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CASE REPORT

A case of corticobasal degeneration studied with positron emission tomography

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We measured cerebral blood flow, oxygen metabolism, glucose utilization, and dopamine metabolism in the brain of a patient with corticobasal degeneration using positron emission tomography (PET). The clinical picture is distinctive, comprising features referable to both cortical and basal ganglionic dysfunction. Brain imagings of glucose and dopamine metabolism can demonstrate greater abnormalities in the cerebral cortex and in the striatum contralateral to the more affected side than those of blood flow and oxygen metabolism. This unique combination study measuring both cerebral glucose utilization and dopamine metabolism in the nigrostriatal system can provide efficient information about the dysfunctions which are correlated with individual clinical symptoms, and this study is essential to diagnosis of corticobasal degeneration.

Keywords: Cerebral blood flow – Corticobasal degeneration – Dopamine metabolism – Glucose metabolism – Magnetic resonance imaging – Oxygen metabolism – Positron emission tomography

INTRODUCTION

In 1968, Rebeiz *et al.* described the clinical and pathological findings in three patients with what they called "corticodentatonigral degeneration with neuronal achromasia". Thereafter, Gibb *et al.* (1989) reported three patients and reviewed the clinical and pathological features of corticobasal degeneration. The diagnosis of corticobasal degeneration can be predicted during life on the basis of clinical findings, but a definitive diagnosis requires confirmation by autopsy (Riley *et al.*, 1990). However, a recent study using positron emission tomography (PET) indicated that distinctive supportive findings for the diagnosis could be obtained with this technique (Watts *et al.*, 1985; Eidelberg *et al.*, 1989; Sawle *et al.*, 1991). In the present study, we measured cerebral blood flow (CBF), cerebral oxygen consumption ($CMRO_2$), cerebral glucose utilization (CMRGlc), and dopamine metabolism in a patient with corticobasal degeneration using PET.

CASE AND METHODS

Case

A 71-year-old right-handed man developed disturbances of mental activity, spontaneity, and change of personality in 1988. He then became unsteady and was unable to walk without assistance in 1989. On examination in March 1991, he was alert and well oriented, and his mental status examination was normal. A neurologist noted generalized hyperreflexia, akinesia, limb rigidity and dystonia which were greater on the left, and prominent slowness and awkwardness of movements of the left hand. A left alien limb was also present with bilateral grasp reflexes. There was apraxia of the left hand with no sensory deficit and constructional disturbance of the right hand when copying figures. He complained of losing his balance and falling due to severe impairment of postural reflexes and his gait was markedly disturbed because of prominent apraxia.

Positron emission tomography

PET study was performed on a scanner, PT-931 (CTI Inc, USA), at the Cyclotron Radioisotope Center, Tohoku University, Sendai, Japan. This study was approved by the Research Ethics Committee of the Tohoku University, School of Medicine. The patient gave his written informed consent after a full explanation of the procedure.

For all studies, the patient was positioned in the scanner with the orbitomeatal (OM) line parallel to the detector rings. Using the bed and gantry coordinates, we tried to position the head in exactly the same position for each study. Before scanning, a short 21-gauge cannula was inserted to a brachial artery for arterial blood sampling. All the procedures were performed in a semidarkened room and the position of the patient enabled him only to see the ceiling of the scanner. A 15-min transmission scan was collected using a retractable germanium 68-gallium 68

ring source. To determine CBF and $CMRO_2$, steady-state emission data were collected for two scans each of 10 min duration, during inhalation of $C^{15}O_2$ and $^{15}O_2$ (370 MBq/min), respectively, with sufficient washout time following each study. Each scan was reconstructed into 14 planes with an 8 mm axial and transaxial resolution. Regional CBF and $CMRO_2$ were calculated according to Frakowiak *et al.* (1980) from the emission scans using arterial oxygen content and whole blood and plasma radioactivity counts measured in triplicate during each scan. To determine CMRGlc, a series of three emission scans each of 10 min duration was commenced 30 min after an intravenous bolus injection of 185 MBq (5 ml) 2[^{18}F]-fluoro-2-deoxy-D-glucose (^{18}FDG). Twenty blood samples were collected to determine the plasma radioactivities and glucose concentrations, taken every 10 min during the study (Hatazawa *et al.*, 1988). Regional CMRGlc was calculated from the emission scans using plasma radioactivity counts and the operational equation derived by Phelps *et al.* (1979) and Huang *et al.* (1980) from Sokoloff *et al.* (1977). A total of 22 regions of interest (ROIs) were manually placed on the calculated images as determined by reference to magnetic resonance images (MRI) and neuroanatomical atlases (Salamon and Huang, 1980; Talairach and Tournoux, 1988).

