Confusion or Delirium in Patients with Posterior Cerebral Arterial Infarction

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Abstract-

Objective: To identify the possible anatomic sites and risk factors for the development of confusion or delirium in patients with posterior cerebral arterial (PCA) infarction.

Materials and methods: Twenty-nine patients aged 34-86 years with PCA infarction were divided into two groups: one with and the other without perturbed mentation. The clinical and laboratory data, including neuroimages, were retrospectively reviewed. Student-t, chi-square and Fisher's exact tests were performed for data analysis.

Results: Confusion or delirium tended to develop in the left (10/13) or bilateral (5/5) PCA infarction as compared to the right PCA infarction (3/15) ($P< 0.05$) and medial occipital-temporal gyri involvement was crucial for its development ($P< 0.05$). The results were also noted in the patients with first-ever stroke. Diabetes mellitus was the sole biochemical factor to be associated with confusion or delirium ($P< 0.01$).

Conclusions: The involvement of the medial occipito-temporal gyri, especially on the left side was the pivotal factor for the development of confusion or delirium in patients with PCA infarction. Higher prevalence of diabetes mellitus was also observed in the group with mental perturbation.

Key Words: Confusion, Delirium, Posterior cerebral arterial infarction

Acta Neurol Taiwan 2007;16:136-142

INTRODUCTION

Since 1952, several case reports have suggested that lesions in the brain supplied by the posterior cerebral artery (PCA) may cause confusion or delirium, especially when bilateral or the dominant PCA are involved[(1,2)]. The inferior medial aspect of bilateral temporo-occipital areas were the most frequently sites of involvement,

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Received October 4, 2006. Revised December 18, 2006.
Accepted March 14, 2007.

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such as lingual gyrus, hippocampus, parahippocampus, and medial occipito-temporal gyri (fusiform gyrus)[3-6]. However, it is uncertain whether there is a hierarchic order of these areas in eliciting confusion or delirium. Medina et al. reported that the fusiform and lingual gyri involvement might be more crucial than the lesion of the limbic area (hippocampus and parahippocampus) in the development of the behavioral changes[3]. However, this viewpoint was not supported by other researchers[1,7] and suspended the issue mandatory to be justified in further. In addition, some reports also revealed that the PCA infarction with delirium was associated with higher mortality, especially in the elderly[5,7]. Although PCA infarction is not uncommon, the patients with concomitant presence of confusion or delirium were not often encountered. Thus the previous studies usually drew conclusion from either single case report or small number of patients[1-7]. In the current report we investigated twenty-nine patients with acute PCA infarction to further elucidate the relationship between the anatomic sites and the development of delirium or confusion. In addition, the possible risk factors causally linked to the development of perturbed mentation in PCA infarction patients were also analyzed.

MATERIALS AND METHODS

The clinical information of twenty-nine admitted patients from May 1st, 2002 to February 28th, 2005 (4 women and 25 men) was retrospectively analyzed from the data bank of the Department of Neurology. Their ages ranged from 34 to 86, with a mean of 65.55 years. To enter the study, the patients had to fulfill the following inclusion criteria: presence of both an acute focal neurological deficit and an acute ischemic stroke located in the territory of PCA on either brain computed tomogram (CT) or magnetic resonance image (MRI). The exclusion criteria were (1) pre-existing impairment or history that might influence cognitive or functional outcome (i.e., history of alcohol or drug abuse, pre-existing cognitive declining), (2) severe systemic infection that might confound or combine with delirium, or (3) associated with acute stroke in areas beyond PCA territory.

The recording of charts was delicately reviewed. The contents included clinical presentation, general physical and neurological examinations, results of blood tests including blood glucose or HbA1c, triglycerides (TG), total cholesterol or low-density lipoprotein (LDL), the data of electrocardiography (ECG), Holter 24-hour ECG or trans-esophageal echography (TEE), and the results of brain CT or MRI. We divided patients into two groups. The first group presented as confusion or delirium. Confusion usually denotes the patient's incapacity to think with customary speed and coherence. Its most conspicuous attributes are impaired attention and concentration, manifest disorientation and an inability to properly register immediate events. Delirium was defined as an acute and transient mental syndrome, which is marked by prominent disorders of perception, terrifying hallucination and delusions, inability of sleep, a tendency to twitch and convulse, and intense fear or other emotional reactions. Delirium is not only extreme inattentiveness, but also overactivities of psychomotor and autonomic nervous system functions. The second group of patients presented as homonymous hemianopia without disturbed cognitive function as aforementioned. We recorded the side (right, left or bilateral) and the locations of ischemic stroke. We further divided the inferior medial temporo-occipital area into medial occipito-temporal gyri (fusiform gyri), lingual gyrus, hippocampus, and parahippocampus associated with thalamus, cuneus, precuneus, and cingulate gyrus. The concomitant existence of vascular risk factors were also reviewed; these included previously diagnosed diabetes mellitus (DM), hypertension, hypertriglyceridemia, hypercholesterolemia, transient ischemic attack, old ischemic stroke, and evidence of cardiac emboli.

