Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.5139-20
Intern Med 60: 629-633, 2021
http://internmed.jp

【 CASE REPORT 】

Low-dose Contrast-induced Encephalopathy During Diagnostic Cerebral Angiography

Teppei Kamimura[1,2], Masahiro Nakamori[1,2], Eiji Imamura[1], Yuki Hayashi[1,2], Hayato Matsushima[1], Tatsuya Mizoue[3], Shinichi Wakabayashi[3] and Hirofumi Maruyama[2]

Abstract:

Contrast-induced encephalopathy (CIE) is a rare complication of contrast agent use. We herein report a case of acute lacunar infarction in a 70-year-old woman. During diagnostic cerebral angiography for asymptomatic common carotid stenosis, she experienced transient drowsiness. After angiography, generalized tonic-clonic seizures occurred in her left arm and leg, with eye deviation to the left. The patient was diagnosed with CIE due to the acute onset of symptoms during angiography and characteristic computed tomography findings of high-density signaling in the cortex. Our findings suggest that it is important to pay close attention to acute neurological symptoms during and immediately after examinations, even with small amounts of contrast agents.

Key words: contrast-induced encephalopathy, acute encephalopathy, contrast agent, cerebral angiography, acute cerebral infarction, small vessel disease

(Intern Med 60: 629-633, 2021)
(DOI: 10.2169/internalmedicine.5139-20)

Introduction

Contrast-induced encephalopathy (CIE) is a rare complication of angiography. The first cases of CIE were reported in 1961, and transient blindness was observed after the use of ionic contrast agents (1). In recent years, although nonionic contrast agents have been used, some cases of CIE resulting from coronary angiography or cerebral endovascular therapy have been reported (2). In addition, CIE can also occur with examinations using low-dose contrast agents; thus, caution should be exercised.

We herein report a case of CIE during cerebral diagnostic angiography with small amounts of contrast agents.

Case Report

A 70-year-old woman with no relevant medical history, such as hypertension, renal dysfunction, or allergic disorders, presented with sudden-onset dysarthria, right facial palsy, and monoparesis of the right arm. Diffusion-weighted imaging (DWI) revealed a high intensity in the left corona radiata. Fluid-attenuated inversion-recovery (FLAIR) imaging showed periventricular and white matter lesions. Magnetic resonance (MR) angiography indicated mild stenosis in the right common carotid bifurcation (Fig. 1). The patient was diagnosed with acute lacunar infarction and asymptomatic right carotid artery stenosis. She received antithrombotic and edaravone treatment.

A close examination showed a high brachial-ankle pulse wave velocity (baPWV; R, 3,297 cm/s; L, 2,778 cm/s) and microalbuminuria level (51.8 mg/gCr). The mini-mental state examination score was 24/30. We performed diagnostic cerebral angiography to examine the carotid artery stenosis at 10 days post-onset. After the innominate artery and right common carotid artery (CCA) were imaged with iopamidol (iodine concentration, 300 mg/mL; osmotic pressure, 620 mOsm/kg H_2O), which is a nonionic water-soluble iodine contrast agent (Fig. 2A, B), she became drowsy, and her blood pressure increased to 201/101 mmHg. She presented with mild unconsciousness with Glasgow Coma Scale (E4 V4 M5) scores of 13, and she had no headache nausea or

[1]Department of Neurology, Suiseikai Kajikawa Hospital, Japan, [2]Department of Clinical Neuroscience and Therapeutics, Hiroshima University Graduate School of Biomedical and Health Sciences, Japan and [3]Department of Neurosurgery, Suiseikai Kajikawa Hospital, Japan
Received: April 27, 2020; Accepted: August 12, 2020; Advance Publication by J-STAGE: September 30, 2020
Correspondence to Dr. Teppei Kamimura, tetetteteppei@gmail.com