On a separate occasion, dynamic emission scans, each of 5 min duration, were performed over 60 min after an intravenous bolus injection of 185 MBq (5 ml) [^{18}F]-6-fluorodopa (FDOPA) in order to assess the presynaptic functional integrity of the nigrostriatal system. Emission data were simultaneously collected from seven contiguous axial sections, each about 6 mm in thickness from OM + 66 to OM + 22 mm. After data collection, the latter six continuous images of the same brain slice scanned between 30 and 60 min after administration of FDOPA were added and composite images were obtained in order to improve the contrast between dopaminergic and non-dopaminergic brain regions. FDOPA metabolism was determined using target-to-background ratio (TBR) values, which were the ratio of the accumulated activity in the caudate nucleus or the putamen to that in the ipsilateral cerebellum of each hemisphere as a reference area (Nagasawa, *et al.*, 1993).

RESULTS

Representative appearances of brain images obtained by MR and those of CMRGlc, CBF, and $CMRO_2$ are shown in Fig. 1. Regional CBF and $CMRO_2$ were markedly decreased with no asymmetry in the bilateral supratentorial brain structures including the cerebral cortex, the thalamus, the caudate nucleus, and the putamen compared with the values of the cerebellum. On the other hand, the brain imagings of CMRGlc were quite different from

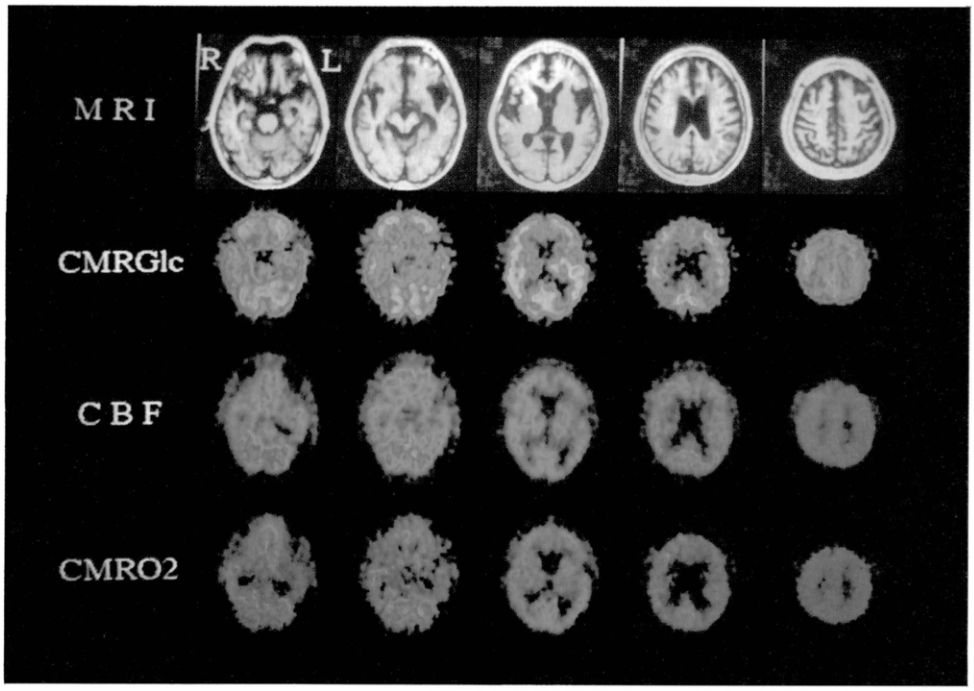

FIG. 1. Representative appearances of brain imagings obtained by magnetic resonance and those of cerebral metabolic rate of glucose (color scale ranged from 0 to 15 mg/100 g/min), cerebral blood flow (color scale ranged from 0 to 100 ml/100 g/min), and cerebral metabolic rate of oxygen (color scale ranged from 0 to 10 mg/100 g/min) in the same brain slices.

TABLE I. Cerebral metabolic rate of glucose of normal control subjects and a patient with corticobasal degeneration