Statistical analysis

Independent t test, chi-square and Fisher's exact tests were adopted where appropriate to compare the differences between the two groups of patients. A two-tailed p value of less than 0.05 was considered to be significant.

RESULTS

The demographic data of patients are shown in Table. Among them, 13 patients had left, 15 had right and 1 had bilateral PCA infarction. Fourteen patients presented as homonymous hemianopia with confusion or delirium, and fifteen patients had only visual field defects. No obvious statistical significant difference could be detected in the mean age of these two groups (Table). Of the 13 patients with left PCA infarction, 10 had confusion or delirium (76.9%), whereas only 3 of 15 patients with right PCA involvement had such a manifestation (20%). Statistical analysis revealed a significant tendency for the confusion or delirium to develop in patients with left PCA infarction ($p< 0.05$) (Table). One of the three right PCA patients with mental confusion or delirium had an old infarction of the left PCA territory (patient 7). One patient (patient 13) with confusion had acute infarction in the territory of bilateral PCA. In the confusion or delirium group, 5 patients had old PCA infarction (4 contralateral, 1 ipsilateral). Disregarding the temporal or chronological order of infarction, there was a tendency for the confusion or delirium to develop in patients with infarcts in the territory of bilateral PCA (patients 1, 7, 9, 13, 14) ($p< 0.05$).

The correlation between the topographic distributions and the development of confusion or delirium was analyzed (Table). Of the 19 patients with medial occipi-

Table. *Comparison between posterior cerebral arterial infarction patients with and without confusion or delirium*

	PCA infarction with confusion or delirium	PCA infarction without confusion or delirium	Statistical significance
Mean age (years)	66.3±13.05	64.8±9.85	NS*
Sex (Male:Female)	10:4	15:0	
Left	10 (76.9%)	3 (23.1%)	P< 0.01
Right	3 (20%)	12 (80%)	P< 0.005
Thalamus	6 (46.2%)	7 (53.8%)	NS
Lingual gyri	10 (52.6%)	9 (47.4%)	NS
Hippocampus	7 (46.7%)	8 (53.3%)	NS
Parahippocampus	7 (46.7%)	8 (53.3%)	NS
Cuneus	7 (46.7%)	8 (53.3%)	NS
Pre-cuneus	2 (50%)	2 (50%)	NS
Cingulated gyri	2 (66.7%)	1 (33.3%)	NS
Medial O-T	12 (63.2%)	7 (36.8%)	P< 0.05
DM	7 (100%)	0 (0%)	P< 0.01
Hypertension	9 (40.9%)	13 (59.1%)	NS
Hyper-TG	1 (20%)	4 (80%)	NS
Hyper-Chol	6 (42.9%)	8 (57.1%)	NS
Heart emboli	2 (33.3%)	4 (66.7%)	NS
Old CVA-POST	5 (100%)	0 (0%)	P< 0.05
Old CVA-Ant	2 (50%)	2 (50%)	NS
Carotid TIA	0 (0%)	1 (100%)	NS
Dependent at discharge	6 (85.7%)	1 (14.3%)	NS
Mortality	1 (50%)	1 (50%)	NS
Total	14	15	

Medial O-T: medial occipito-temporal gyri; DM: diabetes mellitus; Hyper-TG: hypertriglycerolemia; Hyperi-Chol: Hypercholesterolemia; Old CVA-POST: old ischemic stroke over posterior circulation territory, Old CVA-Ant: old ischemic stroke over anterior circulation territory; Carotid TIA: carotid ischemic stroke.

(Mean age was analyzed with Student-t test; The other items were analyzed with chi square test with Fisher exact correction for small numbers. Degree of freedom: 1); *NS: non-significance

to-temporal gyrus lesions, 12 had confusion or delirium (63.2%), whereas only 2 of 10 patients with lesions located outside the medial occipito-temporal area had similar clinical manifestations (20%). This difference was statistically significant ($p< 0.05$) (Table).

For avoiding the confounding of old stroke and to delineate the true topographic effect in developing the perturbation of consciousness, we focused on the first-ever stroke patients. Of the 9 patients with left PCA infarction, 6 patients had confusion or delirium (66.7%), whereas only 1 of 11 patients with right PCA involvement had such a manifestation (9.09%) ($p= 0.017$). Of the 15 patients with medial occipito-temporal gyrus lesions, 8 had confusion or delirium (53.3%), whereas none of 6 patients with lesion located outside the medial occipito-temporal area had similar clinical manifestations (0%) ($p= 0.047$).

