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# Contrast Injection from an Intermediate Catheter Placed in an Intradural Artery is Associated with Contrast-Induced Encephalopathy following Neurointervention

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## ABSTRACT

**BACKGROUND AND PURPOSE:** Contrast-induced encephalopathy can result from neurotoxicity of contrast medium in the affected area. The development of intermediate catheters has allowed guidance of catheters to more distal arteries. This study focused on the association between contrast-induced encephalopathy and contrast injection from an intermediate catheter guided into a distal intradural artery during neurointervention for cerebral aneurysms.

**MATERIALS AND METHODS:** We retrospectively reviewed 420 consecutive aneurysms in 396 patients who underwent neurointervention for extracranial aneurysms and unruptured intracranial aneurysms at our institution from February 2012 to January 2023. Patients were divided into a group with contrast-induced encephalopathy and a group without. To identify risk factors for contrast-induced encephalopathy, we compared clinical, anatomic, and procedural factors between groups by multivariate logistic regression analysis and stepwise selection.

**RESULTS:** Among the 396 patients who underwent neurointervention for cerebral aneurysms, 14 (3.5%) developed contrast-induced encephalopathy. Compared with the group without contrast-induced encephalopathy, the group with contrast-induced encephalopathy showed significantly higher rates of patients on hemodialysis, previously treated aneurysms, intradural placement of a catheter for angiography, nonionic contrast medium, and flow-diversion procedures in univariate analyses. Stepwise multivariate logistic regression analysis revealed intradural placement of a catheter for angiography (OR = 40.4; 95% CI, 8.63–189) and previously treated aneurysms (OR = 8.20; 95% CI, 2.26–29.6) as independent predictors of contrast-induced encephalopathy.

**CONCLUSIONS:** Contrast injection from an intradural artery and retreatment of recurrent aneurysms were major risk factors for contrast-induced encephalopathy. Attention should be paid to the location of the intermediate catheter for angiography to avoid developing contrast-induced encephalopathy.

**ABBREVIATIONS:** CIE = contrast-induced encephalopathy; VA = vertebral artery

Contrast-induced encephalopathy (CIE) after neurointervention is a rare-but-important complication.<sup>1–7</sup> CIE can cause a variety of neurologic abnormalities, including motor, sensory, and visual impairments, aphasia, and seizures, depending on the affected area of cerebrum.<sup>1,5,6,8</sup> The symptoms are generally temporary and curable but may occasionally persist.<sup>1,9</sup> Risk factors

for CIE have previously been considered to include prior stroke, renal dysfunction, hemodialysis, hypertension, diabetes mellitus, posterior circulation aneurysms, higher dosage of contrast medium, and injection of contrast medium under elevated blood pressure.<sup>1–4,6,7,10</sup>

To clarify the mechanisms underlying CIE, animal studies have demonstrated that the BBB is temporarily overcome by either elevated blood pressure or hyperosmolality and that the penetration of contrast medium (including nonionic monomeric contrast medium) causes neuronal cell death in the affected area.<sup>10–14</sup> Furthermore, in clinical practice, Uchiyama et al<sup>15</sup> detected large amounts of iodine in the CSF on neuroimaging after coil embolization for a ruptured intracranial aneurysm, probably due to temporary leakage or destruction of the BBB. Because neurointervention involves repeat injection of contrast medium into a single intracranial artery, the risk of contrast-induced neurotoxicity might be elevated.

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Large-bore intermediate catheters have recently been used extensively in neurointerventional procedures for cerebral aneurysms. The development of intermediate catheters has helped guide catheters to more distal arteries, improved the maneuverability of microcatheters, and facilitated high-density coil packing.<sup>16</sup> One of the problems with contrast injection from a distally guided catheter is thought to be higher pressures and volume loading on distal arteries, which might destroy the BBB and cause neurotoxicity and CIE by leakage of contrast medium.

To verify this hypothesis, we investigated the association between CIE and contrast injection from an intermediate catheter guided into a distal intradural artery during neurointervention for cerebral aneurysms.

