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Case Report

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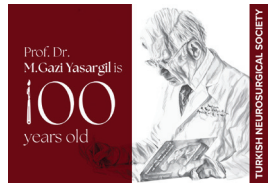

Strategies for Preventing Delayed Leukoencephalopathy: A Case Report on the Efficacy of Separate-Axis Catheter Angiography in Coil Embolization

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ABSTRACT

In recent years, there have been multiple reports of delayed leukoencephalopathy (DL) occurring after endovascular treatment for cerebral vascular lesions, with polyvinylpyrrolidone (PVP) identified as a contributing factor. Herein, we present a case of DL developing after coil embolization for an unruptured aneurysm, and following the implementation of measures, we subsequently performed repeat endovascular treatment. A 65-year-old female with a history of bronchial asthma underwent coil embolization using the double catheter technique for the right internal carotid artery-anterior choroidal artery aneurysm. One month postoperatively, she developed DL accompanied by left hemiparesis, which improved with steroid pulse therapy. Investigation into the cause of DL revealed elevated anti-nuclear antibodies, leading to a diagnosis of Sjögren's syndrome and Hashimoto's disease. Additionally, metal patch testing yielded negative results. At the 1-year follow-up, an enlargement of a known basilar top aneurysm prompted the decision to perform stent-assisted coil embolization. To prevent peripheral scattering of PVP during the procedure, the decision was made to perform all imaging along a different axis guided by a catheter. Despite complications such as stent thrombosis, with no reduction in contrast agent usage, imaging frequency, or surgical time compared to the initial treatment, DL did not manifest in the postoperative course. For the prevention of DL after endovascular treatment, from a procedural aspect, it is important to reduce the peripheral dispersal of PVP that occurs during treatment. Performing angiography during treatment from a separate axis catheter may be a useful strategy in preventing the development of DL.

KEYWORDS: Endovascular treatment, Delayed leukoencephalopathy, Polyvinylpyrrolidone, Separate-axis catheter, Complication

ABBREVIATIONS: DL: Delayed leukoencephalopathy, **PVP:** Polyvinylpyrrolidone, **FLAIR:** Fluid attenuated inversion recovery, **DWI:** Diffusion-weighted imaging, **CIE:** Contrast-induced encephalopathy, **GC:** Guiding catheter, **ICA:** Internal carotid artery, **MRA:** Magnetic resonance angiography, **MRI:** Magnetic resonance imaging, **AchA:** anterior choroidal artery, **BA:** basilar artery, **PGLA:** polyglycolic-polylactic acid, **VA:** vertebral artery

INTRODUCTION

Endovascular interventions for cerebral aneurysms, such as coil embolization and flow diverter placement, are widely used in minimally invasive treatments. Although complications, such as aneurysm perforation and thromboembolic events, are well-known, delayed leukoencephalopathy (DL) has recently emerged as a rare complication. Polyvinylpyrrolidone (PVP), one of the hydrophilic coating materials on catheters used during procedures, has been highlighted as

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a potential cause (3,5,7,8,12,13). This report presents a case of DL that occurred after coil embolization of an unruptured internal carotid artery (ICA) aneurysm, necessitating a second endovascular intervention.

CASE REPORT

A 65-year-old woman presented with an enlargement of a right ICA aneurysm. She had a medical history of bronchial asthma and lipid disorders. Magnetic resonance angiography (MRA) revealed a 7-mm aneurysm at the ICA-anterior choroidal artery (AchA) bifurcation and a 5-mm aneurysm at the top of the basilar artery (BA) (Figure 1A, B). The first treatment involved a double-catheter technique that preserved the AchA while achieving complete occlusion, and the postoperative course was uneventful (Figure 2). The procedure lasted for 2 h 33 min, with 13 imaging sessions and 151 mL of the contrast agent used. One week after discharge, she developed a slight fever for 7 days. Approximately 1 month postoperatively, she developed left hemiparesis, with a 4/5 muscle strength reduction on manual muscle testing. MRI FLAIR (magnetic resonance imaging fluid attenuated inversion recovery) of the head revealed multiple white matter lesions in the right middle cerebral and bilateral anterior cerebral artery regions (Figure 3A, B). Contrast-enhanced MRI T1 images revealed multiple small circular lesions within the white matter lesions, showing contrast enhancement (Figure 3C, D). DL due to a PVP embolism was suspected, and steroid pulse therapy (methylprednisolone, intravenous administration, at a dose of 1000 mg for 3 consecutive days) was initiated. The patient showed improvement the following day, with complete resolution of symptoms after 1 week. The imaging findings showed gradual improvement, and progressive regression of the white matter lesions was observed on FLAIR images acquired at 3 and 6 months after onset (Figure 3E, F). Despite a favorable course, MRA performed 1 year postoperatively showed enlargement of a known BA aneurysm (Figure 1C, D), leading to the decision to proceed with coil embolization.