Structure	Control	Patient	
		Right hemisphere	Left hemisphere
Frontal cortex			
Superior frontal cortex	8.67 ± 0.66	8.03	9.23
Medial frontal cortex	8.63 ± 0.97	8.64	8.94
Medial mesial frontal cortex	8.53 ± 1.10	8.60	8.80
Inferior frontal cortex	8.72 ± 1.31	8.40	8.46
Lateral frontal cortex	8.16 ± 1.30	8.40	8.50
Lateral posterior frontal cortex	8.23 ± 0.92	7.60	7.50
Parietal cortex			
Primary motor and sensory cortex	9.17 ± 0.77	7.40	8.50
Posterior parietal cortex	8.64 ± 0.51	7.10	7.70
Lateral parietal cortex	8.66 ± 1.20	7.12	7.65
Temporal cortex			
Superior temporal cortex	8.70 ± 0.88	8.80	9.40
Medial temporal cortex	8.50 ± 0.77	8.16	7.60
Inferior temporal cortex	7.70 ± 0.80	7.37	7.53
Temporal pole	7.25 ± 0.99	7.10	7.50
Occipital cortex	8.35 ± 0.84	8.70	9.30
Primary visual area	9.51 ± 0.88	9.48	9.48
Associative visual area	9.45 ± 1.11	8.40	9.90
Centrum semiovale	7.34 ± 0.68	6.63	6.43
Thalamus	8.79 ± 0.95	7.65	9.45
Caudate nucleus	9.13 ± 0.88	8.16	7.60
Putamen	8.67 ± 0.88	7.63	9.23
Brainstem	7.06 ± 0.46	6.40	6.43
Cerebellum	7.70 ± 1.23	8.33	8.40

Control values are given in mg/100 g/min (mean ± S.D.) from six subjects.

those of CBF and $CMRO_2$. The values of CMRGlc in each structure of the six normal control subjects and the patient are represented in Table I. The values of regional CMRGlc decreased in the parietal cortex, the thalamus and the putamen, this was more severe on the right side, and these findings were compatible with the asymmetric clinical features of the patient.

Brain CT and FDOPA PET brain slices of a normal subject at the level of the caudate nucleus and the putamen are shown in Fig. 2A. FDOPA and its metabolites were highly concentrated in the caudate nucleus and the putamen of both hemispheres. The values of TBR in the caudate nucleus and the putamen of 10 normal subjects were (mean ± S.D.) 1.81 ± 0.23 and 1.92 ± 0.28, respectively. On the contrary, in the case of the patient, the mean values of TBR decreased to 1.52 in the caudate nucleus and 1.44 in the putamen, and were more reduced in the right hemisphere (Fig. 2B, C, Table II).

DISCUSSION

The clinical diagnosis of corticobasal degeneration was made in this case on the basis of an asymmetric akinetic–rigid syndrome with apraxia and an alien limb (Rebeiz *et al.*, 1968; Gibb *et al.*, 1989). MRI revealed no responsible lesion except for moderate atrophy of the bilateral frontal and parietal cortices. The most remarkable PET findings were a reduction of CMRGlc in the thalamus and the parietal region contralateral to the more affected side, and a reduction of FDOPA accumulation in both caudate nucleus and putamen. Glucose is the main substrate for cerebral metabolism and many studies have confirmed a correlation between physiological function and glucose metabolism in the central nervous system (Sokoloff, 1977). Therefore, measurement of cerebral glucose utilization can provide an index of brain functions. No significant findings with asymmetry in relationship to the clinical features were found by measuring CBF and $CMRO_2$ in the present study. However, there are some reports about the usefulness of measurement of $CMRO_2$ (Sawle *et al.*, 1991) or CBF (Okuda *et al.*, 1992) for the diagnosis of corticobasal degeneration. Okuda *et al.* (1992) reported that the regional CBF decreased in the unilateral frontal and parietal cortices by using a single photon emission computed tomography and that such findings were in agreement with asymmetric clinical symptoms of two patients with corticobasal degeneration. Further detailed investigations for more patients using PET are

