Online October 9, 2021
Journal of Neuroendovascular Therapy 2022; 16: 371–375
DOI: 10.5797/jnet.cr.2021-0061

Case Report

A Case Report of Contrast-Induced Encephalopathy after Repeated Percutaneous Transluminal Angioplasty for Acute Middle Cerebral Artery Occlusion

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Objective: We report a case of contrast-induced encephalopathy (CIE) after repeated percutaneous transluminal angioplasty (PTA) for acute middle cerebral artery (MCA) occlusion.

Case Presentation: An 88-year-old woman with left hemiparesis was transferred to our hospital by ambulance. MRI revealed acute MCA M1 occlusion. We performed intravenous tissue plasminogen activator therapy and PTA for right MCA occlusion, leading to complete recanalization and improvement in hemiparalysis. After approximately one week, restenosis of right MCA developed and PTA was performed again on day 11. However, her left hemiparesis exacerbated shortly thereafter. CT demonstrated leakage of contrast medium, and an extensive high-intensity area (HIA) on the white matter in the right cerebral hemisphere was noted on MRI FLAIR. The HIA on MRI and neurological deficits gradually improved after conservative treatment, but diffuse atrophy of the right cerebral hemisphere occurred and higher brain dysfunction remained.

Conclusion: Repeated ischemia and reperfusion, and the frequent use of contrast media were considered the causes of CIE.

Keywords ▶ contrast-induced encephalopathy, reversible leukoencephalopathy, hyperperfusion syndrome, mechanical thrombectomy, acute large vessel occlusion

Introduction

After the usefulness of endovascular treatment for acute occlusion of major intracranial arteries, including mechanical thrombectomy (MT), was demonstrated, it became widely performed, but many complications have also been reported. Many are hemorrhagic or ischemic complications, but there have also been sporadic reports of contrast-induced encephalopathy (CIE).[1,2] CIE is known to occur after intracranial endovascular treatment, but there are few reports of CIE following MT. In this report, we present a case of complete recanalization of acute middle cerebral artery (MCA) occlusion by intravenous thrombolysis with recombinant tissue plasminogen activator (tPA) and percutaneous transluminal angioplasty (PTA) in which CIE subsequently developed after PTA for restenosis of the MCA.

Case Presentation

Patient: An 88-year-old woman.

Medical history: Hypertension, dyslipidemia, diabetes (stage 1 diabetic nephropathy), chronic atrial fibrillation (no history of antithrombotic medication), and dementia.

History of present illness: The patient was transferred to our hospital by ambulance due to the sudden onset of dysarthria, and hemiparalysis of the left upper and lower limbs. The onset-to-door time was 50 minutes.

Findings on arrival: The blood pressure was 148/101 mmHg, the heart rate was 103 beats/min, and atrial fibrillation was noted. Other findings included right concomitant deviation, central left facial palsy, severe hemiparalysis of the left upper and lower limbs, and left-sided reduction of superficial sensation, and the National Institutes of Health Stroke Scale (NIHSS) score was 13.

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Received: March 31, 2021; Accepted: September 12, 2021
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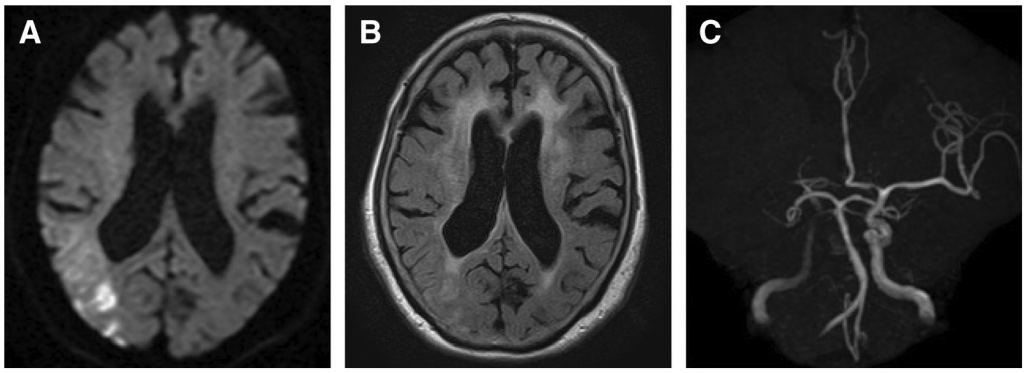