Some patients had more than one type of vascular risk factors. All of the seven patients whose blood glucose levels were elevated and met the criteria of DM [fasting plasma glucose > 126 mg/dL, or glycosylated hemoglobin (HbA1c) > 6.5%] had confusion or delirium (100%), whereas only 7 of 22 patients without DM suffered from cognitive dysfunction (31.8%) ($p< 0.01$). One of the seven DM patients had elevated HbA1c level higher than 11% (patient 1), and three of them (patient 6, 9, 11) had DM for more than 8 years. Four of the seven patients were regularly managed with oral hypoglycemic agents and the others had poor compliance to medical treatments. Five DM patients had blood glucose levels higher than 150 mg/dL at emergency room. The relationship between the perturbed cognitive function and other risk factors, including hypertension and hyperlipidemia, was also analyzed and the finding was unremarkable (Table).

ECGs were conducted in all of the 29 patients. In addition, TEE was conducted in 8, transthoracic Doppler was done in 2 and Holter ECG was done in 5 of 29 patients. Two of the five patients with evidence suggestive of cardiac emboli (left atrial appendix thrombus in TEE, atrial fibrillation, atrial flutter, or sick sinus syndrome in complete or Holter ECG) had confusion or delirium (40%), and 11 of 19 patients with no evidence of cardiac emboli also had perturbed mentation (57.9%). There was no significant difference between the two subgroups.

Brain CT and MRI revealed old ischemic stroke in 8 of 29 patients (Table) and one patient had history of left carotid TIA. All of the five patients with old ischemic stroke in the PCA territory (3 right, 2 left) had confusion or delirium (100%) ($p< 0.01$, Table), whereas only 2 of the 5 patients with old ischemic stroke in the middle cerebral arterial territory or carotid TIA had similar clinical features (40%).

Concerning the disease course and outcome (Table), 6 patients of the delirium group were dependent at discharge and only 3 patients were still dependent 3 months after the stroke. Patient 8 committed suicide 100 days later after the stroke. For the non-delirium group, patient 15 was still dependent due to infarction in the territory of the main trunk of the left middle cerebral artery occurred 10 days after the first episode. Patient 21 with the left PCA infarction died of basilar arterial occlusion 10 days later after the initial stroke. No significant difference could be detected between the two groups in terms of mortality rate.

DISCUSSION

The current study reveals a strong tendency for the patients with infarction of left PCA territory to develop confusion or delirium whether they are first-ever stroke or not. In addition, it is intriguing to find that the involvement of the medial occipito-temporal gyri was crucial for the occurrence of cognitive perturbation in these patients. It has been known that 'agitated delirium' may be caused by disconnection of anterior limbic structures from neocortical inputs, by destruction of posterior limbic structures, or by the severance of the pathway linking dominant temporal neocortex and limbic system[5]. The involvement of cingulate gyri and orbital areas, inferior medial occipito-temporal area or medial-dorsal nucleus of thalamus in stroke patients with confusion had also been documented[2,4-6]. Among these regions, the involvement of the medial occipito-temporal gyri seems responsible for the development of confusion

or delirium in the current patients and the causal link relationship between the two is intriguing. Marco et al. in 2003[8] illustrated that the occipito-temporal region was bridged by two main structures, the direct inferior longituidinal fasciculus (ILF) and indirect U-shaped fiber. ILF is a major white matter associative connection between the occipital and anterior-inferior temporal lobe. The occipital branches of the ILF (Fig.) run forward in parallel to the fibers of the splenium and optic radiation and merge into a single bundle at the level inferior and posterior to the posterior horn of the lateral ventricle.

