Regional Cerebral Blood Flow in Chronic Stroke Patients with Dementia

Fujio YOSHIDA, Seizo SADOSHIMA, Kenichiro FUJI, Kouzo IINO* and Masatoshi FUJISHIMA

Cerebral atrophy and regional cerebral blood flow (CBF) were examined in 52 chronic stroke patients with dementia, pre-dementia or non-dementia (according to the Dementia Scale). The index of cerebral atrophy was estimated on computed tomography, and CBF was determined using $^{133}$Xe inhalation method. Cerebral atrophy indices were not significantly different among various degrees of dementia except a slightly increased cella media index in pre-dementia group. Average values for CBF were bilaterally reduced in dementia, being $28.5 \pm 4.4$ ml/100g/min for affected hemisphere and $31.0 \pm 3.2$ ml/100g/min for non-affected one. Compared with those, CBF were higher in pre-dementia ($37.3 \pm 8.7$ and $39.4 \pm 8.2$ ml/100g/min, $p < 0.05$ vs dementia, respectively) and more higher in non-dementia ($45.8 \pm 10.2$ and $48.5 \pm 10.4$ ml/100g/min, $p < 0.01$ vs pre-dementia, respectively). Of 11 recurrent stroke patients, 5 with newly developed dementia after the second attack presented the preceding CBF reduction 10 to 34 months prior to the recurrence. Present results suggest that bilateral reduction of CBF may be the primarily important factor for the initiation or development of vascular dementia, and the CBF reduction seems to precede the symptom of dementia.

Key Words: Vascular dementia, multi-infarct dementia, cerebral infarction, cerebral circulation, cerebral atrophy

Dilatation of cerebral ventricles and decrease in cerebral blood flow (CBF) are commonly observed in patients with cerebrovascular dementia as well as in senile dementia of Alzheimer type. Positron emission tomography (PET) has shown that cerebral oxygen utilization was also decreased in proportion to the reduction of CBF in vascular dementia. Little is known, however, about the correlations of the degree of dementia to the cerebral atrophy, the site of cerebrovascular lesion, and the derangements of cerebral circulation and metabolism.

In this study, we examined in stroke patients with dementia whether 1) there is any relation between the degree of dementia and cerebral atrophy or decrease in CBF, and 2) there are regional characteristics in CBF pattern in vascular dementia. In patients who had recurrent stroke with newly developed dementia, CBF was determined before (non-dementia) and after the recurrence, to examine whether or not CBF is already decreased prior to manifest dementia.

MATERIALS AND METHODS

Fifty two stroke patients (11 cerebral hemorrhage, 41 cerebral infarction, 70 ± 7 years old), more than one month after ictus, were analyzed in this study. Detailed medical history, physical and...
neurological examinations, CT scan, regional CBF measurements were completed in all patients. Prior to the CBF study, the presence and the degree of dementia were evaluated using Dementia Scale11) which consists of 11 items for orientation, calculation and memory, and the patients were classified into four groups; normal (32.5 to 31 points), subnormal (30.5 to 22), pre-dementia (21.5 to 10.5) and dementia (< 10).

Cerebral atrophy was presented as frontal horn index (FHI) and cella media index (CMI) on CT film12). FHI was calculated as a ratio of the maximum width of frontal horns of the lateral ventricles and outer table of the skull in the slice through foramen Monro. CMI was calculated as a ratio of the minimum width of cella media and outer table of the skull in the slice where the lateral ventricle was separated with septum pericidum.

Regional CBF was measured by $^{133}$Xe inhalation technique using Cerebrograph (Novo). Twenty two collimated scintillation detectors were attached to the lateral surface of the head perpendicular to the sagittal plane. $^{133}$Xe gas mixed with air (3mCi/L) was inhaled for one minute. The $^{133}$Xe clearance curves from the head and from end-tidal air were recorded throughout the ensuing ten minutes of desaturation. F1, flow to the gray matter, was calculated by the two-compartmental analysis13). CBF obtained from each detector was averaged and presented as mean hemispheric CBF. Regional CBF (rCBF) pattern was presented as percent change of CBF in each detector, compared with mean hemispheric CBF. In patients with bilateral lesions on CT scan, the hemisphere responsible for the latest attack was determined by the medical history and neurological examination, and defined as the affected hemisphere.