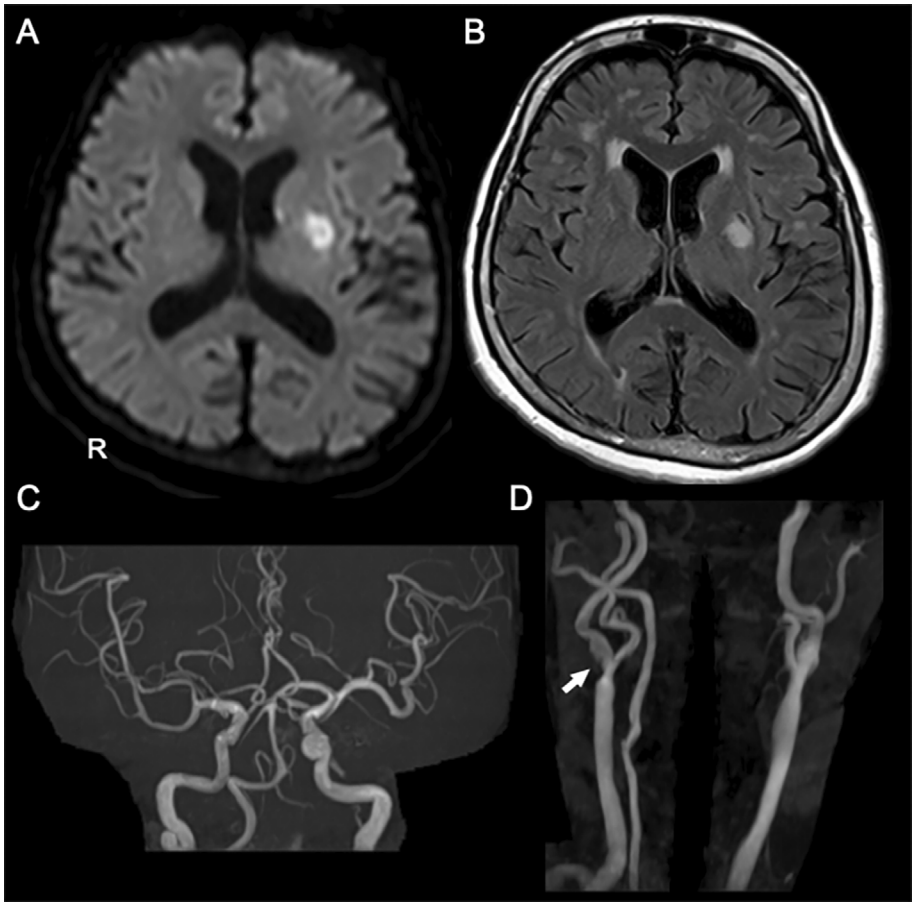

Figure 1. **Magnetic resonance imaging on admission. Diffusion-weighted and fluid-attenuated inversion-recovery (FLAIR) imaging revealed a high-intensity lesion in the left corona radiata (A, B). FLAIR imaging also showed periventricular hyperintensity and a subcortical white matter lesion. Magnetic resonance angiography indicated left vertebral artery occlusion (C) and mild stenosis in <50% of the right carotid bifurcation, suggesting a small ulcer (D, arrow).**

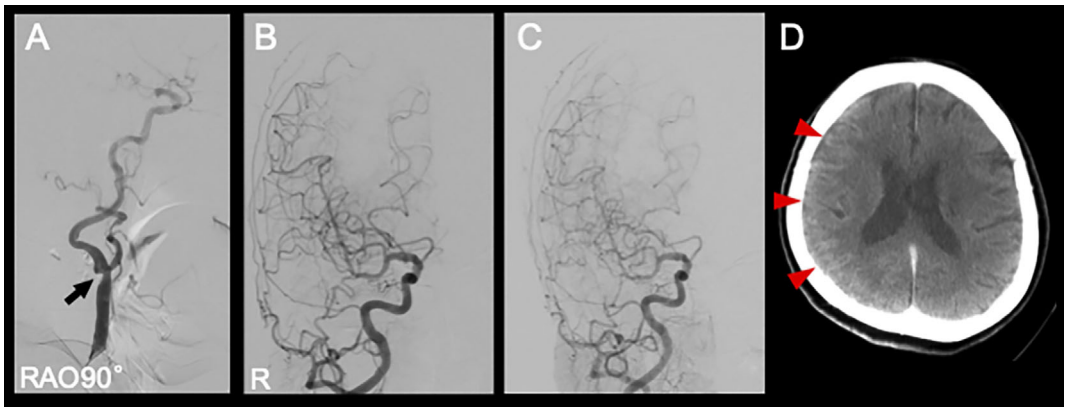

Figure 2. **Cerebral angiography at 10 days after onset. Common carotid artery (CCA) angiography revealed mild stenosis at the bifurcation of the right carotid artery (A, arrow). The posterior cerebral artery is depicted via the posterior communicating artery, and the A1 segment of the right anterior cerebral artery is absent (B). After angiography of the right CCA, she exhibited transient consciousness disturbance. Immediate right CCA angiography revealed no occlusion (C). Cone-beam computed tomography indicated no intracranial hemorrhaging. Retrospectively, the cerebral cortex in the right internal carotid artery exhibited a high signal density (D, arrowheads).**

anisocoria. Dysarthria was detected, but symptoms such as visual field defect, diplopia, new paralysis, involuntary movement, or sensory disturbances were not found. The total contrast agent volume at that time was 43 mL. Re-