Fig. 1 Initial MRI images on admission. (**A** and **B**) DWI showing a hyperintense area in the right MCA territory with few signal alterations on FLAIR. (**C**) MRA indicates the occlusion of M1. DWI: diffusion-weighted imaging; MCA: middle cerebral artery

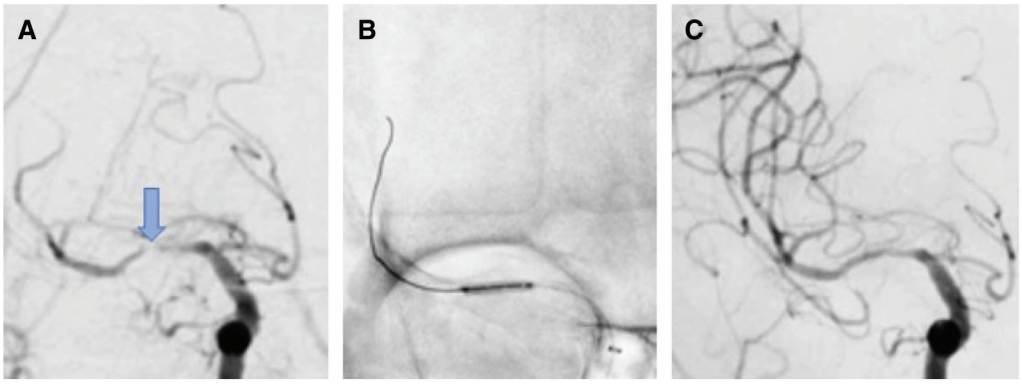

Fig. 2 Cerebral angiography after intravenous administration of tissue-type plasminogen activator on day 1. (**A**) Severe stenosis in the right M1 segment (arrow). (**B**) PTA using a "UNRYU 2.0 × 10 mm" (Kaneka Medix, Osaka, Japan). (**C**) Stenosis improved and complete reperfusion (TICI 3) was achieved. PTA: percutaneous transluminal angioplasty; TICI: thrombolysis in cerebral infarction

Imaging findings on admission

MRI revealed a localized diffusion-weighted imaging (DWI) high-intensity area (HIA) posterior to the right MCA territory (**Fig. 1A**), DWI-Alberta stroke program early computed tomography Score (ASPECTS) was 10, and no FLAIR hyper-intensity was noted (**Fig. 1B**). MRA demonstrated right MCA M1 occlusion (**Fig. 1C**).

Therapeutic course

As DWI–FLAIR mismatch was noted on MRI, the condition was judged to be an indication for intravenous thrombolysis with tPA and thrombectomy. After right femoral artery puncture, exploratory imaging was performed by guiding an 8-Fr Optimo (Tokai Medical Products, Aichi, Japan) to the right internal carotid artery, which revealed recanalization of the right M1 with 90% stenosis, and delineation of the distal vessels was poor (**Fig. 2A**). Concerning the pathogenic mechanism of cerebral infarction in this patient, the condition was diagnosed as atherothrombotic infarction due to severe M1 stenosis. As the risk of reocclusion was judged to be high, PTA was selected. A 0.014-inch CHIKAI 200 cm (Asahi Intecc, Aichi, Japan) was passed through the lesion and the stenosed area was gradually dilated using a UNRYU XP 2.0 × 10 mm (Kaneka Medix, Osaka, Japan) (**Fig. 2B**). After PTA, stenosis improved to 30% and thrombolysis in cerebral infarction (TICI) 3 recanalization was eventually achieved (**Fig. 2C**). After treatment, left upper and lower limb hemiparalysis was markedly alleviated, and the NIHSS score improved to 1 after 24 hours. Thereafter, to prevent restenosis, the oral administration of clopidogrel at 75 mg/day and intravenous infusion of argatroban (60 mg/day × 2 days and 20 mg/day × 5 days) were started in addition to the oral administration of apixaban at 5 mg/day in consideration of the risk of cardiogenic stroke due to atrial fibrillation.

