Electroencephalographic Evaluation of Cerebral Hyperperfusion Syndrome Following Superficial Temporal Artery-Middle Cerebral Artery Anastomosis

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Abstract

Low-flow bypass, such as superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis, can result in cerebral hyperperfusion syndrome (CHS). The present study evaluated the pathophysiological conditions of CHS through the use of repeated electroencephalography (EEG). Among a total of 22 patients who underwent STA-MCA anastomosis over a course of 4 years, 3 patients were diagnosed with CHS based on clinical symptoms and neuroradiological examinations, including cerebral blood flow evaluation. Case 1 and Case 2 developed CHS on postoperative day 1, when EEG demonstrated focal slow waves on the frontal region of the operated side, indicating cortical dysfunction in these areas. Although prompt recovery of these EEG findings was noted with improvement of the clinical symptoms in Case 1, Case 2 developed an intracranial hemorrhage on postoperative day 5, when EEG clearly depicted persistent nonconvulsive status epilepticus (NCSE) after control of convulsive status epilepticus. In contrast, the clinical onset in Case 3 was delayed to postoperative day 6 and EEG revealed frequent ictal discharges in the operated hemisphere, although convulsive seizures were not apparent. Administration of anticonvulsants was performed after the diagnosis of NCSE, and complete recovery from CHS was achieved. Although the pathophysiology of CHS is cortical dysfunction, ictal hyperperfusion associated with NCSE could be included. The present findings emphasize the importance of repeated EEG examinations in the differential diagnosis of the various types of pathophysiological conditions of CHS.

Key words: cerebral hyperperfusion syndrome, nonconvulsive status epilepticus, superficial temporal artery-middle cerebral artery anastomosis, ictal hyperperfusion, electroencephalography

Introduction

Carotid reconstruction surgery, including carotid endarterectomy (CEA) or carotid artery stenting (CAS), in patients with atherosclerotic diseases can cause a rapid increase in cerebral blood flow (CBF) in the chronic ischemic brain, resulting in complications such as cerebral hyperperfusion syndrome (CHS).3,19,23,26–28,31 In contrast to CHS after CEA or CAS, CHS after superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis for atherosclerotic diseases is thought to be rare, since the anastomosis usually provides low-flow revascularization.32 Recent reports have indicated that STA-MCA anastomosis for moyamoya disease as well as atherosclerotic diseases can also result in CHS.5–8,11,16–19,33 However, the exact pathophysiological conditions of CHS following STA-MCA anastomosis are still controversial.1,6,10 The present study investigated the role of the neuronal activities in the development of CHS through the use of repeated
Table 1  Clinical profiles and electroencephalography (EEG) findings of the patients with cerebral hyperperfusion syndrome following superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)/Sex</th>
<th>Diagnosis</th>
<th>STA-MCA anastomosis</th>
<th>Cerebral hyperperfusion syndrome</th>
<th>Outcome (mRS score)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Indication</td>
<td>Onset</td>
<td>Subsequent course</td>
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<td></td>
<td></td>
<td></td>
<td>Method</td>
<td>EEG findings</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Postoperative day</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>67/M</td>
<td>left M1_</td>
<td>decreased CBF and</td>
<td>intermittent delta waves on the</td>
<td>recovery on days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>stenosis</td>
<td>impaired perfusion</td>
<td>left anterior quadrant</td>
<td>5–7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>reserve</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>71/M</td>
<td>left M1_</td>
<td>impaired perfusion</td>
<td>continuous delta waves on the</td>
<td>ICH with SDH on</td>
</tr>
<tr>
<td></td>
<td></td>
<td>stenosis</td>
<td>reserve</td>
<td>left anterior quadrant</td>
<td>day 5, CSE→NCSE (C3)</td>
</tr>
<tr>
<td>3</td>
<td>77/M</td>
<td>right M1_</td>
<td>impaired perfusion</td>
<td>NCSE (originated from O2, P2,</td>
<td>recovery on days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>stenosis</td>
<td>reserve</td>
<td>and C4)</td>
<td>25–28</td>
</tr>
</tbody>
</table>


