Postsurgical Disappearance of Dementia without Increased Cerebral Blood Flow in Hydrocephalic Patients

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Abstract

Cerebral blood flow (CBF) was measured by the ^{133}Xe inhalation method in four hydrocephalic patients without signs of increased intracranial pressure. Dementia decreased markedly after shunting procedures in two patients and after removal of posterior fossa tumors in the other two patients. The preoperative average hemispheric CBF was subnormal in three patients; it did not increase when dementia disappeared, within 7 to 21 days postoperatively, in any of the four patients. The cerebral circulation time, measured by dynamic computed tomography in three patients, was prolonged before operation and returned to normal after operation reflecting improvement in the microcirculation of the affected tissue. The results of this study demonstrate that disappearance of dementia following surgical intervention in hydrocephalic patients, possibly including those with normal-pressure hydrocephalus, is not always accompanied or preceded by increased CBF as measured by the conventional method.

Key words: brain neoplasms, cerebral blood flow, dementia, dynamic computed tomography, hydrocephalus, normal-pressure hydrocephalus

Introduction

Dementia has become a major social problem as the elderly population has grown. Normal-pressure hydrocephalus (NPH) is one well known cause of neurosurgically treatable dementia.^{1,19)} Brain tumors affecting the ventricular system, particularly the third ventricle and below it, can cause dementia *via* alteration of cerebrospinal fluid (CSF) dynamics.^{1,13,19)} When dementia develops insidiously, without signs and symptoms of increased intracranial pressure (ICP), such tumors are often overlooked, particularly in elderly patients.

We treated four elderly patients with dementia who were referred to our clinic with NPH, three of whom were found to have a tumor in the posterior fossa. Dementia disappeared in all four cases after a shunting procedure or removal of the tumor. Regional cerebral blood flow (rCBF) was subnormal

before operation in three patients and remained low postoperatively in all four patients, even though the dementia abated.

Patients and Methods

The patient population comprised four elderly individuals (two males and two females) admitted to our department with dementia and hydrocephalus. Dementia was evaluated by the dementia rating scale proposed by Hasegawa *et al.*⁸⁾: a score of 0 to 10 was rated as dementia, 10.5 to 21.5 as predementia, 22 to 30.5 as subnormal, and 31 to 32.5 as normal. The evaluation was repeated every 2 to 3 days until the score reached the normal range. We measured CBF by the ^{133}Xe inhalation method, using a TASC-5 dynamic rCBF analyzer with eight NaI detectors on each hemisphere. Average CBF values for each hemisphere, including the initial slope index (ISI) at 2 minutes, the gray matter flow (FG), and the white matter flow (FW), were used in the analysis.¹⁶⁾ CBF was measured 2 to 3 days before surgery and

repeated 7 to 21 days postoperatively, when dementia had decreased and the score on the dementia rating scale had reached the normal range. CBF values were also obtained for normal control subjects of 60 years or older.

Dynamic computed tomography (CT) was performed before or 2 to 3 days after operation, while the patient was still demented, and then repeated within 3 days after the postoperative CBF measurement, when dementia had disappeared. For the dynamic assessment we used a GE CT/T 8800 scanner equipped with a special research program (GEDIS/D), which we reported previously.⁶⁾ Among the various parameters derived from the time-density curve, the width (W) and the effective width (area/peak, or A/P) were considered to represent the circulation time in the region of interest.⁶⁾ Dynamic CT was also performed for normal control subjects (not age-matched).

Case Reports

Case 1: A 73-year-old male received a minor head injury when he stumbled and fell 4 months prior to admission. Two months after the fall he began to speak incoherently and shortly thereafter became incontinent. On admission he had a triad of NPH (*i.e.*, dementia, gait disturbance, and incontinence). He had no headache or vomiting either before or after admission. There was no choked disc. A CT scan showed symmetrical dilatation of the lateral ventricles. After a ventriculo-peritoneal (V-P) shunt was performed, his neurological status steadily improved. His scores on the dementia rating scale showed progressive improvement, from 0 before

operation to 15.5 on the 7th postoperative day and 31.5 on the 17th postoperative day. His scores were normal thereafter. The average hemispheric CBF did not change significantly from before to 21 days after the shunting procedure (Table 1). The preoperative dynamic CT was not usable because of motion artifact. Compared with the dynamic CT results obtained on the 2nd postshunt day, the circulation time on the 23rd postshunt day was reduced by 2 to 4 seconds and was entirely restored to the normal range (Fig. 1).

