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Clinical Article

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J Korean Neurosurg Soc 43 : 275-280, 2008 10.3340/jkns.2008.43.6.275

Thromboembolic Events after Coil Embolization of Cerebral Aneurysms : Prospective Study with Diffusion-Weighted Magnetic Resonance Imaging Follow-up

Objective : In order to assess the incidence of thromboembolic events and their clinical presentations, the present study prospectively examined routine brain magnetic resonance images (MRI) taken within 48 hours after a coil embolization of cerebral aneurysms.

Methods : From January 2006 to January 2008, 163 cases of coil embolization of cerebral aneurysm were performed along with routine brain MRI, including diffusion-weighted magnetic resonance (DW-MR) imaging, within 48 hours after the embolization of the aneurysm to detect the silent thromboembolic events regardless of any neurological changes. If any neurological changes were observed, an immediate brain MRI follow-up was performed. High-signal-intensity lesions in the DW-MR images were considered as acute thromboembolic events and the number and locations of the lesions were also recorded.

Results : Among the 163 coil embolization cases, 98 (60.1%) showed high-signal intensities in the DW-MR imaging follow-up, 66 cases (67.0%) involved the eloquent area and only 6 cases (6.0%) showed focal neurological symptoms correlated to the DW-MR findings. The incidence of DW-MR lesions was higher in older patients ($\geq$60 yrs) when compared to younger patients ($<$60 yrs) (p=0.002, odd' s ratio=1.043). The older patients also showed a higher incidence of abnormal DW-MR signals in aneurysm-unrelated lesions (p=0.0003, odd' s ratio=5.078).

Conclusion : The incidence of symptomatic thromboembolic attacks after coil embolization of the cerebral aneurysm was found to be lower than that reported in previous studies. While DW-MR imaging revealed a higher number of thromboembolic events, most of these were clinically silent and transient and showed favorable clinical outcomes. However, the incidence of DW-MR abnormalities was higher in older patients, along with unpredictable thromboembolic events on DW-MR images. Thus, in order to provide adequate and timely treatment and to minimize neurological sequelae, a routine DW-MR follow-up after coil embolization of cerebral aneurysms might be helpful, especially in older patients.

KEY WORDS : Cerebral aneurysm · Embolization · Thromboembolism · Diffusion magnetic resonance imaging.

INTRODUCTION

Following U.S. Food and Drug Administration approval of the Guglielmi detachable coil in 1995, coil embolization of cerebral aneurysm was introduced as an alternative treatment method for cerebral aneurysms. Along with the rapid development of devices and procedural techniques for endovascular treatment, coil embolization is also being increasingly used for the treatment of intracranial aneurysms. When compared to surgical clipping of an aneurysm sac, endovascular treatment is minimally invasive, as it does not require a craniotomy, brain dissection, or even general anesthesia. Other advantages of endovascular treatment include easy access to surgically difficult yet demanding areas, such as the basilar top, and the ability to visualize angiographically the patency of adjacent vessels during the procedure. It is also especially appropriate in the case of a poor medical condition, old age, refusal to undergo surgery, and a difficult anatomical position for a surgical approach[9,10]. Nonetheless, endovascular embolization is not without complications; ischemic lesions due to thrombosis or embolic phenomena are the most frequent complication, and the intra-procedural rupture of an aneurysm is not uncom-

• Received : March 14, 2008
• Accepted : June 13, 2008
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mon[3,4,6,8,11,14-16,18,19,22]. The reported rates of thromboembolic complications during a coil embolization vary widely, ranging from 2.5 to 28%, while the incidence of clinically silent infarcts demonstrated on diffusion-weighted magnetic resonance (DW-MR) imaging is as high as 60 to 80%[2,4-6,7,8,11-16,17,20,22,23]. Accordingly, this study prospectively checked routine DW-MR imaging within 48 hours after coil embolization of cerebral aneurysms to assess the incidence of thromboembolic events and their clinical presentation.

Table 1. Locations of aneurysms (n=166)

Anterior circulation (n=141)		Posterior circulation (n=25)	
Anterior communicating artery	50	Posterior cerebral artery	2
Middle cerebral artery	5	Vertebral artery	4
Posterior communicating artery	37	Top of basilar artery	10
Anterior choroidal artery	3	Anterior inferior cerebellar artery	3
Pericallosal artery	3	Superior cerebellar artery	6
Superior hypophyseal artery	1		
Cavernous internal carotid artery	11		
Paraclinoid Internal carotid artery	22		
Ophthalmic internal carotid artery	6		
Internal carotid Artery Bifurcation	3		

MATERIALS AND METHODS

Patient population

From January 2006 to January 2008, 166 aneurysms in 160 patients were enrolled (41 men, 119 women, mean age 57.9 years [range 27-83], including 94 ruptured aneurysms and 72 unruptured). As some patients underwent multiple procedures, the total number of embolization was counted as 163 cases. The locations of aneurysms are summarized in Table 1. The size of the aneurysm varied from 2 mm to 50 mm (mean : 12.6 mm). Before choosing the method to secure the cerebral aneurysm, the patient's age, medical condition, anatomical location of the aneurysm, and patient's preference were all taken into account.