Those who developed insidious mental deterioration without attack of stroke or whose ischemic score was less than 4 points by Loeb's modified ischemic score10), were not included in the present study. In 11 patients who had recurrent stroke, all examinations described above were repeated after the recurrence. The time interval between the first and second measurements ranged from 10 to 34 months. Thus, totally 63 measurements of CBF, atrophy indices and dementia scale in 52 patients were completed; 24 of normal group, 18 of subnormal, 15 of pre-dementia and 6 of dementia.

The values are expressed as mean ± standard deviation. Statistical comparisons of the data were made using Student's t-test.

RESULTS

Since CBF values and other parameters were not substantially different between normal and subnormal groups of patients, they were combined and shown as non-dementia group. Table 1 summarizes the average values of age and cerebral atrophy indices in each group. There was no difference in the average age among three groups. Concerning with cerebral atrophy, FHI did not differ between the groups. In contrast, CMI in non-dementia (0.233 ± 0.035) was significantly smaller than in pre-dementia (0.254 ± 0.033, p < 0.05), but not different from that in dementia (0.237 ± 0.038).

The average values of CBF in the affected and non-affected hemispheres were 28.5 ± 4.4

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Table 1. Mean values of age and cerebral atrophy indices in 63 determinations of 52 chronic stroke patients with dementia, pre-dementia and non-dementia (normal and borderline).

<table>
<thead>
<tr>
<th></th>
<th>age (yrs)</th>
<th>FHI</th>
<th>CMI</th>
</tr>
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<tbody>
<tr>
<td>dementia (6)</td>
<td>75±10</td>
<td>0.285±0.037</td>
<td>0.237±0.038</td>
</tr>
<tr>
<td>pre-dementia (15)</td>
<td>70±9</td>
<td>0.299±0.023</td>
<td>0.254±0.033*</td>
</tr>
<tr>
<td>non-dementia (42)</td>
<td>69±6</td>
<td>0.289±0.028</td>
<td>0.233±0.033</td>
</tr>
</tbody>
</table>

Parentheses indicate number of cases.
Values are mean ± SD.
FHI: frontal horn index, CMI: cella media index
*p < 0.05 (vs non-dementia)
ml/100g/min and 31.0 ± 3.2 in dementia, 37.3 ± 8.7 and 39.4 ± 8.2 in pre-dementia, 45.8 ± 10.2 and 48.5 ± 10.4 in non-dementia, respectively (Figure 1). The differences in CBF of corresponding hemisphere between dementia and pre-dementia, and between pre-dementia and non-dementia were significant (p < 0.05 and p < 0.01, respectively).

In non-dementia, rCBF of the frontal lobe was about 10% higher than mean hemispheric CBF, i.e. hyperfrontal distribution, which tended to be diminished in dementia. However, the difference of rCBF pattern between dementia and non-dementia did not reach a statistical significance, suggesting that CBF reduction in dementia was diffuse rather than focal.

Fig. 2 shows the changes of CBF in the 11 patients with recurrent stroke. Six patients did not show dementia even after recurrent stroke, but remaining 5 patients developed various grade of dementia, i.e., pre-dementia and dementia after the recurrence. Before recurrent stroke mean CBF was 58.0 ± 15.8 ml/100g/min in the former group and 40.8 ± 5.5 ml/100g/min in the latter, respectively (p < 0.05 vs non-dementia). After the recurrence CBF was markedly reduced to 28.2 ± 4.0 ml/100g/min in those who developed dementia. These CBF data indicate that CBF was significantly lowered 10 to 34 months prior to manifest dementia.

DISCUSSION

Previous studies have shown a poor correlation between cerebral atrophy and the severity of vascular dementia. The present study accords with these results. Enlargement of frontal horn had no relation with the degree of dementia. In this study, cella media in pre-dementia was slightly enlarged than that in non-dementia, suggesting more or less atrophy of the brain in demented patients. No further dilatation of cella media, however, was observed with advance of dementia. Morphometric study may not differentiate the age related brain atrophy from that after stroke.

