Confirmation of a Diagnosis by CSF Analysis in a Case of Symptomatic Contrast-induced Encephalopathy with an Onset Immediately after Coil Embolization of an Unruptured Cerebral Aneurysm

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Objective: A case of contrast-induced encephalopathy, a complication of intracranial endovascular treatment, in which the measurement of the iodine concentration in cerebrospinal fluid (CSF) was effective for the diagnosis is reported.

Case Presentations: An 85-year-old woman underwent coil embolization of an unruptured aneurysm at the left internal carotid artery-posterior communicating artery bifurcation. Since recurrence was noted after one year, additional coil embolization was performed. After the procedure, she presented with right hemiplegia and aphasia, and head CT scans immediately after the procedure showed high-density areas in the cortex and sulci of the left cerebral hemisphere. On the day after the procedure, the high-density areas disappeared, and the symptoms were resolved by conservative treatment. Since CSF analysis after the procedure demonstrated marked elevation of the iodine concentration, a diagnosis of contrast-induced encephalopathy was made on the basis of this finding along with the CT findings and symptomatic course.

Conclusion: Measurement of the iodine concentration in CSF immediately after endovascular treatment is useful for the diagnosis of contrast-induced encephalopathy.

Keywords ▶ contrast-induced encephalopathy, cerebrospinal fluid analysis, intracranial endovascular treatment, iodine concentration

Introduction

The proportion of endovascular treatment among treatments for unruptured cerebral aneurysms is increasing due to increased acceptance of the procedure and the development and improvement in devices. During endovascular treatment for intracranial aneurysms, the contrast agent is repeatedly injected in the same vessel, and some patients exhibit high-density areas in the affected cerebral hemisphere on head CT after the procedure. Many of them are asymptomatic, but a few develop neurological symptoms immediately after the procedure. Since the condition is suspected to be due to adverse reactions to the contrast agent, it is called contrast-induced encephalopathy.1–9) The disorder is diagnosed primarily according to symptoms and imaging findings but is difficult to diagnose definitively.

We encountered a patient who developed hemiplegia and aphasia immediately after coil embolization of unruptured aneurysm and exhibited a high iodine concentration on cerebrospinal fluid (CSF) analysis immediately after the procedure and diagnosed the condition as contrast-induced encephalopathy due to head CT findings and the symptomatic course. This case is reported with a review of the literature.
Case Presentations

An 85-year-old woman with a history of chronic pancreatitis in her 30s and coronary artery stenting for myocardial infarction at the age of 80 years suffered coil compaction following coil embolization for cerebral aneurysm.

In 2014, the patient was found at a local hospital to have an unruptured aneurysm at the left internal carotid artery-posterior communicating artery bifurcation and was since followed up by diagnostic imaging. After 1 year, she developed blepharoptosis of the left eye and was referred to our hospital for treatment. Since she was old and was taking antiplatelet drugs due to the history of myocardial infarction, endovascular treatment was selected, and balloon-assisted coil embolization was performed under local anesthesia for the aneurysm (maximum diameter: 10 mm) (complete occlusion, volume embolization ratio [VER] = 30%). Although paralysis of the right upper extremity was noted immediately after the procedure, it disappeared rapidly and was considered to have been due to temporary obstruction of the internal carotid artery by the balloon during the procedure. She was discharged to home with no marked change in blepharoptosis or persistence of new symptoms. Since MRI performed after one year re-visualized the aneurysm due to coil compaction, additional embolization was designed.

Neurological findings on admission: Mild blepharoptosis of the left eye, diplopia (no clear paralysis of the external ocular muscle on the confrontation test).

Imaging findings on admission: The area from the neck to the body of the aneurysm at the left internal carotid artery-posterior communicating artery bifurcation was re-visualized on head MRA. On cerebral angiography, the coil mass was compressed inferiorty, and the area from the inflow site to the upper part of the aneurysm (9 mm × 5 mm × 5 mm) was re-visualized (Fig. 1A).