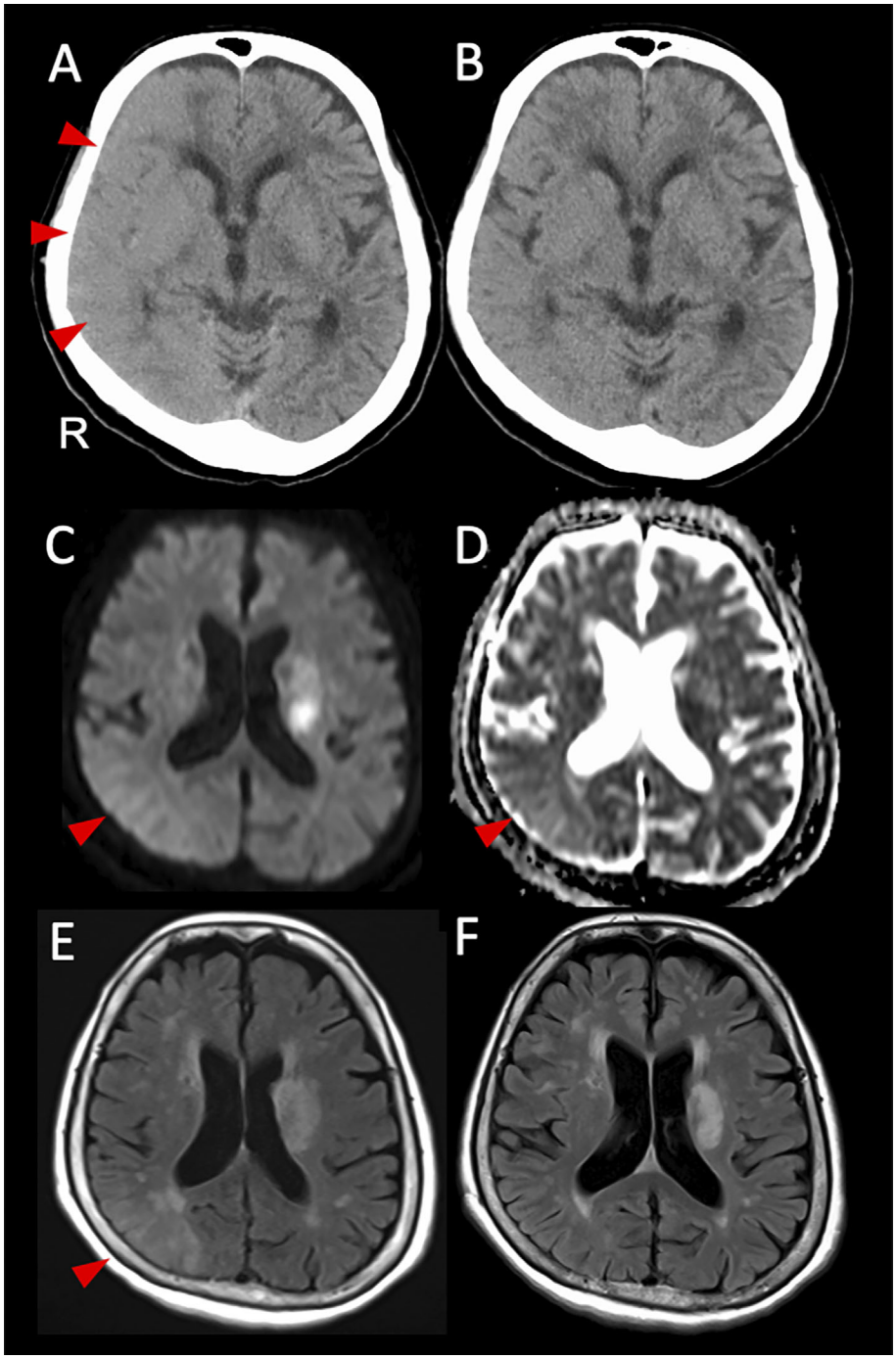

Figure 3. **Imaging after cerebral angiography. Head computed tomography (CT) indicated swelling of the cerebral cortex in the right internal carotid artery (A, arrowheads). Diffusion-weighted imaging (C), apparent diffusion coefficient map (D), and FLAIR imaging (E) revealed a slightly high intensity in the right temporal lobe (arrowhead). The known ischemic area in the left corona radiata was not enlarged. Head CT on the following day revealed no swelling in the right cerebral cortex (B). The high intensity in the right temporal lobe on FLAIR imaging improved gradually until 14 days after angiography (F).**

angiography of the right CCA indicated no occlusion of the right internal carotid artery (ICA), middle cerebral artery, or cerebral venous sinus. Cone-beam computed tomography (CT) revealed no hemorrhaging in the whole brain but showed high-density signaling in the cortex in the right ICA territory (Fig. 2C, D). She recovered after about six minutes, and her blood pressure returned to normal immediately.