Blood Tests and Other Examinations

At the time of DL onset, cerebrospinal fluid analysis was negative. Elevated anti-nuclear antibodies (≥ 2560) and the presence of anti-SS-A(Ro) antibody (40.9 U/mL) in the blood indicated a diagnosis of Sjögren's syndrome, while the presence of thyroid peroxidase antibody (281.0 IU/mL) and thyroglobulin antibody (331.0 IU/mL) indicated a diagnosis of Hashimoto's disease. Dermatology-conducted metal patch tests were negative.

Clinical Course

The second treatment targeted a wide-neck BA aneurysm that required coil embolization with stent assist (Figure 4A). To prevent peripheral scattering of the PVP during the procedure, all imaging was performed along a different axis, guided by a catheter. We chose the Neuroform Atlas stent (Stryker Neuroendovascular, Fremont, CA, USA), which can be deployed without unsheathing. The treatment was performed under general anesthesia, with a 9-Fr Branchor (Asahi Intecc, Aichi,

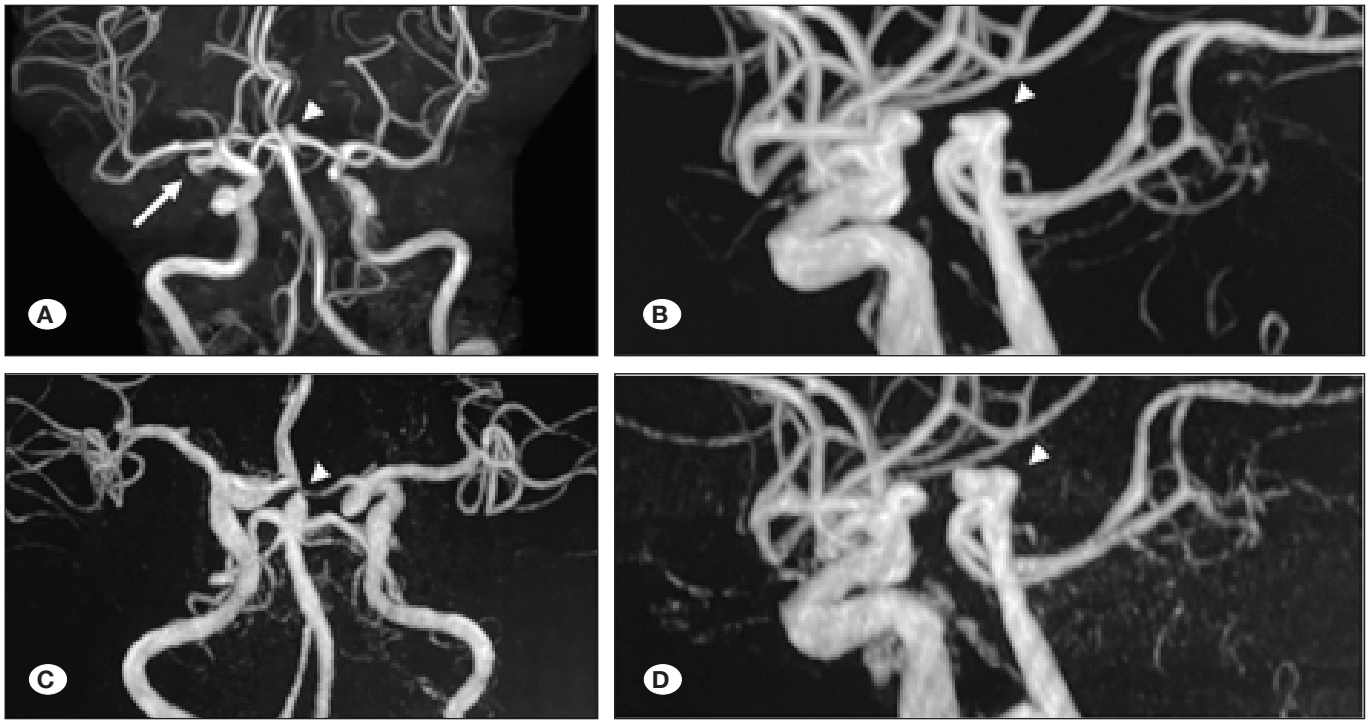