## MATERIALS AND METHODS

### Study Population

This study included 420 consecutive aneurysms in 396 patients who underwent neurointervention for extracranial aneurysms and unruptured intracranial aneurysms at our institution between February 2012 and January 2023. By retrospective review, patients were divided into those with CIE (CIE group; 14 patients, 14 aneurysms) and those without it (Non-CIE group; 382 patients, 406 aneurysms). Groups were compared in terms of clinical, anatomic, and procedural factors. The present study was approved by our institutional review board, and the need for informed consent was waived on the basis of the retrospective design.

### Anatomic Classification of the ICA and Vertebral Artery

Segments of the ICA in the present study were categorized according to the classification of Gibo et al.<sup>17</sup> The extracranial ICA was classified as the C1 segment, and the extradural ICA was subdivided into petrous (C2) and cavernous (C3) segments, ending at the distal dural ring. The entire intradural ICA was categorized as the supraclinoid (C4) segment, including the ophthalmic, communicating, and choroidal subsegments.

The vertebral artery (VA) was classified into 4 segments: V1, representing the preforaminal segment and ranging from the origin of the VA to the transverse foramen of the sixth cervical vertebra; V2, representing the foraminal segment and ranging from the transverse foramen of the sixth cervical vertebra to the transverse foramen of the second cervical vertebra; V3, representing the atlantic, extradural segment and ranging from the transverse foramen of the second cervical vertebra to the penetration of the dura mater; and V4, representing the intradural segment and ranging from after the penetration of the dura mater to the confluence with the contralateral VA.

An intradural artery was defined as the intradural segment of a major artery, including distal to the C4 segment of the ICA in the anterior circulation and distal to the V4 segment of the VA in the posterior circulation.

### Contrast Medium Usage and Endovascular Treatment

All coil embolization procedures were performed solely by certified interventional neurosurgeons (M.F., R.T., A.T., K.I., I.K.) in a standardized manner. Dual antiplatelet therapy with aspirin (100 mg/day) and clopidogrel (75 mg/day) was initiated 1–4 weeks before coil embolization to prepare for unintended rescue

stenting. All coil embolizations were performed with the patient under general anesthesia. Heparin was administered during treatment to maintain an activated clotting time of at least 250 seconds during the procedure. Guiding catheters used included Optimo (Tokai Medical Products), Asahi Fubuki (Asahi Intecc), Shuttle (Cook Medical), FlowGate2 (Stryker Neurovascular), Axcelguide (Medikit), and Envoy (Codman & Shurtleff); and intermediate catheters used included Sofia (MicroVention-Terumo), Navien (Medtronic), Cerulean (Medikit), Asahi Fubuki, and Destination (MicroVention-Terumo). Until July 2017, unless the patient had an allergy to contrast medium, the ionic dimeric contrast medium ioxaglate (Hexabrix 320; Mallinckrodt) was routinely used. After this time, the nonionic monomeric contrast medium iohexol (Omnipaque 300; GE Healthcare) was used. 3D DSA was performed using a biplane flat panel detector C-arm angiography system (Artis zee BA Twin Large Display; Siemens) before and after embolization by injecting a 2:1 diluted contrast medium with an injector through a guiding catheter placed in C1 of the ICA or V1 or V2 of the VA. Control and working projection angiograms were also obtained by manually injecting 2:1 diluted contrast medium from the guiding catheter or intermediate catheter as appropriate during neurointervention.

