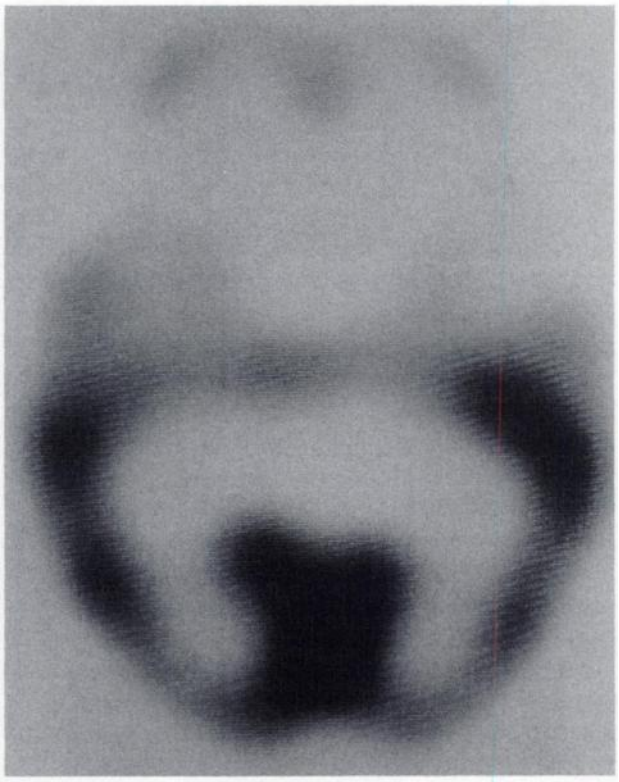

FIGURE 2
An IMP SPECT showed reduction of IMP uptakes in bilateral frontal and temporal regions.

Case 2

A 52-yr-old man was admitted to our institution complaining of weakness of upper extremities over the previous 5 mo. Nine months before admission, personality changes and global intellectual impairment were noted. He had no past history of neurologic and psychiatric disease. On admission, his neurologic and psychologic findings were:

1. Slight dementia, short attention span, and dyscalculia (Intelligence quotient 84, Hasegawa's dementia score, 30.5).
2. Tongue fibrillation.
3. Weakness of upper extremities.
4. Muscle atrophy of upper extremities.
5. Hyperactive muscle stretch reflex in the ankle.
6. Normal sensorium.

Routine laboratory findings, including an examination of spinal fluid and EEG were normal. An EMG showed neurogenic pattern. Magnetic resonance imaging (MRI) of the brain showed mild cortical atrophy in the frontal-temporal lobes without evidence of cerebrovascular attack (Fig. 3). The diagnosis was progressive dementia with MND. An [^{123}I]IMP SPECT study was performed, revealing reduced uptake in the bilateral frontal-temporal regions (Fig. 4) and normal uptake in the parietal and parietal-occipital regions.

DISCUSSION

These case reports and other studies indicate that progressive dementia with motor neuron disease is a new clinicopathologic category of dementia (*1–3*).

The characteristic features include:

1. Slow onset of progressive dementia in the pre-senile period.
2. Neurogenic muscular deterioration during the course of illness.
3. A duration of illness, from onset to death, of one to three years.
4. Absence of extrapyramidal symptoms and definite sensory deficits.
5. Absence of characteristic abnormalities in cerebral spinal fluid or EEG.
6. No known parental consanguinity of familial occurrence.
7. Nonspecific, mild degenerative changes throughout the central nervous system without evidence of cerebrovascular disease or primary degenerative dementia, but with the presence of pathologic findings of MND (*1,2*).

The main mental symptoms include: global intellectual impairment; dysfunctional memory; personality change; emotional disorders; and loss of spontaneous speech (*1,2*). The symptoms of this syndrome usually have been interpreted as unclassified pre-senile dementia. CT scans and MRI of the brain, which showed cortical atrophy in the frontal-temporal lobes, in con-

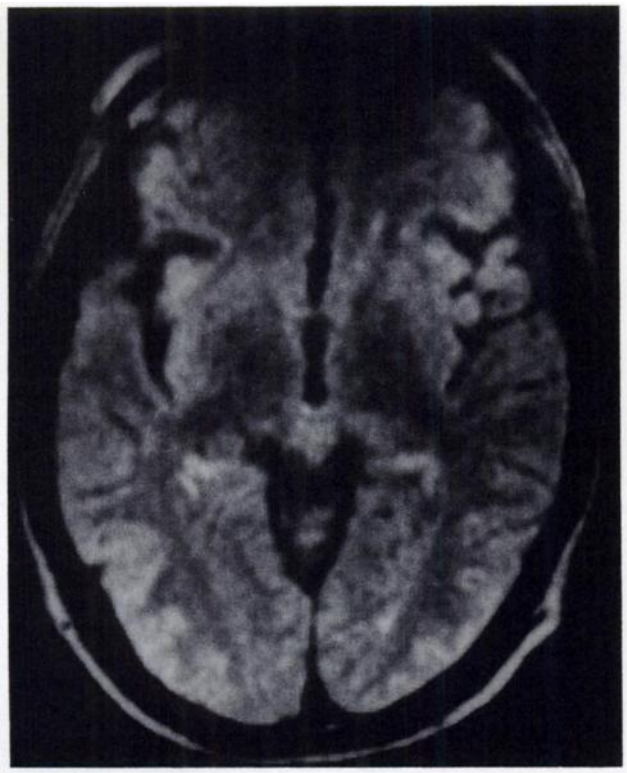

FIGURE 3
A brain MRI showed mild cortical atrophy without evidence of cerebrovascular attack.