Figure 1: A, B) Initial imaging from MRA provides both anteroposterior and lateral views. It reveals evidence suggestive of an aneurysm at the bifurcation of the right IC-AchA (arrow) and at the top of the basilar artery (arrowheads). **C, D)** An MRA image obtained 1 year after coil embolization of the right IC-AchA aneurysm. Enlargement of the basilar top aneurysm is noted when compared with the initial MRA (arrowheads). **IC-AchA:** Internal carotid artery-anterior choroidal artery, **MRA:** Magnetic resonance angiography.

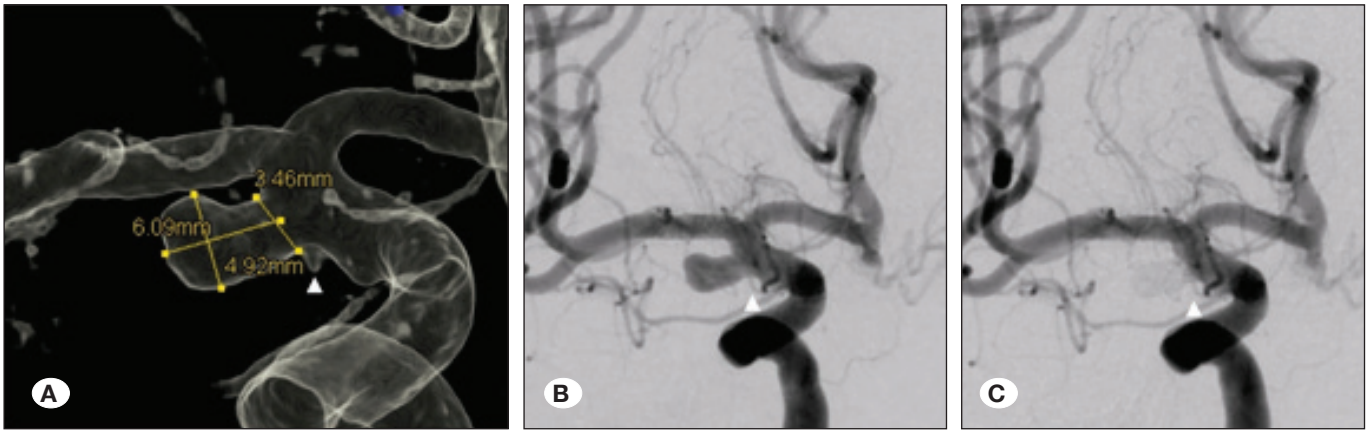

Figure 2: A) In the translucent image of 3D rotation angiography, the right IC-AchA bifurcation aneurysm is depicted. The aneurysm is wide-necked, with a maximum diameter of 6 mm, and the origin of the anterior choroidal artery can be confirmed at the neck of the aneurysm (arrowhead). **B, C)** Preoperative and postoperative frontal working angle images. Preservation of the anterior choroidal artery (arrow) resulted in a Raymond–Roy class II. **IC-AchA:** Internal carotid artery-anterior choroidal artery.