### Diagnostic Criteria for CIE

On the basis of previous studies,<sup>4,5,7</sup> CIE was diagnosed when all 3 of the following criteria were met. 1) Unequivocal postoperative neurologic deterioration compared with the preoperative neurologic status that could not be explained by other reasons. Patients underwent neurologic assessment immediately after waking from general anesthesia and at the onset of any new symptoms. 2) Neurologic symptoms persisting for >24 hours and differentiated from TIA. When imaging findings typical of CIE were present, such as cortical or subcortical contrast enhancement on noncontrast CT or cortical gyriform hyperintensity on a FLAIR sequence or T2-weighted MR imaging, CIE was diagnosed even if symptoms improved within 24 hours.<sup>8,18</sup> 3) Symptoms improved within 1 week after treatment and with re-evaluation on CT or MR imaging showing no obvious abnormality if imaging findings had been abnormal at onset. Noncontrast CT or MR imaging analysis was blinded to the clinical features of the patient and independently reviewed and evaluated by 2 certified interventional neurosurgeons (2 of the following: M.F., R.T., A.T., K.I., and I.K.) who were not the responsible interventional neurosurgeons for the aneurysm treatment. In cases of discrepancies in assessment, a third certified interventional neurosurgeon (One of M.F., R.T., A.T., K.I., and I.K.) other than the initial reviewers verified the consistency of the data and reached a consensus. In addition, the time courses from neurointervention to CIE onset and from CIE onset to recovery and the mRS at 1 month after treatment were also recorded.

### Statistical Analyses

The Mann-Whitney *U* test or Fisher exact test was administered to compare baseline characteristics between the CIE and non-CIE groups. Multivariate logistic regression analysis and stepwise selection were used to assess whether contrast injection from an intermediate catheter guided into an intradural artery was a

**Table 1: Baseline clinical characteristics in CIE and non-CIE groups<sup>a</sup>**

|                                           | CIE              | Non-CIE          | P Value           |
|-------------------------------------------|------------------|------------------|-------------------|
| No. of patients                           | 14 (3.5)         | 382 (96)         |                   |
| Age (yr)                                  | 73 [66–79]       | 68 [57–75]       | .054              |
| Sex, female                               | 8 (57)           | 254 (67)         | .57               |
| Body mass index (kg/m <sup>2</sup> )      | 23.5 [21.4–26.3] | 22.9 [20.3–25.7] | .29               |
| Race                                      |                  |                  |                   |
| Asian                                     | 14 (100)         | 382 (100)        | NA                |
| Medical history                           |                  |                  |                   |
| Hypertension                              | 10 (71)          | 245 (64)         | .78               |
| Diabetes mellitus                         | 3 (21)           | 35 (9.2)         | .14               |
| Hyperlipidemia                            | 6 (43)           | 174 (46)         | 1                 |
| Prior stroke <sup>b</sup>                 | 4 (29)           | 45 (12)          | .081              |
| Ischemic stroke                           | 3 (21)           | 17 (4.5)         |                   |
| Hemorrhagic stroke                        | 2 (14)           | 28 (7.3)         |                   |
| Cerebral hemorrhage                       | 0 (0)            | 6 (1.6)          |                   |
| SAH                                       | 2 (14)           | 22 (5.8)         |                   |
| Renal dysfunction (eGFR <45) <sup>c</sup> | 2 (14)           | 19 (5.0)         | .17               |
| Hemodialysis                              | 2 (14)           | 5 (1.3)          | .022 <sup>d</sup> |
| eGFR, (mL/min per 1.73 m <sup>2</sup> )   | 79.1 [55.5–92.2] | 79.9 [66.1–92.4] | .58               |
| Smoking                                   | 9 (64)           | 155 (41)         | .098              |
| Drinking                                  | 5 (36)           | 146 (38)         | 1                 |
| Allergy <sup>e</sup>                      | 1 (7.1)          | 82 (22)          | .32               |
| Allergy to contrast medium                | 1 (7.1)          | 20 (5.2)         | .54               |

**Note:**—eGFR indicates estimated glomerular filtration rate; NA, not applicable.

<sup>a</sup> Unless otherwise indicated, values represent the number of aneurysms (%) or median [interquartile range]. Not all percentage totals reach 100% because of rounding.

<sup>b</sup> Patients with a history of both ischemic and hemorrhagic stroke were counted in each category.