CBF in patients with dementia is known to be reduced. In most studies, the values of CBF in vascular dementia were compared with age-matched healthy volunteers or senile dementia of Alzheimer type. Thus, it was unclear whether the reduced CBF was compromised secondary to dementia or primarily induced by stroke itself. In the present study, the CBF values in stroke patients with dementia were compared with those in intellectually normal patients who...
also had stroke. The results indicate that CBF in stroke patients with dementia was significantly lower than that in those without dementia, and correlated well with advance of dementia. The measurement of CBF may be a useful mean to estimate the degree of dementia, as compared with the morphometric index of cerebral atrophy.

The stroke patients with dementia showed bilateral reduction of CBF even in the cases with unilateral lesions on CT scan. It has been demonstrated that unilateral brain lesion is associated with contralateral depression of CBF\textsuperscript{14,15}. Transhemispheric metabolic depression\textsuperscript{14} intra- or extra-cranial vascular lesion predisposing to stroke may influence CBF contralateral to the lesion\textsuperscript{16}. Furthermore, unvisualized brain lesions on CT scan in the contralateral hemisphere may also play a role for bilateral reduction of CBF in dementia. Pathological and radiological studies also found the importance of lesions in both hemispheres for the development of vascular dementia\textsuperscript{17,18}. Present results suggest that vascular dementia is associated with bilateral rather than unilateral reduction of CBF.

Previous studies using \textsuperscript{133}Xe clearance method, some investigators found reduced CBF especially in temporo-parietal lobe\textsuperscript{2,4}, while others only noted patchy reduction\textsuperscript{19}. In the present study, the demented patients showed no characteristic rCBF pattern but rather diffuse CBF reduction.

Several reports have presented that in neurologically normal volunteers with risk factors for stroke, reduction of CBF precedes the occurrence of cerebrovascular disease\textsuperscript{20,21} or vascular dementia\textsuperscript{22}. It is also known that CBF is reduced in relation to the severity and duration of hypertension\textsuperscript{23}. Arteriosclerosis of cerebral vessels reduces CBF and increases the susceptibility to stroke. In the present study, five patients who later developed dementia showed the already lowered CBF 10 to 34 months prior to the latest ictus of stroke, followed by a further post-ictal reduction of CBF. Thus, the preceding reduction of CBF possibly due to pathological changes of cerebral vessels may be a primarily important factor for the initiation of vascular dementia.

Our study of PET (position emission tomography) demonstrated in mild dementia that the decrease in cerebral metabolic rate of oxygen (CMRO\textsubscript{2}) was more marked and diffuse, compared with the reduction of CBF (unpublished data). The changes of CBF closely correlate to neuronal function and are usually coupled with those of CMRO\textsubscript{2}. Powers et al., however, found a significant overlap in CBF values between regions of cerebral infarction and those of viable tissue, and suggested that the measurement of CMRO\textsubscript{2} might be more useful to distinguish viable from nonviable cerebral tissue than the measurement of CBF\textsuperscript{24}.

Ujike et al., reported a significant decrease in CMRO\textsubscript{2} in the fronto-temporal cortex, occipital cortex and thalamus in dementia\textsuperscript{9}. Kitagawa et al., using stable Xe contrast CT scanning method, observed correlations between mental test scores and the reduction of CBF in the fronto-temporal lobe and thalamus\textsuperscript{5}. The present results together with the previous studies suggest that the development of dementia in chronic stroke is associated with diffuse reduction rather than focal reduction of CBF, and that such CBF reduction is mainly in the cortex rather than in the deep structure except for the thalamus.

In conclusion, bilaterally diffuse reduction of CBF is suggested to be the primarily important factor for the initiation or the development of vascular dementia. The CBF reduction seems to appear before the symptoms of dementia become manifest. Estimation of CBF may be helpful to predict development of dementia. Further investigation is needed whether restitution of CBF results in recovery of the intellectual performance and prevents dementia.

REFERENCES


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