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Contrast-Induced Encephalopathy after Endovascular Treatment: Two Case Reports

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Abstract

Contrast-induced encephalopathy (CIE) is a rare neurological complication that occurs after the use of contrast medium in various angiographic procedures. Symptoms can be different, from headache to severe neurological deficit and coma. In the articles published to date, symptoms appeared immediately after application of contrast agent or within 24 hours. Here we present two cases of patients in whom CIE developed delayed after endovascular treatment.

Keywords

- case
- cerebral angiography
- contrast-induced encephalopathy
- endovascular treatment
- iodinated contrast

Introduction

Contrast-induced encephalopathy (CIE) is characterized by the appearance of a new neurological deficit after intravenous or intra-arterial administration of iodinated contrast agent.[1] The incidence of CIE ranges between 0.3 and 2.4%.[2,3] The mechanism of CIE was previously explained as the disruption of the blood–brain barrier (BBB), hyperosmolarity, and neurotoxicity from the contrast medium.[4,5]

Although cortical enhancements and hyperintensities in the subarachnoid space are visible on a computerized tomography (CT), the primary diagnostic tool is magnetic resonance imaging (MRI), where hyperintense areas can be seen on a T2-weighted, fluid-attenuated inversion recovery (FLAIR), and diffusion-weighted imaging (DWI). Diagnostic coronary angiography images of an MRI of the brain can help differentiate CIE from cerebral ischemia.

The symptoms can range from a mild headache to a pronounced neurological deficit, such as aphasia, hemiparesis, and coma. Treatment consists of the use of corticosteroids, mannitol, and hydration.[6] In some patients, the symptoms disappear within 24 to 48 hours, but in rare cases, they can last up to 2 weeks.[7] Although the treatment outcome is generally favorable, fatal cases have also been described in the literature.[8]

Herein, we present two case patients who developed CIE after endovascular treatment.

Case 1

A 64-year-old patient presented to our outpatient clinic with MRI findings. She stated that a few months ago, she had frequent headaches. The patient had a medical history of

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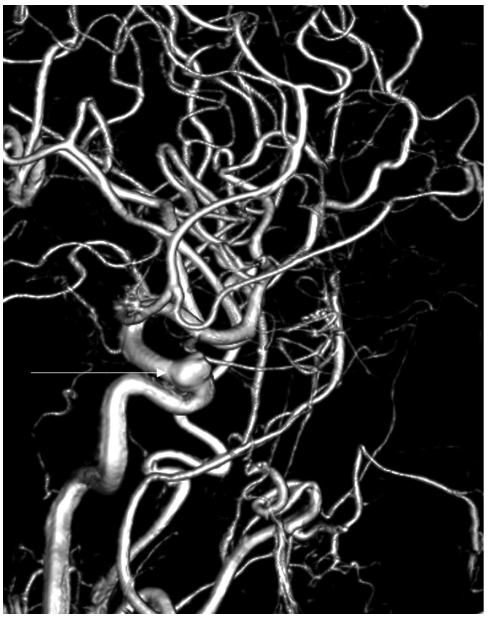

Fig. 1 Three-dimensional reconstruction images of computed tomography angiography showing an aneurysm of the left internal cerebral artery.

hypertension. There was no known family history of a bleeding disorder. The neurological examination was without focal neurological signs. The MRI and CT angiography of the brain showed an aneurysm of the left internal carotid artery (ICA; ►**Fig. 1**). Digital subtraction angiography (DSA) was performed to clarify and assess the aneurysm's anatomy and morphology. During DSA, a total of 60 mL of the nonionic contrast medium iopamidol at an iodine concentration of 370 mgI/mL (Iopamiron 370; Schering, Osaka, Japan) was used.

After interdisciplinary discussion, coil embolization was successfully performed using a transradial approach. The intraoperative and early postoperative course were uneventful. Five days after operation, the patient was discharged from the hospital fully conscious und without any neurological deficit (modified Rankin Scale score: 0).

A follow-up MRI of the brain conducted 2 weeks after intervention showed a hyperintense areal in the T2-weighted image in the left occipital lobe (►**Fig. 2**).

Given that the patient had no symptoms, supportive treatment was recommended. Two weeks later, the patient developed weakness and dysesthesia of the right side as well as numbness in the IV and V fingers.