Three hours after angiography, she became drowsy again, and generalized tonic-clonic seizures occurred in her left arm and leg, with eye deviation to the left. Head CT revealed swelling of the right cerebral cortex (Fig. 3A). DWI, the apparent diffusion coefficient map, and FLAIR imaging depicted a high signal intensity in her temporal lobe (Fig. 3C-E). Electroencephalography indicated no epileptic

Table. Contrast-induced Encephalopathy That Developed with ≤50mL of Contrast Agents.

Reference	Age (years)	Sex	Arteriography	Indication for study	Possible risk factors	Previous angiography	Contrast agents	Amount of contrast agents (mL)	Neurological presentation	CT brain region involved	Clinical resolution	CT brain resolution
8	71	M	Bilateral carotid artery, vertebral artery	Carotid artery stenosis	Not reported	No	Iohexol	46	Cortical blindness, confusion, and ophthalomoplegia	Bilateral occipital	10 day	N/A
8	68	F	Carotid artery, Vertebral artery	Pcom aneurysm	Not reported	No	Iohexol	24	Cortical blindness, confusion, and amnesia	Bilateral occipital	6 day	N/A
9	71	F	Right common carotid artery	Carotid artery stenting	Hypertension, after transient ischemic attack	No	Iopromide 370	25	Confusion, disorientation, and hemiparesis	The territory of the right internal carotid artery	1 day	1 day
Our case	70	F	Innominate artery, right common carotid artery	Carotid artery stenosis	After cerebral infarction	No	Iopamidol 300	43	Confusion and generalized tonic-clonic seizures	The territory of the right internal carotid artery	1 day	1 day

CT: computed tomography, M: male, F: female, Pcom: posterior communicating artery, N/A: not applicable

discharges. The patient was diagnosed with CIE based on the acute onset of symptoms during cerebral angiography and distinctive CT findings (swelling and high-density signaling) in the cortex (2). We initiated methylprednisolone pulse therapy for CIE and levetiracetam treatment for symptomatic epilepsy caused by CIE. Her symptoms disappeared, and the right cerebral swelling on head CT improved on the following day (Fig. 3B). The high signal intensity in the right temporal lobe on the FLAIR imaging gradually disappeared over a period of 2 weeks after cerebral angiography (Fig. 3F).

To determine the effects of low-dose contrast agents on encephalopathy, we performed an electronic search in PubMed for all relevant English-language articles on CIE associated with ≤50 mL of nonionic contrast agent use between 1990 to 2020, as well as cases in literature reviews reported during the same period. The results are summarized in Table.

Discussion

CIE is a rare complication of contrast agent use and manifests as various neurological disorders, such as impaired consciousness, convulsions, cortical blindness, and transient amnesia (2). It has been suggested that the hyperosmotic contrast agent breaks the blood-brain barrier and leaks into the cortex and subarachnoid space, thereby causing acute encephalopathy due to toxicity of the contrast agent (3, 4). One report described complications of cerebral angiography, including puncture site hematoma (0.5-4.2%), pseudoaneurysm of arteriovenous fistula (0.04-0.1%), vessel occlusion (0.14-0.76%), puncture site infection (0-1.0%), transient neurological symptoms due to embolism (1.2-2.5%), ischemic stroke (0.1-1.0%), severe allergic reaction to contrast agent (0.05-0.1%), and contrast agent-related nephropathy (0-3.13%) (5). A previous review from 1981 to 2012 showed that CIE occurs in 0.06% of cases after coronary angiography, 0.3-1.0% of cases after vertebral arteriography, and 2.9% of cases after endovascular coil treatment of posterior circulation aneurysms (2); notably, the CIE incidence seems to be lower in recent years than in the past due to the increased use of nonionic contrast agents. CIE associated with cerebral endovascular therapy often occurs in the territory of blood vessels where the contrast agent has been repeatedly injected. However, CIE associated with coronary angiography often affects the vertebral basilar artery region (2).