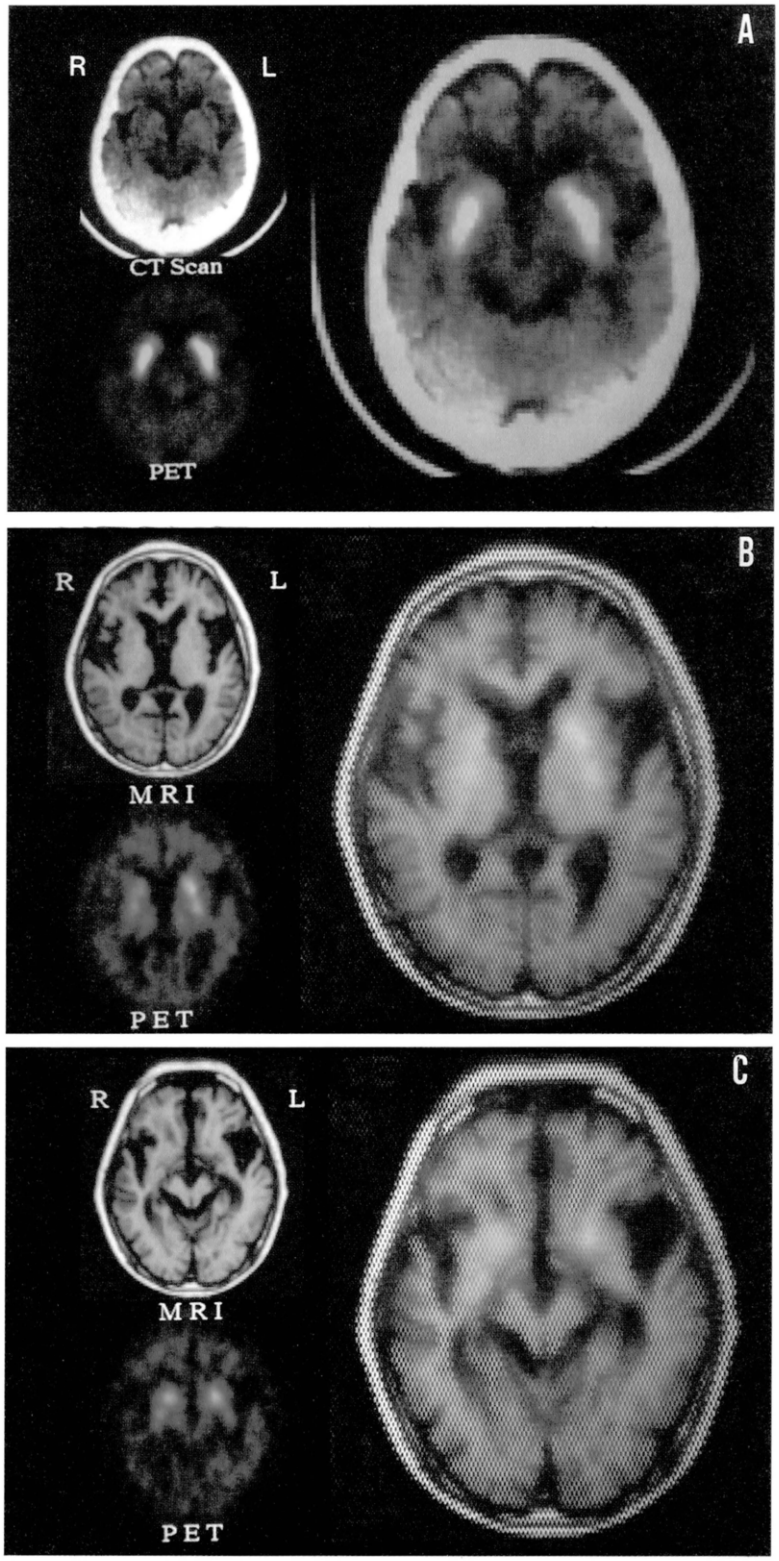

FIG. 2. Two different images obtained using [^{18}F]-6-fluorodopa (FDOPA) positron emission tomography and computed tomography or magnetic resonance at the level of the caudate nucleus and the putamen from a normal control (A) and from the patient with corticobasal degeneration (B, C). FDOPA accumulation was decreased in the caudate nucleus and the putamen. This decrease was more severe on the right side of the brain than the left.

TABLE II. The values of target-to-background ratio of normal control subjects and a patient with corticobasal degeneration

	Caudate/cerebellum	Putamen/cerebellum
Corticobasal degeneration		
Left side	1.58	1.48
Right side	1.46	1.40
Normal control ($n = 10$)	1.81 ± 0.23	1.92 ± 0.28

The mean values of target-to-background ratio of the patient were calculated using two brain slices as shown in Fig. 2B, C.
n, Number of subjects.

required for an analysis of CBF and metabolism in relation to the clinical symptoms of corticobasal degeneration.

The accumulation of FDOPA into striatum reflects its uptake into dopaminergic neurons, conversion into [^{18}F]-dopamine by dopa decarboxylase, and storage in terminal neurotransmitter vesicles (Firnau *et al.*, 1987). We have demonstrated that measurement of FDOPA metabolism with PET using FDOPA, combined with a new anatomical localization method to identify the caudate nucleus and the putamen on the overlapped images as shown in Fig. 2, can reveal specific abnormalities in patient with corticobasal degeneration (Nagasawa *et al.*, 1993). FDOPA metabolism was estimated by using the values obtained as the individual ratio of FDOPA accumulation in the caudate nucleus and the putamen to those in the cerebellum. Reduced accumulation in the caudate nucleus and the putamen are considered to represent a reduction in the number of functioning nigrostriatal dopaminergic neurons (Leenders *et al.*, 1986), and these findings in our case, which are more severe on the right side, reflect the left-sided predominance of the akinetic–rigid syndrome studied.

CONCLUSION

The most important PET findings were a reduction in FDOPA uptake in both caudate nuclei and putamina and thalamoparietal metabolic asymmetries; glucose metabolism was more reduced contralateral to the more affected side. The unique combination study measuring both cerebral glucose utilization and dopamine metabolism in the nigrostriatal system can provide further supportive evidence for the presumptive clinical diagnosis.

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