Impaired Cerebral Autoregulation in a Case of Severe Acute Encephalitis

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The status of cerebral autoregulation (CA) is an important prognostic factor for acute head trauma, but the role of CA in patients with acute encephalitis has not been previously discussed. We present the case of a 30-year-old woman with severe acute encephalitis who underwent craniectomy for intractable increased intracranial pressure (ICP). Preoperatively, adjustments of blood pressure (BP) with simultaneous recording of changes in cerebral blood flow velocity with transcranial Doppler indicated increased ICP and impaired CA. Postoperatively, ICP declined remarkably but CA remained impaired when the relationship between spontaneous fluctuation of mean BP and ICP was analyzed. Increased ICP recurred again within 24 hours of the decompression surgery and caused death of the patient. We propose that evaluating the status of CA could be of prognostic importance in patients with severe encephalitis. [J Formos Med Assoc 2007;106(2 Suppl):S7–S12]

Key Words: cerebral autoregulation, craniectomy, encephalitis, intracranial pressure

Under physiologic conditions, cerebral autoregulation (CA) maintains a constant cerebral blood flow (CBF) despite fluctuations in cerebral perfusion pressure, which normally ranges from 50 to 150 mmHg.1 In some pathologic conditions, CA may be impaired or lost, rendering the patients vulnerable to either cerebral ischemia or hyperperfusion injury. Several studies have documented an association between disturbed CA and unfavorable outcome after head injury.2–5 However, the role of CA in patients with acute encephalitis has not been discussed.

Recently, several methods have been devised to evaluate the state of CA either by clinical testing such as the leg-cuff test6,7 and norepinephrine infusion test8,9 or by analysis of the physiologic signals.2–5 Some studies used transcranial Doppler (TCD) sonography as a noninvasive measurement for evaluation of human CA. By using inotropic agent or changing body position, we can manipulate the blood pressure (BP) during simultaneous recording of CBF8,9 with continuous TCD monitoring. Impaired CA is defined as when the flow velocity changes are proportional to the BP changes. The status of CA can also be represented by the pressure reactivity index (PRx), which is the relationship between the spontaneous fluctuation of mean BP and ICP.2–5 The PRx is obtained by calculating the correlation coefficient between the mean BP and ICP; the value ranges between −1 and +1. A negative value reflects a normally reactive vascular bed, whereas a positive value reflects passive and nonreactive vessels.

We report a case of severe acute encephalitis who underwent craniectomy for medically
uncontrolled ICP. We demonstrate the clinical condition as well as CA status with the PRx.

Case Report

After an influenza-like respiratory tract infection, a 30-year-old woman had acute-onset headache, impaired consciousness, and unsteady gait. She did not have any major systemic disease or relevant drug, trauma, or travel history. On admission, she was mildly drowsy and could not follow commands well. Her body temperature was normal, and the physical examination did not find any significant abnormality. The neurologic examination found bilateral papilledema and symmetric pupil size with prompt light responses. Her brainstem reflexes including corneal, oculocephalic, and cough reflexes were all preserved. There was no gaze limitation or focal motor weakness. The plantar responses were extensor bilaterally.

Magnetic resonance imaging (MRI) showed multiple lesions of high-signal intensity mainly in the deep and subcortical white matter of bilateral cerebral hemispheres, medulla, and right cerebellum on T2- and gadolinium-enhanced T1-weighted images (Figure 1A). Diffuse brain swelling was also noted. MR angiography and venography did not reveal any vascular abnormality. Cerebral spinal fluid (CSF) study on the same day indicated an elevated ICP (26 mmHg), a cell count of 16 lymphocytes, a protein level of 73.5 mg/dL, and a glucose level of 76 mg/dL. Bacterial and fungal cultures of serum and CSF were negative. Virus isolation and antibody testing and polymerase chain reaction for herpes simplex virus DNA from a CSF sample were negative. Serum immunologic studies were unremarkable and C-reactive protein level was 0.25.
Electroencephalography showed diffuse slow waves occurring bilaterally intermittently without epileptiform discharges.

After admission, the patient was treated with intravenous acyclovir, pulse steroid, and osmotic diuretics therapies and her condition stabilized with an oriented level of consciousness. However, acute deterioration of the consciousness level occurred 4 days after admission. Intubation with mechanical ventilation was performed for acute respiratory distress. A repeated head MRI study showed aggravated brain swelling and extension of the previously noticed lesions (Figure 1B).

At that time, TCD of the middle cerebral artery (MCA) showed reversed diastolic blood flow consistent with severely raised ICP (Figure 2A). Within a short period of time, as mean BP increased from 90 mmHg to around 130 mmHg under inotropic agent therapy, the Doppler signals shifted to a hyperemic flow pattern (high systolic and diastolic velocity with low flow resistance) (Figure 2B). The change in flow pattern could not be simply explained by reduction in ICP or increase in BP; thus the impression of impaired CA was obtained. Her condition improved (Glasgow coma scale changed from E1M2V1 to E1M5V1) after resuscitation and intensive care. A unilateral craniectomy with ICP monitoring was performed to further control the increased ICP. ICP decreased from 58 mmHg before to 18 mmHg after the operation.