Previous reports have indicated that hypertension, renal disorder, and the low temperature of contrast agents might be risk factors for CIE (2, 3, 6). Acute cerebral infarction is also reported to be a risk factor for CIE (7). In addition, several reports have described CIE associated with endovascular surgery, which might require a higher dose of contrast agents. However, there are some cases of CIE occurring during diagnostic angiography, which does not require a high dose of contrast agents (2). In the present case, it is unlikely that the right cerebral cortex was vulnerable to ischemia tolerance because the right carotid bifurcation stenosis was not severe. Furthermore, the total amount of contrast agents used in this case was lower than that in previous reports (2). Table shows CIE cases with contrast agent use of ≤50 mL (8, 9). Our case was characterized by the absence of known risk factors in addition to the acute phase of cerebral infarction. This case presented with lacunar infarction,

periventricular and white matter lesion, a high level of baPWV, and mild cognitive impairment, which might be the underlying pathogenesis of cerebral small vessel disease with a certain degree of vascular endothelial damage. We hypothesized that the repeated injection of contrast agents into the right cerebral cortex with vascular endothelial damage as small vessel disease disrupted the blood-brain barrier, thereby leading to localized vasogenic edema and leakage of the contrast agent, which resulted in confusion and a temporarily elevated blood pressure due to localized encephalopathy, followed by generalized tonic-clonic seizures.

We diagnosed CIE based on the acute onset of symptoms during cerebral angiography, typical CT findings, and rapid improvement in clinical and imaging findings (2). Posterior reversible encephalopathy syndrome (PRES) and hypertensive encephalopathy are also known to cause disorientation and brain imaging changes associated with angiography. In the present case, unconsciousness and elevated blood pressure improved immediately after six minutes. Therefore, the transient elevated blood pressure might have been due to the localized encephalopathy because of contrast agent toxicity. Furthermore, PRES or hypertensive encephalopathy generally results in bilateral lesions; however, the lesion in this case was related to the site of contrast injection, providing a further basis for diagnosing this patient with CIE. A few cases have been diagnosed with CIE by measuring the concentration of iodine in the cerebrospinal fluid (4), but we did not examine the cerebrospinal fluid because due to concerns of brain hernia.

The efficacy of corticosteroid therapy for CIE is controversial because most cases of CIE improve smoothly without any immunotherapy (2). However, the use of corticosteroids in severe cases to induce anti-inflammatory effects has been reported (2, 8, 10). The present case was also a severe case of CIE with generalized seizure, and treatment with corticosteroids resulted in improved symptoms by the next day. Further investigations will be necessary to develop evidence-based treatment for CIE.

In conclusion, we encountered a case of CIE with acute neurological symptoms during and immediately after diagnostic cerebral angiography with small amounts of contrast agents. The findings suggest that CIE should be considered in the differential diagnosis if any acute neurological symptoms are noted during and immediately after examinations with even small amounts of contrast agents.

The authors state that they have no Conflict of Interest (COI).

References

1. Silverman SM, Bergman PS, Bender MB. The dynamics of transient cerebral blindness. Report of nine episodes following vertebral angiography. Arch Neurol **4**: 333-348, 1961.
2. Leong S, Fanning NF. Persistent neurological deficit from iodinated contrast encephalopathy following intracranial aneurysm coiling. Interv Neuroradiol **18**: 33-41, 2012.
3. Iwata T, Mori T, Tajiri H, Miyazaki Y, Nakazaki M. Repeated injection of contrast medium inducing dysfunction of the blood-brain barrier. Neuro Med Chir **53**: 34-36, 2013.
4. Uchiyama Y, Abe T, Hirohata M, et al. Blood brain-barrier disruption of nonionic iodinated contrast medium following coil embolization of a ruptured intracerebral aneurysm. Am J Neuroradiol **25**: 1783-1786, 2004.
5. Alakbarzade V, Pereira AC. Cerebral catheter angiography and its complications. Pract Neurol **18**: 393-398, 2018.
6. Wilcox J, Sage MR. Is viscosity important in the production of blood-brain barrier disruption by intracarotid contrast media? Neuroradiology **26**: 511-513, 1984.
7. Zhang G, Wang H, Zhao L, et al. Contrast-induced encephalopathy resulting from use of lobversol and lopromide. Clin Neuropharmacol **43**: 15-19, 2020.
8. Lantos G. Cortical blindness due to osmotic disruption of the blood-brain barrier by angiographic contrast material: CT and MRI studies. Neurology **39**: 567-571, 1989.
9. Potsi S, Chourmouzi D, Moumtzouoglow A, et al. Transient contrast encephalopathy after carotid angiography mimicking diffuse subarachnoid haemorrhage. Neurol Sci **33**: 445-448, 2012.
10. Shinoda J, Ajimi Y, Yamada M, Onozuka S. Cortical blindness during coil embolization of an unruptured intracranial aneurysm. Neurol Med Chir (Tokyo) **44**: 416-419, 2004.