<sup>c</sup> Renal dysfunction was defined as an eGFR of <45 mL/min/1.73 m<sup>2</sup>.

<sup>d</sup>  $P < .05$ .

<sup>e</sup> History of allergy included allergy to any food or drug.

predictor of the development of CIE. This analysis was adjusted not only for factors that appeared significant in univariate analyses in the present study but also for the following previously reported risk factors for CIE: prior stroke, renal dysfunction, hemodialysis, hypertension, diabetes mellitus, posterior circulation aneurysm, and total volume of contrast medium.<sup>1–4,6,7</sup> Because renal dysfunction and hemodialysis were strongly correlated, only variables with lower  $P$  values in univariate analyses were included in the multivariate analysis. All statistical analyses were performed with Easy R (EZR) (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is based on R and R commander [Bone Marrow Transplant].<sup>19</sup> Values of  $P < .05$  were considered significant.

## RESULTS

### Background of Aneurysms

Among the 396 patients who underwent neurointervention for cerebral aneurysms, 14 (3.5%) fulfilled the diagnostic criteria for CIE. Of the 420 aneurysms, 417 (99%) were unruptured cerebral aneurysms, including 5 (1.2%) dissecting aneurysms. The remaining 3 (0.7%) were ruptured extracranial cerebral aneurysms, 2 of which caused epistaxis and 1 that caused otorrhagia.

### Baseline Clinical Characteristics

The baseline clinical characteristics of patients are shown in Table 1. No significant differences between groups were seen with respect to age, sex, body mass index, smoking or drinking history, or allergies. In terms of medical history, no significant difference was observed between groups in hypertension,

diabetes mellitus, hyperlipidemia, prior stroke, or renal dysfunction. Compared with the non-CIE group, the CIE group showed a significantly higher rate of hemodialysis ( $P = .022$ ).

### Anatomic and Procedural Characteristics

No significant differences were found between groups for aneurysm characteristics, including aneurysm size, neck size, aneurysm volume, aneurysm location, access site, or size of catheter used for angiography (Online Supplemental Data). The rate of retreatment for previously treated aneurysms was significantly higher in the CIE group than in the non-CIE group ( $P = .017$ ).

Distributions of locations of the guiding catheter used for angiography in the CIE and non-CIE groups were 0 (0%) and 3 (0.8%) for the common carotid artery, 8 (100%) and 325 (87%) for the ICA C1 segment, 0 (0%) and 8 (2.1%) for the VA V1 segment, and 0 (0%) and 37 (9.9%) for the VA V2 segment, respectively. Distributions of locations of the intermediate catheter used for angiography in the CIE and non-CIE groups were 1 (17%) and 13 (39%) for the ICA C2 segment, 1 (17%) and 9 (27%) for the ICA C3 segment, 3 (50%) and 3 (9.1%) for the ICA C4 segment, 1 (17%) and 0 (0%) for the horizontal (M1) segment of the MCA, 0 (0%) and 1 (3%) for the VA V1 segment, 0 (0%) and 3 (9.1%) for the VA V2 segment, 0 (0%) and 1 (3%) for the VA V3 segment, 0 (0%) and 2 (6.1%) for the VA V4 segment, and 0 (0%) and 1 (3%) for the basilar artery, respectively. The rate of intradural placement of catheters used for angiography was significantly higher in the CIE group than in the non-CIE group ( $P < .001$ ).

No significant differences between the CIE and non-CIE groups were seen regarding procedure time, fluoroscopy duration, total volume of contrast medium, embolization result, or volume embolization ratio. On the other hand, compared with the non-CIE group, the CIE group significantly used nonionic monomeric contrast medium more frequently, underwent a higher proportion of flow diverter treatment, and required a longer hospital stay ( $P = .002$ ,  $P = .026$ , and  $P = .028$ , respectively) (Online Supplemental Data).