An urgent MRI of the brain showed increased hyperintensity on T2 and FLAIR (►**Fig. 2**). The apparent diffusion coefficient had not changed. A diagnosis of contrast-induced encephalopathy was made.

In addition to adequate hydration, corticosteroid therapy was started, after which the patient's clinical neurological status improved.

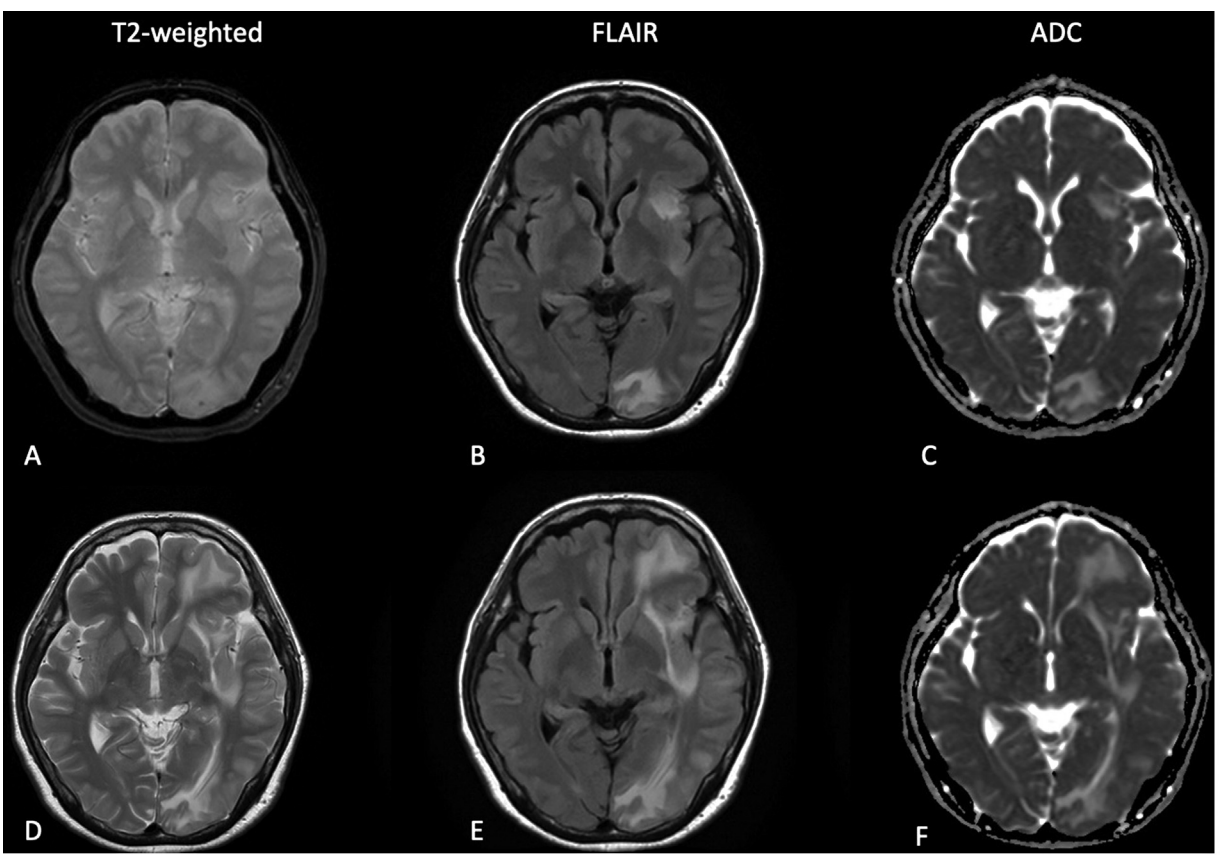

Fig. 2 Brain magnetic resonance imaging at the 2 weeks (**A**–**C**) and 2 months follow-up (**D**–**F**). ADC, apparent diffusion coefficient; FLAIR, fluid-attenuated inversion recovery.