MRI performed on the 2nd hospital day demonstrated no novel lesion, and delineation of the distal right MCA on MRA was satisfactory (**Fig. 3A**–**3C**). CTA and CT

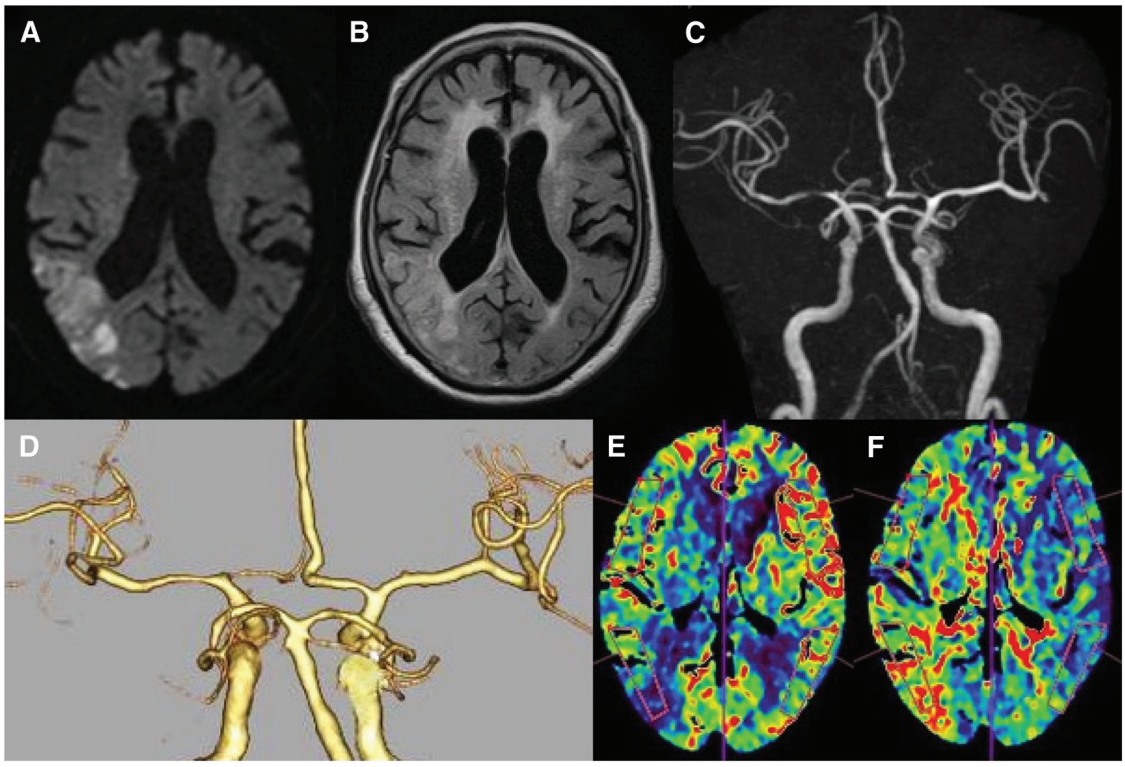

Fig. 3 MRI images on day 2 and enhanced CT images on day 6. (**A**) DWI showing no new HIA. (**B**) FLAIR showing HIA along the posterior region of the MCA, which exhibited an HIA on DWI at admission. (**C** and **D**) MRA and CTA showing the reperfusion and remaining right M1 stenosis. (**E** and **F**) CT perfusion indicates hypoperfusion of the MCA region; rCBF value decreased and the MTT was significantly longer on the right. DWI: diffusion-weighted imaging; HIA: high-intensity area; MCA: middle cerebral artery; MTT: mean transit time; rCBF: regional cerebral blood flow

perfusion performed on the 6th hospital day revealed approximately 80% stenosis in the right M1, and a reduction of the ratio of cerebral blood flow (CBF) to the opposite side to 0.6 and prolongation of the mean transit time (MTT) to ≥6 seconds were noted on CT perfusion, suggesting marked hypoperfusion in the right MCA territory (**Fig. 3D**–**3F**). As restenosis occurred in a short time, we judged the risk of reocclusion to be high and performed PTA again on the 11th hospital day. At the time of retreatment, 65% stenosis was observed in the right M1. PTA was performed by increasing the balloon size compared with the first PTA using the UNRYU XP 2.5 × 10 mm, and stenosis was improved to approximately 25%. The duration of blood flow occlusion was approximately 2 minutes, and the volume of the contrast medium used was approximately 200 cc. Although the stenosed area was able to be dilated, disturbance of consciousness and left hemiplegia developed immediately after PTA, and the NIHSS score deteriorated to 15. CT of the head immediately after surgery revealed diffuse leakage of contrast medium primarily in the subarachnoid space of the right cerebral hemisphere (**Fig. 4A**).