### Contrast-Induced Encephalopathy

Of the 14 patients who developed CIE, the median age was 73 years (interquartile range, 66–79 years), with a predominance of female patients ( $n = 8$ , 57%). All patients presenting with CIE showed normal laboratory values with the exception of 2 patients undergoing hemodialysis with severely impaired renal function. The location of the aneurysm was the ICA in 10 patients (71%), the MCA in 3 (21%), and the anterior cerebral artery in 1 (7.1%).

**Table 2: Multivariate logistic regression analysis and stepwise selection of risk factors for CIE**

| Parameter                                                               | OR (95% CI)                    | P Value           |
|-------------------------------------------------------------------------|--------------------------------|-------------------|
| Variables with $P < .05$ or previously reported as risk factors for CIE |                                |                   |
| Intradural placement of catheter for angiography                        | 50.2 (7.25–347)                | $<.001^a$         |
| Previously treated aneurysm                                             | 7.46 (1.47–37.9)               | .015 <sup>a</sup> |
| Prior stroke                                                            | 4.30 (0.756–24.5)              | .1                |
| Hemodialysis                                                            | 7.91 (0.504–124)               | .14               |
| Hypertension                                                            | 0.985 (0.233–4.17)             | .98               |
| Diabetes mellitus                                                       | 1.64 (0.241–11.1)              | .62               |
| Posterior circulation aneurysm                                          | $7.52 \times 10^{-10}$ (0–Inf) | .995              |
| Total contrast medium volume (mL)                                       | 0.997 (0.988–1.01)             | .58               |
| Nonionic contrast medium                                                | $7.85 \times 10^7$ (0–Inf)     | .99               |
| Endovascular technique (flow diversion)                                 | 7.15 (0.642–79.7)              | .11               |
| After the stepwise selection using the $P$ value (until $P < .05$ )     |                                |                   |
| Intradural placement of catheter for angiography                        | 40.4 (8.63–189)                | $<.001^a$         |
| Previously treated aneurysm                                             | 8.20 (2.26–29.6)               | .001 <sup>a</sup> |

**Note:**—Inf indicates infinitesimal or infinity.

<sup>a</sup>  $P < .05$ .

In addition, 5 (36%) of the 14 aneurysms had been previously treated. The catheter used for angiography was a Sofia in 4 patients (29%), an Optimo in 4 patients (29%), an Asahi Fubuki in 3 patients (21%), and Navien, Axcelside, and Destination in 1 patient each (7.1%) (Online Supplemental Data).

The location of the catheter used for angiography was the ICA C1 in 8 patients (57%), ICA C2 in 1 (7.1%), ICA C3 in 1 (7.1%), ICA C4 in 3 (21%), and MCA M1 in 1 (7.1%), with the left side predominating (64%), and 4 catheters (29%) were placed intradurally. The contrast medium used was iohexol (Omnipaque 300) in 13 cases and iopamidol (Iopamiron 370; Bayer) in 1 case. The median volume of contrast used was 173 mL (interquartile range, 131–208 mL). There was a higher percentage of hypertension in 10 patients (71%), prior stroke in 4 (29%), diabetes mellitus in 3 (21%), and hemodialysis in 2 (14%) patients with CIE. Most patients presented with a disturbance of consciousness (12/14; 86%) and cortical symptoms (13/14; 93%), including hemiparesis, aphasia, agnosia, hemispatial neglect, and cortical blindness. The most frequent cortical symptoms were hemiparesis (10/14; 71%) and aphasia (6/14; 43%).

Imaging findings were abnormal in 8 (89%) of 9 patients on CT and 5 (38%) of 13 patients on MR imaging. Treatment for CIE mainly comprised anticonvulsants and adequate hydration, and patients with end-stage renal failure were treated with hemodialysis to remove contrast medium from the body. The median time from neurointervention to CIE onset was 1 hour (interquartile range, 0.5–1 hour), and the median time from CIE onset to recovery was 4 days (interquartile range, 2–5.75 days). One month after neurointervention, 12 (86%) of the 14 patients showed normalization of mRS compared with pre-neurointervention, while 1 patient showed mild sequelae (mRS 1) and 1 patient showed severe sequelae (mRS 5) due to CIE.