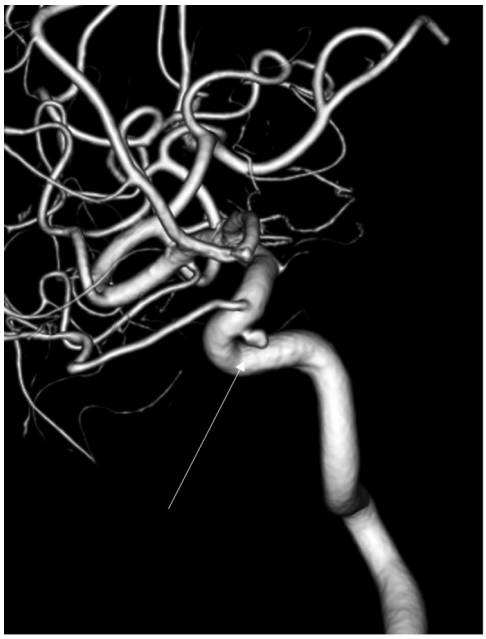

Fig. 3 Three-dimensional reconstruction images of computed tomography angiography showing an aneurysm of the right internal cerebral artery.

Upon discharge from the hospital, the patient completely recovered from sensory dysfunction, but slight weakness of the right-hand grip remained.

Case 2

A 75-year-old male patient was admitted to our hospital for endovascular treatment of an ICA aneurysm (►**Fig. 3**). The patient had two aneurysms: a basilar artery-superficial cerebellar artery (BA-SCA) aneurysm and an ICA aneurysm. He underwent stent embolization of the BA-SCA aneurysm 3 years earlier in another hospital.

Upon examination, the patient was alert, cranial nerves were intact, and no sensorimotor neurological deficits were present.

The medical history includes hypertonia and hyperlipidemia. Laboratory findings at the time of admission were in the normal range.

After admission, he underwent cerebral angiography, resulting in successful occlusion of the right ICA aneurysm with endovascular coiling using a transfemoral approach.

During DSA, a total of 60 mL of contrast-medium iopamidol (Iopamiron 370; Schering, Osaka, Japan) was used. The intraoperative and early postoperative clinical courses were uncomplicated.

On the 5th day after endovascular treatment, the patient developed weakness, numbness, and involuntary movements on the left side.

The urgent MRI of the brain showed a hyperintense signal in the right parietal lobe on the DWI (►**Fig. 4A**). The patient was admitted to the hospital with a suspected cerebral infarction. Atrial fibrillation was observed on the electrocardiogram during a routine clinical examination, and Eliquis therapy was initiated after ablation. The patient was discharged home after a few days.

At the follow-up MRI after 3 months, it was observed that the hyperintense area had increased and spread to the right frontal and temporal lobes (►**Fig. 4B**).

Given that the patient had no new neurological symptoms, supportive treatment was continued. After a month, the patient came to the emergency department due to vertigo and was admitted to the cardiology department with a diagnosis of sinus sick syndrome. Given that the hyperdense areal in the MRI scan continued to increase, a biopsy of the lesion was performed. Pathohistological findings showed a granuloma, suggesting an allergic reaction to the stent.

After an interdisciplinary consultation, therapy with prednisolone 60 mg/per day was started, which was considered effective and was gradually reduced. A follow-up MRI 1 month after the introduction of corticosteroid therapy showed reduced hyperintense areas (►**Fig. 4C**). In addition, the patient's neurological status slightly improved. The vertigo has completely disappeared, but the patient still has numbness in her lower left leg.

Discussion

CIE is a rare transient phenomenon that occurs after the administration of contrast media during endovascular

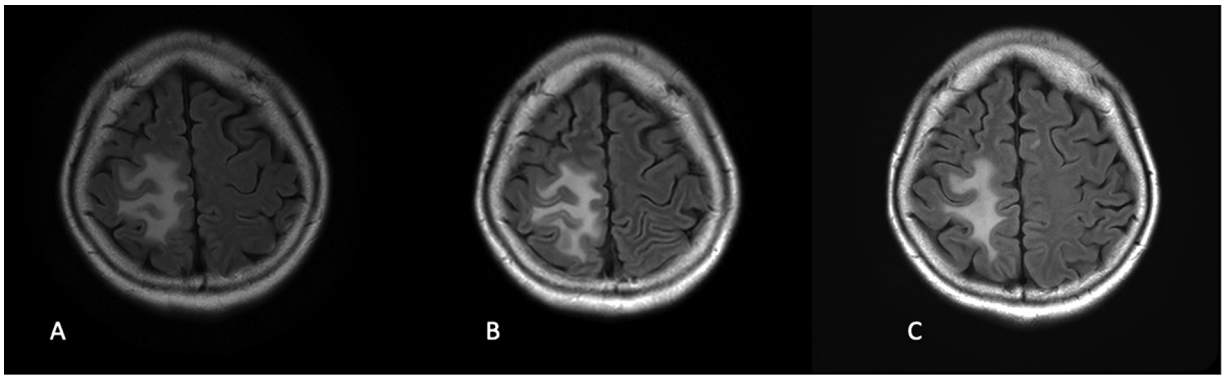

Fig. 4 Brain magnetic resonance imaging showing hyperintense signal in the right parietal lobe (**A**), increase in the hyperintense signal at the 3-month follow-up (**B**), and resolution of hyperintense area at the 1-month follow-up after prednisolone treatment (**C**).