Materials and Methods

Twenty-two STA-MCA anastomoses were performed in 22 patients for moyamoya disease in 7, M1 stenosis in 6, occlusion of the internal carotid artery in 5, and occlusion of M1 in 4, by a single surgeon (second author) between July 1, 2008 and July 31, 2012 in our hospital. The patients with moyamoya disease were one man and 6 women aged from 15 to 58 years (mean 39.1 years), and the patients with atherosclerotic disease were 13 men and 2 women aged from 51 to 77 years (mean 66.4 years). Postoperatively, the systolic blood pressure was strictly controlled at 100–140 mmHg with intravenous administration of diltiazem hydrochloride. During the postoperative period, the diagnosis of CHS was made based on clinical findings, neuroimaging examinations including computed tomography (CT), magnetic resonance (MR) imaging, and MR angiography, and CBF findings with single-photon emission computed tomography (SPECT). The diagnostic criteria for CHS included all of the following according to the previous authors:3,5–7,11,20,31) presence of neurological symptoms, absence of any de novo lesion that explains neurological deterioration on MR imaging including diffusion-weighted images, presence of apparent visualization of STA-MCA bypass on MR angiography, and concomitant hyperperfusion visualized in the region of the bypass on CBF imaging with SPECT. If the diagnosis of CHS was determined, repeated EEG examinations were performed. Recordings were obtained from 12- or 16-channel EEGs with electrode placement according to the International 10–20 System. Functional outcomes were assessed at 1–3 years postoperatively using the modified Rankin scale (mRS).32

Results

During the postoperative period after STA-MCA anastomosis, 3 of 22 (13.6%) patients exhibited CHS. The detailed clinical courses and EEG findings for these three patients are described below and summarized in Table 1.

Case 1: A 67-year-old man with an old infarction in the left corona radiata was introduced to our hospital. He had mild right hemiparesis, but was independent in his activities of daily living. CT demonstrated a small infarction in the left corona radiata (Fig. 1A). Left carotid angiography revealed severe stenosis of the left M1 portion (Fig. 1B). Iodine-123 N-isopropyl-p-iodoamphetamine (123I-IMP) SPECT showed decreased CBF in the left MCA territory (21.00 ml/100 g/min) compared with the right MCA territory (25.93 ml/100 g/min) (normal value in our hospital: 42.5 ml/100 g/min) (Fig. 1C). The vascular reserve capacities in the right MCA territory were also compromised (Fig. 1D). With acetazolamide loading, the regional cerebrovascular reactivities in the left and right MCA territories were +21.1% and +22.9%, respectively. Thus, the parietal and frontal branches of the STA were
anastomosed to the M1 portions of the frontal and temporal lobes, respectively, through a right fronto-temporo-parietal craniotomy.

On postoperative day 1, the patient experienced deterioration in the level of consciousness with confusion and worsening of dysarthria. Although CT and MR imaging, including T1-/T2-weighted, diffusion-weighted, and fluid-attenuated inversion recovery sequences, failed to reveal additional abnormalities that could explain his neurological deterioration, MR angiography showed an apparently patent STA-MCA bypass as a thick high signal intensity line (Fig. 1E). EEG demonstrated intermittent slow waves (2–3 Hz) on the left hemisphere, especially on the left anterior quadrant (Fig. 1F). Although CBF evaluation could not be performed at that time based on the diagnosis of CHS, stricter blood pressure control (systolic blood pressure of <120 mmHg) was continued and a free radical scavenger (edaravone) was given in accordance with previous reports.10,26)

On postoperative day 5, the patient became well orientated. Technetium-99m ethyl-cysteinate dimer (99mTc-ECD) SPECT on postoperative day 6 still showed slightly increased perfusion in the right MCA territory (Fig. 1G). Ultrasonography of the STA was performed on postoperative day 6, according to previous reports1,10 which demonstrated no increase in the peak flow velocity of the left STA in the systolic period (left STA: 107.0 cm/sec, right STA: 97.7 cm/sec), although a marked increase in the peak flow velocity of the left STA was noted in the end-diastolic period (left STA: 27.5 cm/sec, right STA: 11.8 cm/sec).