### Risk Factors for CIE

Intradural placement of a catheter for angiography (OR = 40.4; 95% CI, 8.63–189) and a previously treated aneurysm (OR = 8.20; 95% CI, 2.26–29.6) were identified as independent predictors of

CIE by multivariate logistic regression analysis and stepwise selection (Table 2).

### Illustrative Case

A 70-year-old man with hemodialysis due to end-stage renal failure was scheduled for coil embolization of a right MCA aneurysm with a maximum diameter of 9 mm (Fig 1A). The aneurysm was treated by guiding a 6F Sofia catheter as an intermediate catheter into the right MCA M1; then coil embolization was performed using a stent-assisted technique (Fig 1B). Contrast medium was injected through the intermediate catheter to examine the embolization status.

Coil embolization achieved complete occlusion, with a volume embolization ratio of 30% (Fig 1C). A total of 120 mL

of iohexol (Omnipaque 300) was used. Half an hour after completion of treatment, the patient presented progressively with stupor, disorientation, and severe left upper- and lower-extremity paralysis. MR imaging found no obvious ischemic or hemorrhagic lesions (Fig 1D, -E), and MR angiography did not detect any arterial occlusion, dissection, or vasospasm. Noncontrast CT showed enhancement in the right cerebral cortex and subcortex (Fig 1F).

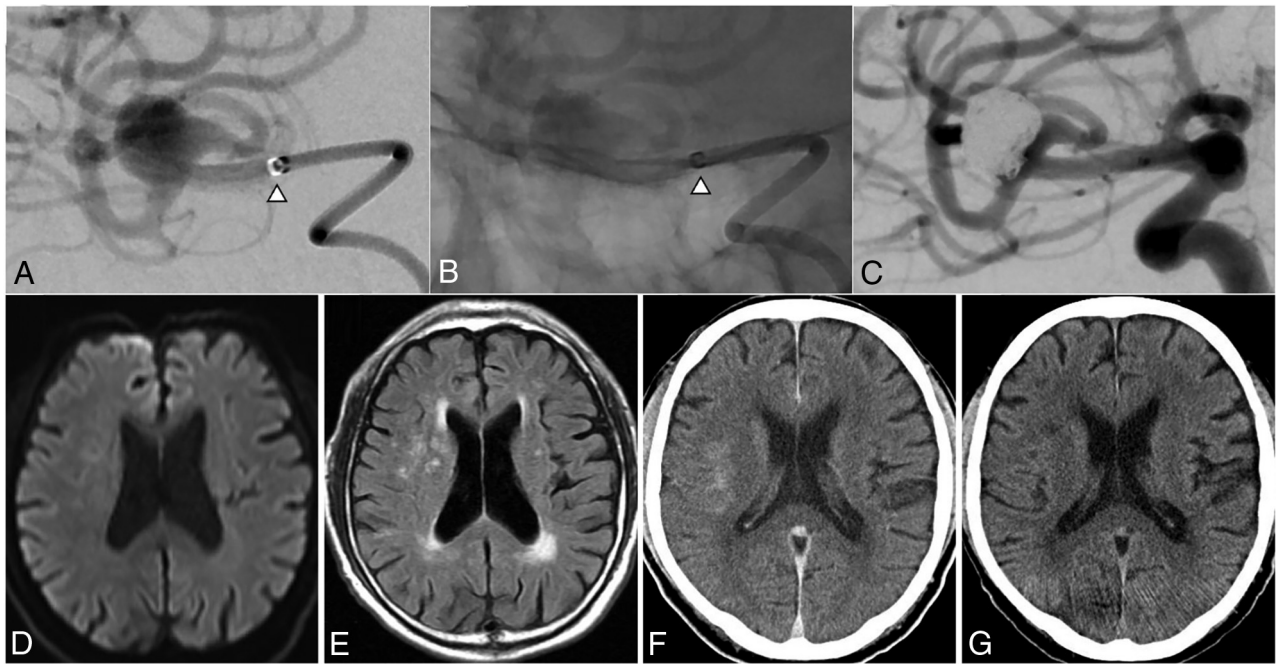
On the basis of the above, CIE was diagnosed and the patient was administered anticonvulsant and underwent emergency hemodialysis to drain the contrast medium. After hemodialysis, disturbance of consciousness and left hemiparesis gradually improved. Noncontrast CT 5 days after treatment demonstrated disappearance of contrast-induced enhancement from the right cerebral cortex and subcortex (Fig 1G). Six days after coil embolization, neurologic abnormalities had completely resolved (mRS 0).