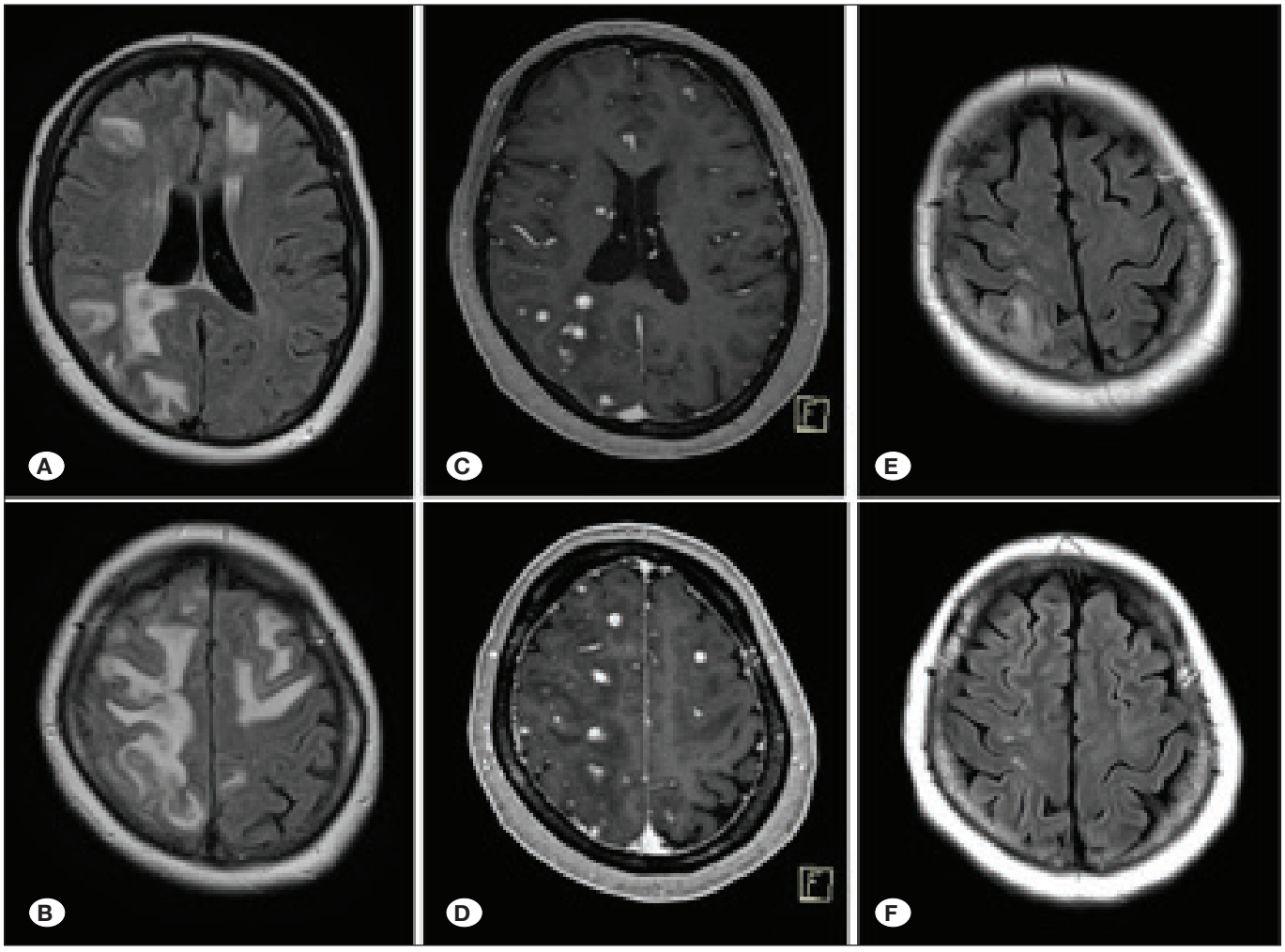

Figure 3: A, B) FLAIR images show multiple white matter lesions predominantly located in the right cerebral hemisphere. **C, D)** Contrast-enhanced MRI T1 images reveal multiple small lesions with oval shapes within the white matter lesions, showing contrast enhancement. **E, F)** FLAIR images acquired 3 months **(E)** and 6 months **(F)** after DL onset. Residual white matter lesions in the right frontal and parietal lobes also disappeared. **DL:** Delayed leukoencephalopathy, **FLAIR:** Fluid attenuated inversion recovery, **MRI:** Magnetic resonance imaging.

Japan) introduced into the left subclavian artery and a 125-cm 6-Fr Sofia select (MicroVention TERUMO, Aliso Viejo, CA, USA) guided to the mid-BA through left vertebral artery (VA) access. A diagnostic catheter was placed in the contralateral VA for imaging. We guided the Excelsior SL-10 (Stryker) into the left posterior cerebral artery for stent placement and inserted the Phenom17 (Medtronic, Minneapolis, MN, USA) into the aneurysm. After fully deploying the stent, we inserted coils through the jail catheter to complete embolization. The stent thrombosis was observed on postoperative imaging, requiring intra-arterial infusion therapy with Ozagrel sodium (AK Scientific Inc., CA, U.S.A.) and additional administration of Prasugrel (Figure 4B). On postoperative MRI, no diffusion-weighted imaging (DWI)-positive findings were observed, and the patient had a good course and was discharged without the development of any neurological sequelae. The surgical duration for the second treatment was 4 h 40 min, with 14 imaging sessions and 187 mL of contrast agent used. Subsequently, the patient underwent MRI follow-up at the outpatient clinic at 1, 3, and 6 months postoperatively, and no signs of DL were observed.