On postoperative day 7, the patient’s neurological conditions had completely returned to those in the preoperative period. EEG showed well-organized background activities in the bilateral occipital region, although intermittent slow waves (5–6 Hz) were noted in the left frontal region (Fig. 1H). 123I-IMP SPECT on postoperative day 20 revealed disappearance of the hyperperfusion in the left MCA territory (Fig. 1I). The CBFs in the left and right MCA territories were 39.88 and 41.93 ml/100 g/min, respectively. With acetazolamide loading, the
vascular reserve capacity in the left MCA territory had improved compared with the preoperative period. The regional cerebrovascular reactivities in the left and right MCA territories were +28.7% and +37.8%, respectively. On postoperative day 40, the patient was transferred to another hospital for further rehabilitation. At 13 months postoperatively, the mRS score was 2 (unchanged from the preoperative state).

Case 2: A 71-year-old man with multiple infarctions was admitted to our hospital. He had mild right hemiparesis and aphasia caused by an infarction in the left insular cortex to the corona radiata (Fig. 2A), but was independent in his activities of daily living. Left carotid angiography revealed severe stenosis of the left M₁ portion (Fig. 2B). ¹²³I-IMP SPECT showed that the vascular reserve capacities in the left MCA territory were compromised. The CBFs in the left and right MCA territories were 26.92 and 32.49 ml/100 g/min, respectively. With acetazolamide loading, the regional cerebrovascular reactivities in the left and right MCA territories were +24.1% and +37.1%, respectively. Thus, the parietal and frontal branches of the STA were anastomosed to the M₄ portions of the frontal and temporal lobes, respectively.

On postoperative day 1, the patient experienced deterioration of the level of consciousness with drowsy state and worsening of right hemiparesis and dysarthria. Although CT and MR imaging failed to reveal additional abnormalities (Fig. 2C), MR angiography showed an apparently patent STA-MCA bypass as a thick high signal intensity line (Fig. 2D). EEG demonstrated almost continuous slow waves (2–3 Hz), predominantly on the left anterior quadrant (Fig. 3A). Based on the diagnosis of CHS, intensive control of blood pressure (systolic blood pressure of <120 mmHg) was continued. However, on postoperative day 5, the patient developed convulsive status epilepticus (CSE) of the right face and CT demonstrated an intracerebral hemorrhage in the left frontal lobe with subdural and subarachnoid hemorrhage (Fig. 2E). Although the CSE was controlled with intravenous diazepam administration, subsequent EEG showed frequent ictal discharges on the left centro-parietal region (Fig. 3B). Ictal discharges originating from the left central region (C3 in the International 10–20 System) extended to the left parietal region (T3). Duration of the seizure activities was 21–59 seconds (43.5 sec average). Twelve episodes of ictal discharges were recorded during 18 minutes. ⁹⁹mTc-ECD SPECT on postoperative day 6 showed hyperperfusion in the left hemisphere, especially around the intracranial hematoma (Fig. 2F).

Based on the diagnosis of nonconvulsive status epilepticus (NCSE), intravenous administration of a phenytoin loading dose, followed by oral carbamazepine administration were performed. Ultrasonography of the STA on postoperative day 8 demonstrated no increase in the peak flow velocity of the left STA in the systolic period (left STA: 116.0 cm/sec, right STA: 95.4 cm/sec), although an increase in the peak flow velocity of the left STA was noted in the end-diastolic period (left STA: 19.9 cm/sec, right STA: 15.8 cm/sec).