Endovascular treatment: From 1 week before the procedure, 100 mg of aspirin and 75 mg of clopidogrel were orally administered. After an 8 Fr 25 cm sheath was inserted under local anesthesia, heparin was administered intravenously, and the activated clotting time (ACT) was maintained at ≥250 seconds. ASAHI FUBUKI 8F, 90 cm (Asahi Intecc, Aichi, Japan) and Cerulean DD6, 118 cm (Medikit, Tokyo, Japan) were placed as a triple-axial system at a high position of the left internal carotid artery. PROWLER SELECT Plus (Johnson & Johnson, Raynham, MA, USA) was guided to the middle cerebral artery using GT wire 0.012” (Terumo, Tokyo). Excelsior SL-10 (Stryker, Kalamazoo, MI, USA) was placed in the aneurysm using ASAHI CHIKAI 0.014” (Asahi Intecc). After deploying Enterprise VRD 4.0 mm × 23 mm (Johnson & Johnson), another Excelsior SL-10 was guided into the aneurysm by the trans-cell technique using Traxcess 14 (Terumo). Embolization was started with the jailed Excelsior SL-10. After overall framing using Orbit GALAXY Complex Fill 9 mm × 25 cm (Stryker), HydroSoft 10 Helical 4 mm × 10 cm (MicroVention TERUMO, Tustin, CA, USA), embolization was performed serially using Target XL HELICAL 5 mm × 15 cm (Stryker), HydroSoft 10 Helical 4 mm × 10 cm (MicroVention TERUMO, Tustin, CA, USA), ED Coil ES 3 mm × 4 cm (Kaneka Medix, Osaka, Japan), HyperSoft 3D 2.5 mm × 4 cm (MicroVention TERUMO), and ED Coil ES 1.5 mm × 3 cm. At this point, the Excelsior SL-10 that had been jailed was kicked back out of the aneurysm. Next, embolization was performed by the trans-cell...
cerebral hemisphere, and no irreversible change that might cause symptoms such as acute cerebral infarction was noted (Figs. 3A and 3B). Head MRA clearly delineated the major arteries. Suspecting contrast-induced encephalopathy, we collected CSF by lumbar puncture 10 hours after the procedure for a definitive diagnosis. CSF was watery and clear, the pressure was normal at 13 cmH₂O, and the cell count, protein concentration, and electrolyte concentrations were normal. However, the iodine concentration, which was examined as an additional item, was 122 µg/ml and was markedly elevated compared with 0.159 µg/ml obtained as a reference value 21 days after the procedure (Fig. 4). Concerning symptoms, motor aphasia and hemiparesis of the right upper and lower extremities were gradually alleviated by conservative treatment from about 5 days after the procedure, and, after rehabilitation, the patient was discharged to home with no residual symptoms.

Course after embolization: Immediately after the procedure, the patient exhibited motor aphasia and hemiparesis of the right upper and lower limbs, and head CT scans showed high-density areas in the cortex and sulci of the left cerebral hemisphere (Figs. 2A and 2B). The high-density areas disappeared on head CT scans on the day after surgery (Figs. 2C and 2D). Also, diffusion-weighted imaging (DWI) of MRI on the day after the procedure showed only a few small high-intensity areas in the left cerebral hemisphere, and no irreversible change that might cause symptoms such as acute cerebral infarction was noted (Figs. 3A and 3B). Head MRA clearly delineated the major arteries. Suspecting contrast-induced encephalopathy, we collected CSF by lumbar puncture 10 hours after the procedure for a definitive diagnosis. CSF was watery and clear, the pressure was normal at 13 cmH₂O, and the cell count, protein concentration, and electrolyte concentrations were normal. However, the iodine concentration, which was examined as an additional item, was 122 µg/ml and was markedly elevated compared with 0.159 µg/ml obtained as a reference value 21 days after the procedure (Fig. 4). Concerning symptoms, motor aphasia and hemiparesis of the right upper and lower extremities were gradually alleviated by conservative treatment from about 5 days after the procedure, and, after rehabilitation, the patient was discharged to home with no residual symptoms.