Written informed consent was obtained from the patient and her family for publishing this clinical report. Approval from the hospital's ethics committee was secured for the intra-arterial infusion therapy of Ozagrel sodium.

DISCUSSION

The estimated incidence of DL is 0.14–2.3%, with a higher prevalence among middle-aged women. The onset of DL has been reported to range from 2 weeks to 14 months post-treatment; however, most cases manifest symptoms within the first month after the procedure (5,7,8,9,13). The majority of symptomatic DL cases occur following aneurysm treatment procedures, while occurrence after diagnostic catheterization is considered extremely rare (8). Steroid pulse therapy has been found to be a highly effective treatment, typically resulting in a positive prognosis with considerable resolution of neurological symptoms as well as enhancement of MRI findings (3,5,9,12). However, clinical and neuroradiological relapses have been reported during corticosteroid tapering or discontinuation, with some patients exhibiting steroid dependence. Furthermore, caution is warranted in cases with persistent imaging abnormalities (8,13). The involvement of type IV allergies in the onset of DL has been considered, and it is possible that multiple factors, including patient background-related risk factors, in addition to procedural factors, are involved (5). Our patient had a history of bronchial asthma, and after the onset, further examination led to the diagnosis of Sjögren's syndrome and Hashimoto's disease. Although there are no comprehensive reports to date, based on the reviewed literature, cases of DL in patients with a history of allergic or autoimmune diseases have been sporadically observed (4,12). Further detailed investigations are necessary regarding the risk of DL.

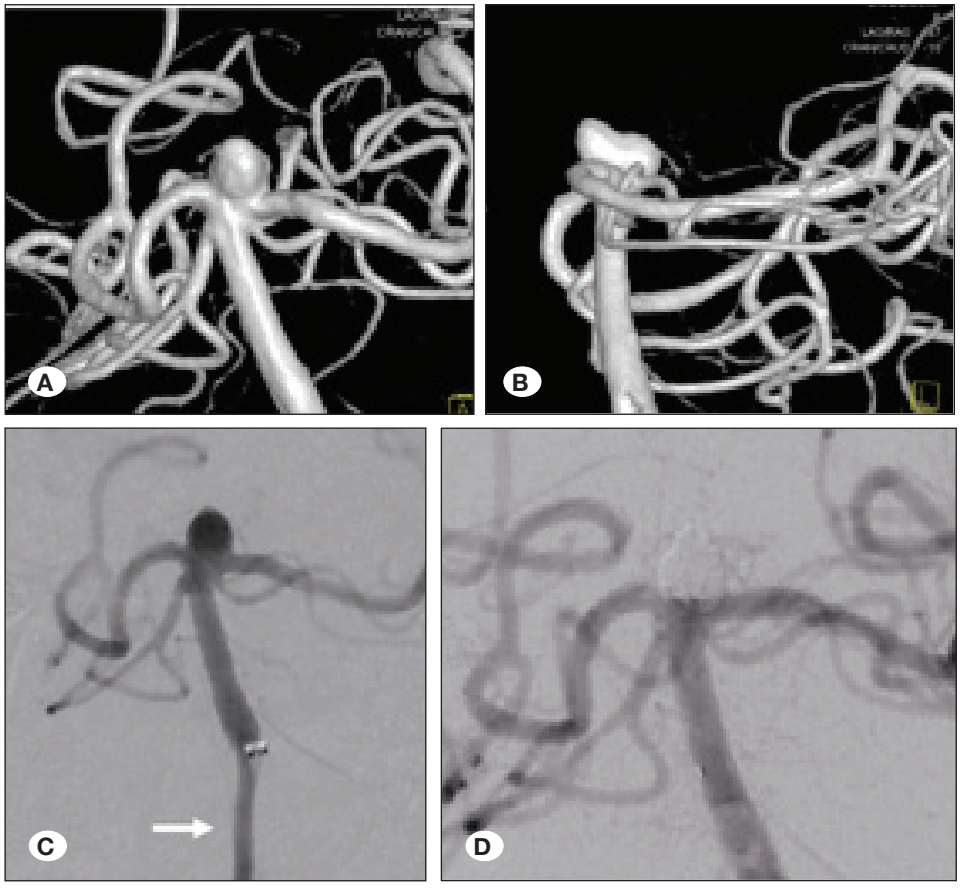

Figure 4: A, B) 3DRA images demonstrate the working angle of the basilar top artery aneurysm. It is a wide-necked aneurysm that is slightly saddle-shaped, tending toward the left posterior cerebral artery side, and exhibits a bilobed shape in the anterior-posterior direction. **C, D)** DSA shows pre and postoperative working angles of anteroposterior view. A distal access catheter is introduced into the proximal part of the basilar artery through the VA (arrowhead), and intraoperative imaging is performed from the right VA (arrow). **D:** Postoperative DSA demonstrates the final view of the stent-assisted coil embolization, achieving Raymond–Roy class I. **3DRA:** 3D rotation angiography, **VA:** vertebral artery, **DSA:** digital subtraction angiography