Case 2: Five years prior to admission a 60-year-old male noted hearing difficulty and tinnitus of the right ear, and 1 year later became deaf in that ear. Six months before admission he developed forgetfulness and gait disturbance, which gradually worsened. On admission the neurological examination disclosed a slow, narrow-based gait; the patient was indifferent to his environment, slow in responding to verbal commands, and deaf in the right ear. He was not incontinent, nor did he have headache or vomiting. There was no choked disc. His score on the dementia rating scale was 20. The CSF was watery clear, with a protein content of 59 mg/dl. A CT scan revealed symmetrical ventricular dilatation and a small, enhanced mass in the right cerebellopontine angle. The gait disturbance and dementia improved dramatically for about 2 days following a right suboccipital craniectomy and total removal of the acoustic tumor. The dementia score increased to 29.5. However, 6 days postoperatively the score decreased to 20 and the gait disturbance recurred. A V-P shunt was inserted, and 7 days later the patient's dementia rating was normal and he no longer had disturbed gait. The CBF study showed no significant changes from

Table 1 Average hemispheric cerebral blood flow before and after surgical procedure

Case No.	Age, Sex	Before operation (dementia present)			After operation (dementia absent)					
		ISI	FG (ml/100 g/min)	FW	ISI	FG (ml/100 g/min)	FW	ISI	FG (ml/100 g/min)	FW
1	73, M	39.1	58.9	17.2	43.1	60.8	16.4**	—	—	—
2	60, M	49.1	65.8	19.6	48.4	65.3	18.9*	53.3	67.8	18.8**
3	68, F	39.1	59.9	16.2	35.2	64.6	15.7*	36.6	55.7	16.2***
4	73, F	38.0	56.4	17.6	36.3	54.3	18.9*	—	—	—
Mean $\pm$ SD		41.4 $\pm$ 4.6	60.3 $\pm$ 3.4	17.7 $\pm$ 1.2	40.8 $\pm$ 5.4	61.3 $\pm$ 4.4	17.5 $\pm$ 1.4			
MABP (mmHg)		105.0 $\pm$ 13.3			108.5 $\pm$ 13.6					
PaCO ₂ (mmHg)		32			32					

*7 days; **21 days; ***2 years. ISI: initial slope index at 2 minutes, FG: gray matter flow, FW: white matter flow, MABP: mean arterial blood pressure, PaCO₂: partial pressure of carbon dioxide in arterial blood. Note: In age-matched controls the average hemispheric ISI, FG, and FW were 54.0 $\pm$ 7.4, 75.9 $\pm$ 6.3, and 21.3 $\pm$ 2.0, respectively.

Fig. 1 Case 1, dynamic CT. *upper*: Second postshunt day, when dementia was still present. *lower*: Twenty-third postshunt day, by which time the dementia had completely disappeared. Functional image of width (see *Patients and Methods*) (*left*) showing less intensity on the 23rd postshunt day. Time-density curve (*right*) obtained from the region of interest in the frontal lobe (indicated by circle in center) showing reduced circulation time on the 23rd postshunt day, although the lateral ventricles were still enlarged. Note: In normal controls, W was 7.3 ± 1.6 seconds and A/P was 8.5 ± 1.5 seconds.

before operation to the 7th day after shunt emplacement, at which time he achieved a normal score on the dementia rating scale. The repeat CBF measurement on the 21st postshunt day showed no significant increase (Table 1). A preoperative dynamic CT was not obtained. Compared with the dynamic CT data obtained on the 3rd postshunt day, when he was still demented, the circulation time on the 10th postshunt day was reduced by a few seconds to within the normal range; by that time the dementia had already disappeared.