On postoperative days 25–28, the patient’s neurological conditions had completely returned to those of the preoperative period. On EEG, well-organized background activities were observed in the bilateral occipital region, although intermittent slow waves...
Fig. 3 Case 2. A: Electroencephalogram on postoperative day 1 revealing almost continuous slow waves (2–3 Hz) on the left hemisphere, especially on the left anterior quadrant (Fp1, F7, and T3; black lines). B: Electroencephalogram on postoperative day 6 showing frequent ictal discharges that originate from the left central region (C3; arrow) and extend to the left parietal region (P3; dotted arrow).

were noted in the left frontal region. $^{99m}$Tc-ECD SPECT on postoperative day 25 revealed disappearance of the hyperperfusion in the left MCA territory. The CBFs in the left and right MCA territories were 30.09 and 35.45 ml/100 g/min, respectively. With acetazolamide loading, the vascular reserve capacity in the left MCA territory had improved compared with the preoperative period. The regional cerebrovascular reactivities in the left and right MCA territories were +30.09% and +35.45%, respectively. On postoperative day 40, the patient was transferred to another hospital for further rehabilitation. At 22 months postoperatively, the mRS score was 2 (unchanged from the preoperative state).

Case 3: Since this case was previously reported, only a brief clinical course with long-term observations is described. A 77-year-old man with an old infarction in the right corona radiata developed temporal deterioration of the consciousness level and worsening of left hemiparesis on postoperative day 6 following STA-MCA anastomosis for severe stenosis of the right M1. Although convulsive seizures were not apparent, EEG revealed frequent ictal discharges (rhythmic slow waves originating from the right temporo-occipital region posterior to the anastomosis site) in the right hemisphere. This area corresponded with a cortical hyperintense area on diffusion-weighted imaging and a hyperperfused area on $^{99m}$Tc-ECD SPECT. Based on a diagnosis of NCSE, with rapid improvement of the EEG findings following phenytoin administration, complete recovery from CHS was achieved. At 3 years postoperatively, the mRS score was 2 (unchanged from the preoperative state).

Discussion

In the present study, 3 of 22 (13.6%) patients exhibited CHS during the postoperative period after STA-MCA anastomosis. Since the incidence of CHS after STA-MCA anastomosis is considered to be rare in contrast to that of CHS after CEA or CAS,34) this percentage was higher than expected. Although patients with moyamoya disease were clearly demonstrated to have a lower threshold for developing CHS following STA-MCA anastomosis compared with those of atherosclerotic disease,7) in our study, all three patients who developed CHS had atherosclerotic disease. The exact reason was not determined, but the small number of the moyamoya disease patients in our study is one of the possible reasons.

The diagnosis of CHS is usually based on the clinical symptoms and CBF findings such as CBF images with SPECT.11,23,24,31) In Case 1 and Case 2, the clinical symptoms at onset were subtle, and conventional CT and MR imaging failed to reveal additional abnormalities, whereas MR angiography showed an apparently patent STA-MCA bypass as a thick high signal intensity line. One of the disadvantages of CBF images with SPECT is that correctly timed SPECT examination often cannot be performed,
since the radioisotope is unavailable on weekends or outside working hours in local hospitals. Actually, in Case 1 and Case 2, the timing of their SPECT examinations was delayed for this reason. In some institutes, a CBF analysis is routinely scheduled within 72 hours after vascular reconstruction surgery to overcome this disadvantage.\textsuperscript{[7,11,24,33]} In our previous report on Case 3, we demonstrated that measurement of the flow velocity of the STA by ultrasonography was useful for evaluating the hyperperfusion state of the MCA territory through an STA-MCA anastomosis, since ultrasonography is a noninvasive technique and easily repeatable.\textsuperscript{[10]} However, in Case 1 and Case 2, ultrasonography failed to reveal the hyperperfusion state, probably because of the delayed performance of the examinations. As is often the case with CHS after CEA, no diagnostic examinations have 100% sensitivity.\textsuperscript{[23,31,33]} and the diagnosis of CHS requires a high level of awareness in all patients after STA-MCA anastomosis.\textsuperscript{[23,33]}

Surprisingly few previous reports described EEG findings,\textsuperscript{[10,15,31]} although seizures or epilepsy are one of the major symptoms in patients with CHS after CEA or CAS.\textsuperscript{[13,23,25,31]} Only EEG examinations of 10 patients with CHS for several days after CEA revealed periodic lateralizing epileptiform discharges on the operated hemisphere, even in the absence of seizures or during the postictal state.\textsuperscript{[28]} Since periodic lateralizing epileptiform discharges are one of the EEG patterns in patients with NCSE,\textsuperscript{[2,12,22]} these cases probably had similar pathophysiological conditions to those of Case 3 in the development of CHS.