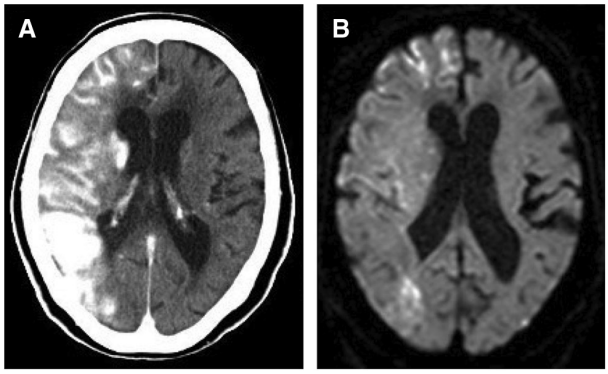

Fig. 4 (**A**) Non-contrast CT findings after second PTA. CT shows extensive contrast medium leakage mainly in the subarachnoid space in the right cerebral hemisphere. (**B**) DWI shows an HIA in the right cerebral cortex on day 12 (the day after second PTA). DWI: diffusion-weighted imaging; HIA: high-intensity area; PTA: percutaneous transluminal angioplasty

On the next day (12th hospital day), the M1 and distal MCA were delineated satisfactorily on MRA, and no novel infarction foci were detected by DWI (**Fig. 4B**), but a wide HIA primarily in the white matter of the right cerebral hemisphere was observed on FLAIR imaging (**Fig. 5A**). In consideration of the risk of hyperperfusion,

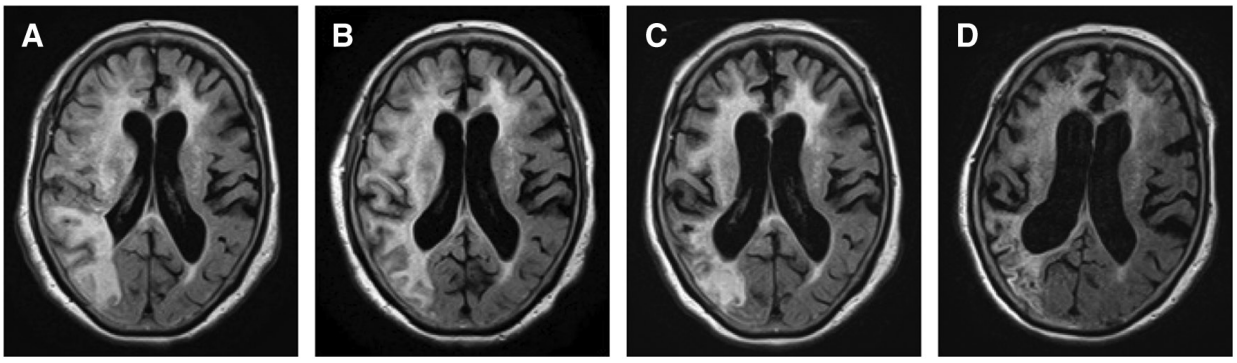

Fig. 5 Changes in MRI findings over time. Hyperintense lesions in the right subcortical white matter on FLAIR gradually disappeared. (**A**) Day 12 (the day after second PTA), (**B**) day 16, (**C**) day 25, and (**D**) day 43. PTA: percutaneous transluminal angioplasty

antihypertensive therapy using nicardipine and sedation using propofol were performed. A decrease in CBF in the right MCA territory (ratio to the opposite side: 0.4) and prolongation of MTT (5 sec) were noted on CT perfusion performed on the 18th hospital day, excluding hyperperfusion. However, symptoms suggestive of allergy to contrast medium, such as reddening of the trunk and mild respiratory discomfort, were observed after CT examination. Thereafter, sedation was discontinued, and treatment and fluid replacement for atherothrombotic cerebral infarction and rehabilitation were continued. There was no exacerbation of renal function due to repeated contrast-enhanced imaging. The size of the HIA in the right cerebral white matter on MRI FLAIR gradually decreased, and the FLAIR HIA other than the areas that exhibited irreversible change due to cerebral infarction nearly disappeared on MRI after the 25th hospital day, but diffuse atrophy was noted in the right cerebral hemisphere (**Fig. 5B**–**5D**). Left hemiplegia was gradually alleviated with shrinking of the FLAIR HIA, but impairment of higher brain functions, such as left spatial neglect, persisted. Based on the findings on CT of the head immediately after treatment and the clinical course, a diagnosis of CIE was made.