Biopsy has identified PVP, a hydrophilic coating material used on endovascular catheters as a causative agent of granuloma formation leading to DL (6,8). Additionally, similar delayed-type allergic reactions have been reported in cases using polyglycolic-polylactic acid (PGLA)-coated coils (4), suggesting that PGLA may be implicated in some DL cases (15). In this case, DL was strongly suspected based on the patient's postoperative course and imaging findings. Rapid resolution of the lesions with medical treatment obviated the need for biopsy of the contrast-enhancing lesions, and DL was diagnosed based on the clinical course.

Differential diagnoses of post-endovascular white matter lesions include contrast-induced encephalopathy (CIE) and metal allergies. CIE occurs in 0.38–1.7% of diagnostic imaging and endovascular procedures, presenting with both localized and general symptoms (6,15). These side effects stem from direct neurotoxicity due to blood-brain barrier disruption and endothelial dysfunction triggered by iodinated contrast agents and are characterized as non-immune-mediated allergic reactions (6). It manifests within 48–72 hours and typically improves within this timeframe (6). No clear correlation exists between the dosage of contrast agents and neurological outcomes. Metal allergies related to endovascular treatment are extremely rare; however, nickel, a common allergen more prevalent in women, is found in flow diverters and intracranial stents (1,9,14). Average serum nickel ion levels typically peak approximately 1 month after the placement of nickel-containing devices in the vasculature, which could potentially be relate to the onset timing of reactions (11). However, positive results from skin patch tests do not necessarily correlate with clinical outcomes. One small study of seven patients with nickel allergy showed no complications after treatment with nickel-containing devices (2).

The mechanism of PVP embolism is linked to procedural factors and techniques. The number of catheters, contrast agent volume, and fluoroscopy time are associated with DL occurrence (5). PVP detachment, leading to embolism, can result from contact or friction between catheters within the guiding catheter (GC) or frequent passage of devices like coils. Therefore, it is advisable to avoid tight-fitting catheter systems (7,10). We speculate that performing angiography directly from the GC contributes to scattering detached PVP to the periphery, making it a primary factor in DL occurrence. As increased imaging frequency from the GC is associated with higher contrast agent volumes and prolonged fluoroscopy times, we prioritized imaging from a separate axis from the GC in the second treatment to prevent DL. Due to the occurrence of intraoperative thrombosis, we could not reduce procedure time, imaging frequency, or contrast agent volume compared to the initial treatment. However, the absence of DL suggests that imaging from a separate axis may effectively prevents DL.

In this case, the first and second treatment sites were different, but both were treated with an adjunctive technique using a single GC system. The number of imaging sessions, amount of contrast media used, and treatment time were comparable. Previous reports have shown that treatment in the anterior circulation has been documented in some cases, but treatment in the posterior circulation is also common, and the frequency should not differ according to the site (5,8,13). Given that the same patients were treated under generally similar conditions, we believe that imaging from a different axis played a significant role.

CONCLUSION

This report presents a case of DL that occurred after coil embolization of an unruptured cerebral aneurysm, which required a second coil embolization procedure. DL development involves procedural and patient-specific factors, and in the procedural aspect, imaging from a different axis rather than from the guiding catheter can help prevent PVP dispersal and may contribute to DL prevention.

Declarations

Funding: No external funding was received for this study.

Availability of data and materials: The datasets generated and/or analyzed during the current study are available from the corresponding author by reasonable request.

Disclosure: The authors declare no competing interests.

AUTHORSHIP CONTRIBUTION

Study conception and design: NT
Data collection: NT, RF
Analysis and interpretation of results: NT
Draft manuscript preparation: NT
Critical revision of the article: SM, TS
Other (study supervision, fundings, materials, etc...): TS
All authors (NT, RF, SM, TS) reviewed the results and approved the final version of the manuscript.

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