### DISCUSSION

In the present study, contrast injection from an intradural artery and retreatment of a previously treated aneurysm were identified as risk factors for CIE by multivariate analysis.

Contrast medium can cross the BBB and leak into brain tissue, resulting in neurotoxicity.<sup>10–14,20</sup> Uchiyama et al<sup>15</sup> proposed that CIE might be caused by temporary disruption of the BBB as evidenced by elevated concentrations of iodine levels in the CSF of patients with CIE. Recently, large-bore, flexible intermediate catheters such as the Navien and Sofia have become available for neurointervention. Guiding the intermediate catheter into an intradural artery is expected to improve maneuverability of the microcatheter.<sup>16</sup> However, the present study demonstrated that direct contrast injection from an intermediate catheter guided into an intradural artery might raise the risk of CIE. Diamandis et al<sup>21</sup> experienced CIE after multiple angiograms from an intermediate catheter (AXS Catalyst6; Stryker Neurovascular) placed in an intradural artery during flow-diverter treatment of an aneurysm of the left ICA C4 segment. Close attention may need to be





**FIGURE.** A 70-year-old man undergoing hemodialysis due to end-stage renal failure underwent coil embolization for a right MCA aneurysm with a maximum diameter of 9 mm. Right middle cerebral arteriography (A) and fluoroscopic view (B) show contrast of the right MCA aneurysm from the 6F Sofia catheter, an intermediate catheter guided to the right MCA horizontal segment. Right middle cerebral arteriography (C) shows complete embolization of aneurysm achieved by a stent-assisted technique. Half an hour after completion of the treatment, the patient's condition with stupor, disorientation, and severe left upper and lower extremity paralysis progressively deteriorated. No obvious ischemic and hemorrhagic lesions were seen on MR imaging (D, DWI; E, FLAIR sequence). MRA did not detect arterial occlusion, dissection, or vasospasm. Noncontrast CT (F) shows enhancement due to leakage of contrast medium into the right cerebral cortex and subcortex. After hemodialysis, disturbance of consciousness and left hemiparesis gradually improved. Noncontrast CT (G) 5 days after treatment demonstrates that the contrast-induced enhancement in the right cerebral cortex and subcortex had disappeared. The arrowhead indicates the tip of Sofia catheter.

paid to the location of the intermediate catheter for angiography to avoid CIE.

The present study also revealed retreatment of a previously treated aneurysm as a risk factor for CIE. Prior stroke may pose a risk factor for CIE due to disruption of the BBB in the same or adjacent vascular territories,<sup>4</sup> resulting in tissue damage and cerebral edema via leakage of contrast medium into a wide range of cerebral parenchyma.<sup>22</sup> Recent SAH might compromise the BBB via endothelial cell damage.<sup>6,23</sup> In the present study, 3 of the 4 patients with recurrent aneurysms who developed CIE had previously undergone treatment of a ruptured aneurysm (2 after coil embolization, 1 after clipping). In addition, the remaining case involved a recurrent aneurysm after coil embolization of an unruptured cerebral aneurysm, with complications of cerebral infarction at the time of initial treatment. These results suggest previous SAH or cerebral infarction as a potential cause of damage to the BBB, allowing direct neurotoxicity and CIE via leakage of contrast medium into the cerebral parenchyma. Predisposing surgical insults of craniotomy or neuroendovascular surgery including brain injury, SAH, and cerebral infarction might thus represent key risk factors for CIE, especially when repeating treatment for recurrent aneurysms. This issue warrants investigation in the future.