Discussion

In this case, exacerbation of neurological symptoms was observed after PTA was performed twice in a short period for acute occlusion and restenosis of the MCA, and a diagnosis of CIE was made based on the clinical course and characteristic imaging findings.

There have been few reports of CIE after intracranial endovascular treatment.[1–3] Chu et al.[1] reported that CIE was observed in 7 (1.7%) of the 421 patients who underwent MT, and they defined a condition that fulfills both of the following clinical and imaging criteria as CIE. The clinical criteria are clear exacerbation of neurological findings within 24 hours after MT (exacerbation of 4 or more points in the NIHSS score or 2 or more points in the Glasgow Coma Scale [GCS] score) or a delay in improvements of neurological findings not explained by cerebral infarction, and the imaging criteria are edematous change with contrast enhancement beyond the ischemic core. As for imaging findings characteristic of CIE, abnormal contrast enhancement in the cortex, brain edema, and subarachnoid contrast enhancement resembling that in subarachnoid hemorrhage on CT[2]; hyperintensity on T2-weighted imaging; and DWI on MRI without an increase in apparent diffusion coefficient (ADC)[4] have been reported. The exacerbation of neurological findings immediately after treatment, and the CT and MRI findings in this case did not contradict previous reports about CIE. Plain CT after retreatment also demonstrated leakage of contrast medium in the territory of the anterior cerebral artery (ACA), but contrast medium was considered to have spread to the subarachnoid space in the ACA territory as a large amount of contrast medium leaked out of the MCA territory.

Clinical symptoms of CIE often resolve within 24–48 hours and the prognosis is considered to be favorable,[2,5] but impairment of higher brain functions persisted in this patient. However, there have also been reports of persistent sequelae and death,[6,7] and the present case is considered to have been a severe case of CIE.

Pathologically, CIE is ascribed to brain edema caused by disruption of the blood–brain barrier (BBB) induced by the toxicity of contrast medium or its leakage into the subarachnoid space.[5] There have also been reports that a specific reaction to contrast medium itself is related to CIE and that CIE occurs when contrast medium is used in large amounts.[2] In the present case, we also evaluated continuation or

intensification of internal treatment at the time of restenosis after the first PTA but judged retreatment to be more appropriate in consideration of the high risk of reocclusion in addition to the risk of hemorrhage due to the addition of antiplatelet medication because stenosis progressed rapidly in a short period despite 3-drug antithrombotic therapy including an anticoagulant. However, in retrospect, BBB disruption was considered to have been induced by the repeated use of contrast medium in a short period under conditions that were likely to invite BBB disruption, such as ischemia and hypoperfusion, eventually leading to CIE.

In this case, hyperperfusion syndrome and CIE were considered in the differential diagnosis, but their possibility was considered low according to the MRA and CT perfusion findings on the day after surgery. Posterior reversible encephalopathy syndrome (PRES) is known to cause reversible leukoencephalopathy, as does CIE.[8] PRES presents with symmetric lesions primarily in the occipital and parietal lobes, and its symptoms are considered reversible,[3] but the lesions in our patient were localized in the right cerebral hemisphere, and the changes in both clinical symptoms and imaging findings were partly irreversible. Therefore, we also considered PRES to be unlikely.

Recently, indications of endovascular treatment for occlusion of large intracranial arteries are widening and we recommend that CIE be regarded as a possible complication, as observed in our patient.

Conclusion

We treated a patient who developed CIE after repeated PTA for acute MCA occlusion. Repeated ischemia and reperfusion were considered to have further exacerbated vascular endothelial injury and BBB disruption, leading to CIE.

Disclosure Statement

The authors declare no conflicts of interest.

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