Case 3: A 68-year-old female first developed gait

disturbance 5 years prior to admission. Following a fall 6 months prior to admission the gait disturbance progressively worsened and forgetfulness, incoherence, and urinary incontinence became marked. She had no headache or vomiting. On admission the patient was demented (her score was 18.5), incontinent, and unable to walk. Neurological examination disclosed diminished corneal reflex, peripheral facial paresis, and hearing difficulty, all on the left side. There was no choked disc. A CT scan revealed symmetrical enlargement of the lateral ventricles with periventricular lucency and a large meningioma in

Fig. 2 Case 3, dynamic CT. *upper*: Before operation, when dementia was present. *lower*: After removal of meningioma of the posterior fossa and complete recovery from dementia. Functional image of width (see *Patients and Methods*) (left) showing lower intensity postoperatively. The meningioma in the left posterior fossa appeared as a high-intensity area. Time-density curve (right) obtained from the region of interest in the frontal lobe (indicated by circle in center) showing reduction of prolonged circulation time to the normal range after surgery, although some enlargement of the ventricles and periventricular lucency persisted. Note: In normal controls, W was 7.3 ± 1.6 seconds and A/P was 8.5 ± 1.5 seconds.

the left side of the posterior fossa. The tumor was totally removed and within 2 days the patient's bladder control was restored and her leg mobility was considerably improved. On the 7th postoperative day her score on the dementia rating scale reached 31.5, which is within the normal range. However, a CBF study on the same day yielded subnormal values; they had not significantly changed from the preoperative values (Table 1). On her last follow-up visit 2 years after surgery there was still no significant increase over the preoperative CBF values (Table 1).

A dynamic CT scan obtained 10 days after operation showed a reduction in the circulation time in the frontal lobes (Fig. 2). The ventricles had become smaller and the periventricular lucency less marked. **Case 4:** A 73-year-old female experienced a generalized seizure, following which she became progressively demented and developed gait disturbance. She had no headache or vomiting. On admission, 40 days after the seizure, she was incontinent and unable to walk. Her score on the dementia rating scale was 7. There was no choked disc. A CT scan revealed sym-

metrically enlarged lateral ventricles and a contrast-enhancing mass in the left cerebellum. The mass was totally removed and the histological diagnosis was papillary adenocarcinoma, which was discovered to be metastatic from the lung. The CBF values had not significantly changed by the 7th day after the operation (Table 1), although the dementia and incontinence had disappeared. Dynamic CT was not carried out.

Results

The average preoperative hemispheric CBF was below normal in three of the four patients, relative to that of healthy control subjects (Table 1). All four patients had marked clinical improvement within 1 to 3 weeks after V-P shunting or suboccipital craniectomy for tumor excision. However, there was no corresponding improvement in the average hemispheric CBF; these values did not significantly increase after treatment, when dementia had improved (Table 1). The mean arterial blood pressure and PaCO₂ also did not change significantly from before to after treatment. In Case 2 CBF measurement 21 days after operation disclosed no significant increase over the preoperative findings. In Case 3 the CBF had not increased by 2 years after operation. Dynamic CT scanning was performed in Cases 1, 2, and 3, although preoperative data were not available for Cases 1 and 2. In Case 1 the circulation time was prolonged slightly beyond the normal range (by 1 to 2 seconds) on the 2nd postshunt day, at which time the patient was still demented. It was reduced by 2 to 4 seconds and entirely restored to the normal range by the 23rd postshunt day, and he was also completely normal clinically (Fig. 1). In Case 2 the circulation time was markedly prolonged on the 3rd postshunt day, when the patient was still demented, and was entirely normal on the 10th postshunt day, by which time the patient's mentation also became normal. In Case 3 the prolonged circulation time before operation also returned to normal, along with the disappearance of dementia, following removal of the tumor (Fig. 2). The mean values of W (see *Patients and Methods*) in these three patients were 13.0 seconds when they were demented and 7.5 seconds when dementia had abated. The patients with hydrocephalus tended to have a longer circulation time in the frontal lobe than in other areas of the brain.