For embolization, about 210 ml of a non-ionic and low-osmotic pressure contrast agent (Iopamiron 300) was used. At this point, the Excelsior SL-10 was kicked back out of the aneurysm, and the aneurysm was not visualized by imaging techniques, embolization of the aneurysm was ended (complete occlusion) (Fig. 1B). For embolization, about 210 ml of a non-ionic and low-osmotic pressure contrast agent (Iopamiron 300) was used.
symptoms other than blepharoptosis and diplopia, which were presented from before the procedure.

Discussion

Contrast-induced encephalopathy is a rare complication of intracranial endovascular treatment considered to be caused by temporary disruption of the blood–brain barrier (BBB) associated with the use of a non-ionic contrast agent and subsequent neurotoxicity. According to previous reports, focal neurological symptoms are often observed from immediately after the procedure, and high-density areas appear in the cerebral cortex on head CT immediately after the procedure. MRI is often negative for lesions that explain the symptoms, and the high-density area on head CT often disappears rapidly.\(^1-9\) Although contrast-induced encephalopathy may be suspected from the symptomatic course and imaging findings, it is difficult to diagnose definitively. In the patient reported here, we strongly suspected contrast-induced encephalopathy from the focal neurological symptoms and imaging findings immediately after the procedure and sampled CSF 10 hours after the procedure. Uchiyama et al. measured the iodine concentration in CSF on day 0 in four non-contrast-induced encephalopathy patients after embolization of ruptured cerebral aneurysms and reported that it was 10–40 µg/ml.\(^10\)

In our patient, the iodine concentration in CSF was 122 µg/ml 10 hours after the procedure and 0.159 µg/ml 21 days after the procedure. Even considering that disruption of the BBB is milder in the treatment for unruptured aneurysms compared with ruptured aneurysms, the CSF iodine level 10 hours after the procedure is considered to have been extremely high, and, in consideration also of the head CT findings and symptomatic course, contrast-induced encephalopathy was diagnosed. The iodine concentration in CSF is measured by spectrocolorimetry. A problem with this study was that it took about 10 days before the establishment of the diagnosis because the iodine assay was commissioned to an outside institution. Hypertension and kidney disorders have been reported as risk factors for contrast-induced encephalopathy. Although...
the occurrence of contrast-induced encephalopathy has been suggested to depend on the dose of the contrast agent or number of its injections into the same vessel, there has also been a report of its occurrence even at a low dose,\(^{11}\) and consensus has not been reached. There have also been reports that angiography performed before and after an episode of contrast-induced encephalopathy did not induce symptoms.\(^{12,13}\) In our patient, a relatively large amount of contrast agent (210 ml) was used, and the possibility that the temporary right hemiplegia observed immediately after the first session was contrast-induced encephalopathy cannot be excluded. Although contrast-induced encephalopathy is considered to be a specific response to a contrast agent, its causation has not been clarified. In addition, Iwata et al. reported that individual variation was observed in disruption of the BBB and neurotoxicity associated with endovascular administration of a contrast agent.\(^{14}\) Minimization of the use of a contrast agent and a review of the presence or absence of focal neurological symptoms in previous procedures may be helpful for the prevention of contrast-induced encephalopathy. However, hypertension and kidney disorders, suggested as risk factors, are common conditions, and its preprocedural prediction is extremely difficult.

Although steroid drip infusion has been reported to be effective for the treatment of contrast-induced encephalopathy,\(^{15}\) we conservatively treated our patient by fluid supplementation and rehabilitation in consideration of her old age and obtained a favorable outcome. Since symptoms may persist or appear in the subacute period, although very rarely,\(^{16,17}\) attention to contrast-induced encephalopathy is considered necessary as a complication of intracranial endovascular treatment.

## Conclusion

A case diagnosed with certainty as contrast-induced encephalopathy by the measurement of the iodine concentration in CSF after coil embolization of unruptured cerebral aneurysm was reported. Contrast-induced encephalopathy is often suspected due to the symptomatic course and imaging findings, but the measurement of the iodine concentration in CSF may be helpful for its diagnosis.

## Disclosure Statement

The top author and all of the coauthors have no conflicts of interest concerning this paper.

## References