In Case 1 and Case 2 of the present study, the onset of the clinical symptoms occurred on postoperative day 1, and EEG at that time clearly demonstrated localized slow waves on the operated frontal region, indicating cortical dysfunction of these areas.\textsuperscript{[9,20]} Another notable EEG finding was the prompt recovery of the localized slow waves with improvement of the clinical symptoms. In Case 1, EEG on postoperative day 7 showed well-organized background activities in the bilateral occipital region, although intermittent slow waves were noted in the operated frontal region, which were probably caused by the old infarction that was present preoperatively. These reversible EEG findings suggested that the occurrence of CHS was not attributed to a destructive lesion, but to a functional lesion. In a patient with CHS after CEA, EEG showed pathological slowing over the operated hemisphere at the onset, but became normalized on postoperative day 5.\textsuperscript{[5,14]} Since this patient developed partial seizures of the left extremities at the onset of CHS, this reversible EEG slowing was thought to be attributable to post-ictal changes.

Despite the strict control of postoperative blood pressure, Case 2 developed an intracranial hemorrhage on postoperative day 5, when the patient also developed CSE. Patients with CHS after CAS appear to show no relationship between blood pressure control and intracranial hemorrhage, although strict control of postoperative blood pressure prevents intracranial hemorrhage in patients with CHS after CEA.\textsuperscript{[27]} In our Case 2, EEG clearly depicted persistent NCSE after the control of CSE with intravenous diazepam administration. Regarding EEG monitoring after initial treatment of CSE, >14% of patients had subsequent NCSE, and EEG was an important diagnostic test to guide treatment plans and evaluate prognosis in the management of CSE.\textsuperscript{[4]} Since the ictal discharges originated from the left central region where the intracranial hematoma was located in our Case 2, the development of CSE and subsequent NCSE was thought to be secondary to the intracranial hemorrhage. The prognosis of CHS patients with associated intracranial hemorrhage is well known to be poor.\textsuperscript{[23,27]} NCSE also indicates a bad prognosis, and prompt diagnosis and subsequent treatment are important, although the mortality was reported to be mainly dependent on the underlying etiology and age.\textsuperscript{2,4,21,30} One of the possible reasons why patients with CHS and intracranial hemorrhage have a poor prognosis is that associated NCSE could be overlooked. Fortunately, our Case 2 had a good outcome following appropriate anticonvulsant therapy for NCSE.

In contrast to Case 1 and Case 2, the clinical onset of CHS in Case 3 was delayed to postoperative day 6 and EEG revealed NCSE.\textsuperscript{[10]} Administration of anticonvulsants was performed and complete recovery from CHS was achieved. CHS is generally thought to be delayed after STA-MCA anastomosis.\textsuperscript{[16]} A possible explanation for this finding is that the lower-flow bypass may take a while to mature and this could affect the dysautoregulated brain.\textsuperscript{16,18} Another explanation may be the delayed occurrence of seizure activity, such as in our Case 2 and Case 3. Three moyamoya disease patients developed simple partial seizures following manifestation of hyperperfusion on postoperative routine CBF images with SPECT.\textsuperscript{24} Although whether epilepsy or hyperperfusion was the first phenomenon cannot be precisely determined, repeated EEG indicated that the first phenomenon was hyperperfusion in Case 2 and epilepsy in Case 3.

In conclusion, although the pathophysiology of CHS is cortical dysfunction, ictal hyperperfusion associated with NCSE could be included. The present
study emphasizes the importance of EEG in the differential diagnosis of the various types of pathophysiological conditions of CHS.

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Conflicts of Interest Disclosure

The authors have no personal financial or institutional interest in any of the drugs, materials, or devices in the article. T. Morioka, T. Sayama, T. Shimogawa, N. Mukae, T. Hamamura, and T. Sasaki have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

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EEG of Hyperperfusion Syndrome


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