In addition to prior stroke, factors of renal dysfunction, hemodialysis, hypertension, diabetes mellitus, posterior circulation aneurysms, and a higher dosage of contrast medium might

contribute to the risk of CIE.<sup>1-4,6,7,10</sup> Unexpectedly, multivariate analysis in the present study failed to identify any of those factors as significant, along with the class of contrast medium, in comparisons between patients with and without CIE. Some researchers have found no relationship between contrast volume and CIE.<sup>3,24</sup> Lantos<sup>24</sup> reported CIE in 4 patients who received <40 mL of contrast medium (ionic and nonionic). Unlike the field of interventional cardiology, repeat injection of contrast medium into a single intracranial artery during neurointervention, regardless of the total volume of contrast medium injected, could cause local increases in intravascular pressure and contrast concentration, resulting in transient disruption of the BBB and subsequent CIE. Furthermore, CIE can develop regardless of the type of contrast medium. Animal studies have demonstrated that iodixanol and iopamidol can cross the BBB at comparable rates.<sup>25</sup> CIE occurred even with the use of iodixanol, which shows the same osmotic pressure as physiologic saline.<sup>26</sup>

Renal dysfunction may decrease contrast clearance, which may, in turn, exacerbate the osmotic accumulation and neurotoxicity of contrast medium. Patients with renal dysfunction requiring hemodialysis should be carefully followed up for CIE.<sup>2</sup> Similarly, in the present study, hemodialysis was a significant risk factor for the development of CIE in univariate analysis after neurointervention. One of the 2 patients receiving hemodialysis had developed frequent generalized seizures. The day after the procedure, MR imaging showed no abnormal findings and

noncontrast CT demonstrated cortical and subcortical contrast enhancement throughout the left hemisphere, meeting the criteria for CIE. However, the delayed treatment of CIE using hemodialysis to remove contrast medium resulted in severe neurologic sequelae due to brain damage secondary to generalized seizures. As shown in the illustrative case, the other patient in whom CIE was suspected from the onset underwent hemodialysis to remove contrast medium immediately after onset, resulting in complete neurologic recovery. CIE that develops in patients with hemodialysis can be improved by rapid induction of hemodialysis to remove contrast medium from the body.<sup>2,27,28</sup>

Our study has several limitations. First, uniform diagnostic criteria for CIE are lacking. As a result, potential underdiagnosis of CIE in our study cohort could not be ruled out. However, patients with SAH were not included in the present study, and only patients with cerebral aneurysms without impaired consciousness were included, allowing more sensitive judgments regarding potential discrepancies between postoperative neurologic changes and imaging findings. These inclusion choices may have contributed to an improved diagnostic accuracy of CIE. Second, control and working-projection angiography from the guiding or intermediate catheter during neurointervention was performed by injecting contrast medium manually, rather than with an injector. Injection pressure varied individually, and the pressures used for injection of contrast medium in each operation were not precisely measured. Third, this study was performed exclusively on East Asian patients. Further validation studies are needed before our findings can be generalized to other ethnic groups. Finally, this study was conducted as a retrospective, single-center study of a moderate-sized cohort. The low incidence of CIE may have limited the statistical power.<sup>2-4,7</sup> Despite these limitations, the present study showed that injection of contrast from an intradural artery and retreatment of a previously treated aneurysm warrant careful follow-up for CIE.

## CONCLUSIONS

Contrast injection from an intradural artery and retreatment of recurrent aneurysms were the main risk factors for CIE. The location of the intermediate catheter for angiography may need to be considered to minimize the risk of developing CIE.

Disclosure forms provided by the authors are available with the full text and PDF of this article at [www.ajnr.org](http://www.ajnr.org).

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