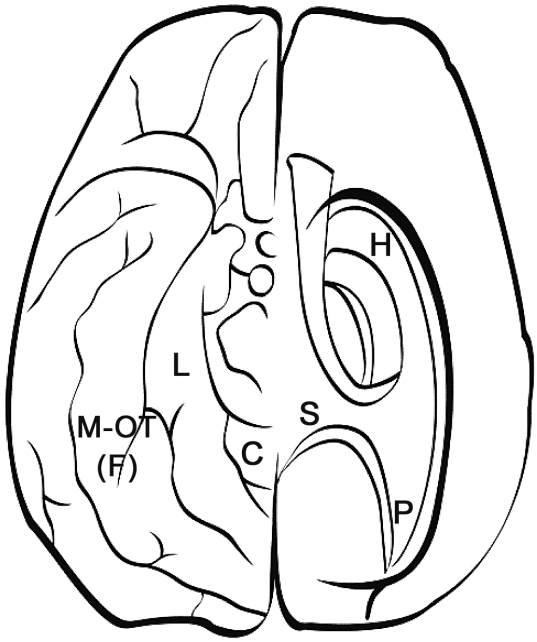

Figure. Illustration of the inferior surface of the brain at the transection level at the midbrain.
The inferior and posterior horns of the left lateral ventricle wereopened and portions of the temporal and occipital lobes were removed. The occipital branches of the inferior longitudinal fasciculus (ILF) arise from (1) the extrastriate cortical regions on the dorso-lateral surface of the occipital lobe and (2) the posterior lingual gyrus and fusiform gyri ventro-medially. The fasciculus terminates medially at the uncus / parahippocampus gyrus close to the amygdala and the hippocampus (M-OT: medial occipito-temporal gyrus; F: fusiform gyrus; L: lingual gyrus; C: cingulate gyrus; S: splenium of corpus callosum; H: hippocampal formation; P: posterior horn of lateral ventricle; bald solid line: ILF)

Through this pathway there is a reciprocal connection between the human visual cortex (V4) and lateral temporal and medial temporal parahppocampal regions where the amygdala is located in. Functionally, ILF appears to mediate the fast transfer of visual signals to temporal regions and conveys neuromodulatory projections from the amygdala to visual areas. Thus transection of this fiber may result in visually specific semantic emotion or memory deficit, such as visual agnosia, prosopagnosia and visual amnesia. In addition, the dominant hemisphere is primarily responsible for language processing, arithmetic and analytic functions. Under these regards, the lesion in the neural circuit of the dominant hemisphere might result in more severe cortical dysfunction than the lesion involving the non-dominant hemisphere. McDonald et al. in 2000[9] described 10-13%-reduction of the mean volume of the left hippocampal and fusiform gyri in patients with schizophrenia suggesting that dominant hemisphere lesions could play a pivotal role for the development of the alteration of normal cognitive processing. Moreover, all of the five patients with bilateral PCA infarction, no matter concomitantly developed or in different chronological order, presented with confusion or delirium. Taken together with these findings, it is likely that lesions in the fusiform branch of the left ILF might cause cognitive dysfunction and additional contralateral PCA infarction may complicate the clinical features by perturbing the non-dominant hemispheric, i.e. spatial concept and facial recognition, or the dominant hemispheric functions.

Among the vascular risk factors, DM was the only significant one that was correlated to the development of delirium or confusion in patients with PCA infarction. There is currently no report concerning the correlation between DM and the development of delirium in ischemic stroke. Bucerius et al.[10] described DM as an independent predictor of delirium in cardiac surgery and the authors proposed that there was close association between atherosclerotic disease burden and DM. Besides, Northam et al.[11] described possible cognitive impairment in diabetic patients, particularly those involving novel learning, memory, abstract reasoning, and psychomotor coordination. Mooradian et al.[12]

described several detrimental impacts of DM, including cerebrovascular atherosclerosis, repeated hypoglycemic reaction, and autonomic neuropathy, on cerebral function. In addition, altered brain metabolism, reduced levels of aromatic amino acids and increased levels of branched chain amino acids, alterations in the levels of brain monoamines and their metabolites, and reduced blood-brain-barrier glucose transport had all been reported in diabetic animals[12]. Mooradian et al. also proposed two phenomena: (1) poor control of diabetes (HbA1c > 11%) was associated with poor attention and increased reaction time and (2) type II diabetic patients with poor performance on psychometric testing showed a significant improvement after a reduction of blood glucose levels to 90-150 mg/dL. In the current DM patients with mental confusion, one was found to have HbA1c levels higher than 11% and five were found to have glucose levels higher than 150 mg/dL. Although we do not know the pre-morbid cognitive conditions of these patients, it is conceivable that they may have pre-existing minimal cognitive dysfunction according to the Mooradian's observation[13]. Eight patients had DM for longer than 8 years and the detrimental impacts of DM on the brain could be far more severe in this group of patients than those of shorter duration[12]. With these gathered, it is possible that chronic hyperglycemia may set the brain in a state that may simmer the development of delirium or confusion in patients with PCA infarct.

Emboli might be more common than thrombi to cause PCA infarction[14]. Since emboli may be allocated randomly to a more widespread vascular territory than the local arterial thrombi, it is intriguing to know whether embolic stroke would trigger disturbed mentation more frequently than thrombotic one. The current data, however, revealed no evidence of such a difference. Since not every individual patient underwent investigation to determine the possible embolic sources, it is premature to draw the conclusion in this regard.

Previous reports had found poor outcome and higher mortality in patients of PCA infarction with confusion or delirium[2,7]. However, the phenomenon was not observed in the current study.

ACKNOWLEDGEMENT

The authors thank Dr.s Chi-Chung Kuo and Yu-Wan Yang for their help in patient referral. We also thank Mr. Jung-Chun Chang for his help in data analysis. The study was supported by grants from NMRP (NSC 94-2314-B-039-005) and DMR-94-011.

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