Discussion

All four patients reported here had dementia and hydrocephalus. In Case 1 the patient had a triad of

NPH, dementia, gait disturbance, and incontinence, the pathogenesis of which was not immediately clear. In Case 2 the small acoustic tumor was an unlikely cause of the hydrocephalus because there was no mass effect exerted by the tumor, such as a shift or an obstruction of the aqueduct or the fourth ventricle. There was only a slight increase in the protein content of the CSF, to 59 mg/dl, which was an unlikely cause of the hydrocephalus. It was considered that the acoustic tumor might be merely coincidental to the NPH. The temporary improvement in mental status after removal of the acoustic tumor and the patient's eventual recovery from dementia and gait disturbance after V-P shunting would imply that the clinical manifestations were related to an alteration in CSF dynamics. In Cases 3 and 4 the tumor in the posterior fossa was considered to be the cause of the hydrocephalus, which presented as the triad of NPH. Removal of the tumor brought about remarkable clinical improvement in both patients. There were no signs and symptoms of increased ICP, such as headaches, vomiting, or choked disc, during the clinical course of any of these patients. In addition, ICP was not elevated at the time of surgery and, although it was not monitored continuously, the clinical picture did not differ from that of NPH in any of these cases.

The preoperative average hemispheric CBF of three patients was decreased compared to that of normal control subjects 60 years of age and older (Table 1). This finding agrees with those of many other reports.^{2,5,9,14,18,23)} However, the CBF did not increase postoperatively in any of these four patients, although their dementia had markedly decreased. This is contrary to the results in other published reports, most of which indicate an increase in CBF after lowering of the CSF pressure by either lumbar puncture or a shunting procedure.^{4,14,15,17,18,21,23)}

It has been reported that after a shunting procedure the circulation time shortened, while the CBF increased.^{4,23)} Our dynamic CT studies showed that the circulation time shortened and normalized after successful shunting or removal of the tumor in the posterior fossa.

Salmon and Timperman²¹⁾ ascribed neurological improvement after shunting in low-pressure hydrocephalus patients to an increase in CBF. Sano *et al.*²²⁾ observed a patient with NPH whose neurological symptoms improved prior to an increase in CBF, and proposed that the increase in CBF might have been secondary to recovery of neuronal function. On the other hand, in some cases CBF does not increase—in fact, may decrease—after shunting, even though the neurological status improves.^{7,10,11)} These

contradictory results have not yet been adequately explained.

All of our patients were examined within 3 weeks after operation and one was studied 2 years postoperatively. None had an increase in CBF over the preoperative value. Thus, in this study the time elapsed after operation did not make a difference in terms of CBF values. Kushner *et al.*¹⁰⁾ also observed that CBF did not increase after successful shunting in patients with NPH. They postulated that "persistently low flow may reflect irreversible alterations in the brain structure brought about by the process responsible for NPH" and that "recovery of neuronal function is not related to a change in bulk tissue perfusion." Our results, which demonstrated that the abatement of dementia was not accompanied by a corresponding increase in CBF but was accompanied by a reduction in the cerebral circulation time, suggest that the cerebral blood volume (CBV) had decreased. Raichle *et al.*²⁰⁾ and Grubb *et al.*⁵⁾ found a slight but not significant increase in CBV in patients with NPH, compared to that of normal control subjects. Thus, our finding of the reduction in CBV at the time of disappearance of dementia seems to support their results. However, they also noted a slight but not significant increase in CBV after ICP reduction in patients with NPH. A ¹³³Xe rCBF study detects blood flow in cortical gray matter better than in subcortical white matter, whereas dynamic CT, which we employed, depicts circulation in subcortical white matter better than in cortical gray matter. In addition, CT scanner is superior to rCBF detector in terms of spacial resolution. This might explain the discrepancy between the results obtained by the Xe inhalation method and the data recorded from dynamic CT.

We treated a 52-year-old female with hydrocephalus that was thought to be caused by a meningioma in the posterior fossa. She had no signs or symptoms of increased ICP and was not at all demented. According to dynamic CT, her cerebral circulation time was normal. The CBF was lower than average for her age but was within the normal range. Thus, the cerebral circulation time of hydrocephalic patients may be a significant factor in the development of dementia, although it is not clear whether the delay in circulation time is a cause or a consequence of dementia. Since cerebral microcirculation is disturbed by enlarged ventricles,^{3,18)} it is logical that dynamic CT reveals a decreased circulation time. Reduction and normalization of circulation time reflect an improvement in microcirculation. Since CBF and cerebral metabolism are dynamically related,¹²⁾ an improvement in microcirculation that

cannot be detected by the conventional ¹³³Xe inhalation method should be accompanied by an escalation in cerebral metabolism. This is expected to be clarified in the near future by positron emission tomography and other new technologies.

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