Table 1 Reported risk factors of CIE

Risk factors
Chronic hypertension
Diabetes mellitus
Renal dysfunction
Administration of large volumes of iodinated contrast
History of stroke
Percutaneous coronary intervention
Selective angiography of internal mammary grafts
Previous adverse reaction of iodinated contrast
Posterior cerebral circulation

Abbreviation: CIE, contrast-induced encephalopathy.

interventions.[7] It was first described in 1970, when it manifested as transient cortical blindness after coronary angiography.[9]

Although the underlying mechanism of CIE is still debated, its pathophysiological process is at the level of the BBB.[6] The BBB should be impermeable to contrast agents.[5] After the administration of a contrast agent, in some cases, there is a disturbed osmotic balance, which leads to hyperosmolarity and causes dehydration of the endothelial cells. Disruption of the junctions between the cells leads to disturbance of the BBB's integrity.[10,11]

Several risk factors can influence the development of CIE. One of the main factors is renal dysfunction, which can impair the clearance of contrast medium and exacerbate the accumulated osmolality.[12] Chronic hypertension due to cerebral autoregulatory dysfunction can also cause damage to the BBB.[7]

Furthermore, the posterior cerebral circulation is the most sensitive to potential damage due to its sympathetic innervation.[13] A previous stroke can disrupt the BBB and affect the leakage of the contrast agent, which can cause tissue reaction and cerebral edema.[12] ►**Table 1** shows some reported risk factors of CIE.[7,8,12,14]

Diagnosis of CIE can be very challenging, especially when symptoms appear delayed after the procedure. Therefore, it is important to perform a thorough diagnostic workup to rule out differential diagnoses. A differential diagnosis can be posterior reversible encephalopathy syndrome, reperfusion syndrome, recurrent ischemic stroke, or subarachnoid hemorrhage.[10,12]

Typical radiological CIE findings include cerebral edema and cortical enhancement. MRI is the gold standard for diagnosis and differentiation from other pathologies.[15] Some authors have suggested other diagnostic methods, such as cerebrospinal fluid (CSF) analysis, measurement of contrast concentration in CSF, and measurement of the Hounsfield unit on a CT scan.[16,17]

There is no exact period between the application of contrast and the onset of symptoms.[7] Some authors have reported that CIE occurs 0.5 to 18 hours after contrast agent administration.[18] In our first case, the appearance of symptoms was preceded by the appearance of hyperdense arreales on T2-weighted and FLAIR MRI. The symptoms appeared almost 4 weeks after the endovascular intervention.

To the best of our knowledge, there are no guidelines for the management of treatment for CIE. The treatment strategy is based on adequate hydration with intravenous crystalloids and antiedematous therapy with mannitol and corticosteroids.[19] In our patients, we administered intravenous corticosteroids during the hospital stay and oral corticosteroids after discharge from the hospital.

The treatment outcome is mostly favorable, with complete recovery within a few days, and permanent neurological deficits are uncommon.

In conclusion, CIE is a serious condition that must be promptly recognized. Although it generally appears within a few hours of the application of the contrast agent, it can also appear delayed. Timely initiation of treatment is of crucial importance.

Given that most of the literature is based on case reports due to this condition's rarity, a multicenter study is needed. In addition to investigating the mechanisms of CIE further, future research should focus on CIE's potential impact on complications and the outcome of patient treatment.

Authors' Contributions

D.J. was involved in collection of the data, analysis of the results, and the writing of the manuscript. R.T., K.S., K.M., S.C., M.N., and T.T. were involved in collection of the data and analysis of the results. F.K., Y.Y., and Y.K. supervised the findings of this work. All authors reviewed the results and approved the final version of the manuscript.

Conflict of Interest

None declared.

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