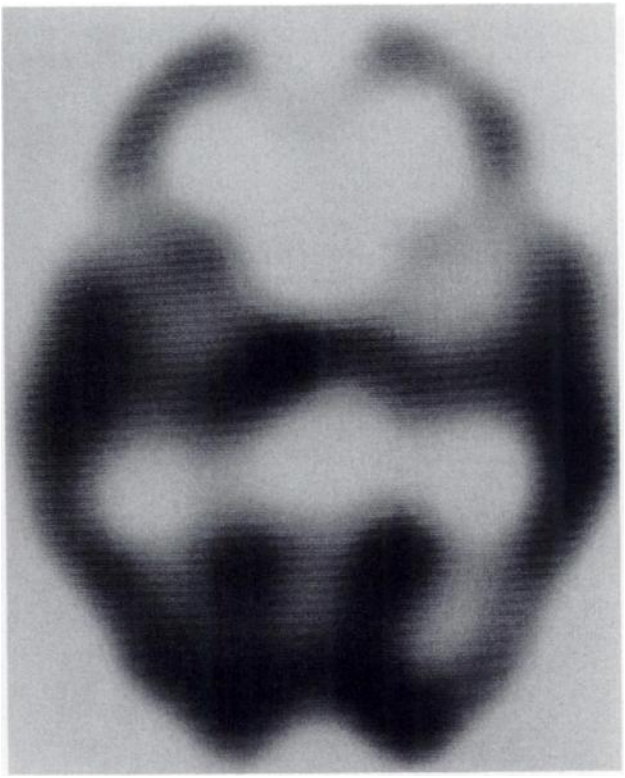

FIGURE 4
An IMP SPECT showed reduction of IMP uptake in bilateral frontal and temporal regions.

junction with the psychologic findings are suggestive of Pick's disease. The personality change experienced by these patients, however, was also mild to slight, and personal contact was preserved fairly well (*1,2*).

Other factors differentiating Pick's disease, Alzheimer's disease, or amyotrophic lateral sclerosis (ALS) from progressive dementia with MND, include the lack of observed Pick's cell or the neurofibrillary tangles associated with Alzheimer's (*1,3*) and the presence of mild, nonspecific neuropathologic changes in the cortex, brain stem, spinal cord, and basal ganglia. The memory disturbance, global intellectual impairment, and loss of spontaneous speech are not seen in classical ALS. The absence of any neuropathologic evidence of other disease suggested that these cases of progressive dementia with MND were etiologically different from ALS, Pick's disease, or Alzheimer's disease (*1–3*).

Our IMP SPECT study in progressive dementia with MND showed reduced uptake in the frontal and temporal regions, without reduction in IMP uptake in parietal and parietal-occipital regions. These findings were similar to those of Pick's disease and progressive supranuclear palsy, but different from those of classical Alzheimer's disease or multi-infarct dementia. Many radiopharmaceutical studies of regional changes in CBF and metabolism in pre-senile dementia have been reported (*4–13*). In Alzheimer's disease, Holman reported that the posterior parietal cortex was the most sensitive marker of Alzheimer's disease (*4*). The symmetric reduction of IMP uptake in bilateral posterior temporal and posterior parietal lobes was a characteristic finding in patients in early stages of Alzheimer's disease (*4–9*). The hypothesis has been advanced that reduction in IMP uptake in the posterior parietal lobes, can be associated with visuospacial problems (*4*). In positron emission tomography (PET), similar findings of metabolic changes and rCBF change have been reported (*10–13*). Momose reported that for Pick's disease, IMP SPECT showed reduced IMP uptake in the bilateral frontal and temporal lobes without parietal deficits (*14*). Similar changes of rCBF were reported with technetium-99m-HM-PAO in progressive supranuclear palsy (*9*). Similar reductions were observed in our IMP SPECT studies. Previous PET studies of cerebral metabolic rates for glucose (rCMRGlc) in patients with ALS, revealed hypometabolism throughout the cortex and basal ganglia that was at its greatest in the motor-sensory cortex and putamen (*15–16*).

We conclude that low perfusion in the anterior cerebral hemispheres appears to be characteristic of progressive dementia with MND and that IMP SPECT may be a useful method for the differentiation of this unique syndrome from the other established types of dementia.

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