To assess the status of postoperative CA, PRx was calculated through continuous monitoring of arterial BP and ICP at around 6 and 12 hours after the operation. Three average values of the arterial BP and ICP were calculated for 5-second intervals using waveform time integration. The PRx was obtained by a moving linear (Pearson’s) correlation coefficient between the most recent 50 consecutive 5-second averages of the mean BP and ICP. At about 6 hours after craniectomy, the PRx was at near-zero to mild positive values (Figure 3A). At about 12 hours after craniectomy, progressively increasing ICP with positive values of PRx (approximately 1.0) was noted despite aggressive medical treatment (Figure 3B). Although PRx data were not available at about 8 hours (mean arterial BP [MABP] 96–102 mmHg, ICP 25–27 mmHg, mean flow velocity [MFV] 86.4 m/s, pulsatility index [PI] 0.725 in the left MCA) and 10 hours after craniectomy (MABP 85–96 mmHg, ICP 15–18 mmHg, MFV 131 cm/s, PI 0.675 in the left MCA after manitol), both TCD data indicated a hyperemic flow pattern with high flow velocities and low resistance. Within 24 hours, ICP increased gradually to 70 mmHg with MABP between 80–85 mmHg and poor MCA flow. During the postoperative course, hourly transcranial color-coded sonography (TCCS) studies did not detect rapid change in midline shift, abnormal hyperechoic regions, or asymmetry of PI in the MCA, so the possibility of massive intracranial hemorrhage was very scant.

Due to the grave prognosis, her family refused craniectomy on the other side or any further aggressive treatment and the patient died.
Discussion

The patient had acute encephalitis with diffuse brain swelling. Based on the clinical presentation, imaging findings and results of laboratory studies on serum and CSF, postinfectious acute disseminated encephalitis or virus encephalitis were the most probable etiology. The patient received pulse steroid therapy, intravenous acyclovir, and osmotic diuretics after admission but her level of consciousness declined 4 days later. On the 1st day of admission, CSF study was performed to clarify the underlying etiology, so the possibility of lumbar puncture induced acute herniation should be considered. However, there was no contraindication to lumbar puncture for the patient at the time of CSF study and the change in neurologic status occurred several days after the puncture.\textsuperscript{15,16} Therefore, progression of the underlying encephalitis and increased ICP could be the most possible causes responsible for neurologic deterioration after admission.

Craniectomy has been used as a treatment for brain edema due to severe encephalitis.\textsuperscript{17,18} All of the reported cases had received maximum medical treatment for elevated ICP while brainstem compression signs later appeared. Unilateral craniectomy was performed in nine patients and bilateral craniectomy was performed in one patient to control ICP, either unilateral or bilateral craniectomy was effective. Both articles concluded that craniectomy was life-saving in the acute stage of the disease and was also able to protect the brain tissue of patients with severe encephalitis.

In this case, craniectomy was performed because the increased ICP could not be controlled by medical therapy. Although the ICP decreased remarkably after the craniectomy, it elevated again within 24 hours despite concomitant intensive medical therapy. In addition to the underlying

![Figure 3. Observations of changes in intracranial pressure (ICP), arterial blood pressure (ABP), flow velocity (FV) in the middle cerebral artery, and pressure reactivity index (PRx). (A) At about 6 hours after craniectomy, the ICP remains low but the PRx is at around zero to mild positive levels. (B) At about 12 hours after craniectomy, the ICP has progressively increased and the PRx is close to 1.](image-url)
malignant process of the disease, persistently im-
paired CA throughout the course of treatment
could be an important factor in this fatal outcome.

Determination of CA depends on accurate as-
ssessment of CBF, which could be difficult in clinical
practice. Therefore, measurement of flow velocity instead of CBF by TCD is often used as a
surrogate marker considered proportional to CBF.
Thus, TCD sonography has been used as a non-
invasive measurement to evaluate CA in human
subjects and clinical population. As already
mentioned, CA can be represented by PRx which
has the advantage of continuous monitoring of
cerebrovascular pressure reactivity without artifi-
cial manipulation of the MAP. Another strength
of this global index of cerebrovascular pressure
reactivity is that it reflects graded loss of autoreg-
ulation, not just “present or absent”. Previous
studies have shown a significant correlation be-
tween PRx and outcome after head injury, which
included a time-dependent element: if PRx per-
sisted above 0.2 for more than 6 hours, this was
usually associated with fatal outcome.

In this case, before the craniectomy, a rapid shift
of Doppler signals from reversed diastolic flow
to hyperemic flow within a small range of BP on
TCD highly suggested either loss of CA or a nar-
rrowed CA plateau. At about 6 hours after the
craniectomy, assessment of the PRx revealed per-
sistently impaired CA despite decreased ICP. The
CA was further impaired as ICP increased again.
Under the condition of impaired CA, it is very
difficult to maintain an optimal cerebral perfusion
even with aggressive medical therapy and surgical
intervention. Therefore, persistently disturbed CA,
as in this case, would easily cause hyperperfusion
or ischemic injury, which resulted in the unfa-
vorable outcome.

There are several limitations of this report. First,
postmortem examination was not performed to
confirm the clinical diagnosis. Second, we depen-
ded on TCCS rather than head computed tomog-
raphy (CT) to rule out postoperative massive
intracranial hemorrhage. However, transporting
the patient to undergo head CT in such a critical
condition could easily aggravate the patient’s

intracranial hypertension. Besides, TCCS has been
shown to be a reliable method to image the brain
parenchyma, ventricular system, and also measure
the intracranial flow velocity and resistance espe-
cially in patients with craniectomy, so the
possibility of postcraniectomy massive intracra-
nial hemorrhage in this patient was scant.

Finally, this is an observation from a single case;
we need to study more cases to confirm the prog-
nostic significance of CA in patients with severe
encephalitis.

In conclusion, we reported a case of severe en-
cephalitis complicated with intractable increased
ICP. Impaired CA was found throughout the
course of treatment. We propose that evaluation
of the status of CA is of prognostic importance in
patients with severe encephalitis as it is in pa-
tients with acute head trauma. In this report, we
have demonstrated the status of CA in different
stages of a case with fatal encephalitis.

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