The coil embolization procedure

Two experienced neuro-radiologists conducted the diagnostic selected angiography. The angiogram information included not only the morphological character of the aneurysm, but also the presence of any arterial vasospasm and other vascular findings, allowing a plan to be determined for obliterating the aneurysm. In most cases of ruptured aneurysms, the coil embolization was performed as soon as possible to avoid rebleeding of the aneurysm and start 3 "H" therapy (Hypertensive, Hypervolemic, Hemo-optimizational) early. The endovascular coil (GDC, Boston Scientific, Fremont, CA; Microplex, Microvention, Aliso Viejo, CA ; Trufil DCS Orbit, Cordis Neurovascular, Miami Lakes, FL) embolization procedure was performed in the neuro-angiography unit with no general anesthesia. However, if a patient was uncooperative due to neurological deterioration or irritability, propofol was used intravenously according to their body weight. After guiding catheter approach to lesion site, intravenous heparinization amounted 3,000 unit was performed.

In the case of technical difficulties due to a wide-neck aneurysm, the balloon remodeling system (Hyperform, Micro Therapeutic, Irvine, CA ; Hyperglide, Micro Therapeutic, Irvine, CA) or stent assisted system (Neuroform, Boston Scientific, Fremont, CA) was applied. After placement and before the electrolytic detachment of each coil, serial angiograms were obtained based on manual injection through the guide catheter to confirm proper position of the coil and patency of the adjacent arterial flow. The total procedure time for embolization was recorded based on minutes.

Following the coil embolization, an immediate brain computed tomography (CT) scan was conducted and the patients sent to the neurosurgical intensive care unit or neurosurgical ward, where they received neurosurgical care until being discharged.

Brain MRI evaluation

Within 48 hours after coil embolization, a brain MRI, including diffusion-weighted (DW) imaging, was routinely performed to check for any silent thromboembolic events, regardless of any neurological changes. Meanwhile, in the event of neurological changes, such as motor weakness or mental deterioration, an immediate follow-up brain MRI was performed. High-signal intensity lesions on the DW-MR images were considered acute thromboembolic events, and the number and locations of the lesions were recorded. Lesions located in the vascular territory downstream from the treated aneurysm were described as aneurysm-related lesions, whereas vascular distributions remote from the treated aneurysm were described as aneurysm-unrelated lesions.

Statistical analysis

The association of high-signal-intensity lesions on DW-MR with the patient's age, aneurysm size, and total procedure time was analyzed using a logistic regression (SPSS

12.0 windows). A p value of less than 0.05 was considered a statistically significant association.

RESULTS

Coil embolization procedure

Among the 163 coil embolization procedures, 5 patients (3.0%) experienced an intra-procedural rupture. Fortunately, all cases were immediately secured and no neurological deterioration was observed after the procedure. Meanwhile, 4 cases involved the use of a balloon-assisted technique, and an intra-luminal stent assisted technique was applied in 16 cases. The total procedure time varied from 22 minutes to 219 minutes (mean : 93.5 ± 12.7 minutes).

Magnetic resonance imaging findings

Among the 163 coil embolization procedures, 98 cases (60.1%) exhibited high-signal-intensity lesions in follow-up DW-MR imaging, 76 cases (77.5%) showed multiple lesions, ranging from 2 to 29 in number (mean : 4.35), while 22 cases (22.4%) showed single lesions. Among the 98 cases that showed abnormal-signal-intensity lesions on DW-MR, 66 cases (67.0%) involved the eloquent area (primary motor, sensory and visual cortices, thalamus, hypothalamus, brainstem, and cerebellar peduncle), while 32 cases did not (Fig. 1). Forty-two patients (42.8%) showed lesions only in aneurysm-related territories, while 56 patients (57.2%) also showed lesions in aneurysm-unrelated territories. The incidence of DW-MR lesions was higher in older patients (≥60 yrs) compared to younger patients (<60 yrs) (p=0.002, odd's ratio=1.043). The older patients also showed a higher incidence if abnormal DW-MR signals were in aneurysm-unrelated territories (p=0.0003, odd's ratio=5.078) (Fig. 2). The size of the aneurysm and procedure time did not show a significant association with the incidence of DW-MR lesions (p=0.68, 0.17).

Clinical presentation

Among the 98 cases with DW-MR positive findings, only 6 cases (6.0%) exhibited focal neurological symptoms correlated to the findings (Table 2). No focal neurological symptoms were observed for the cases with negative DW-MR findings. After conservative treatment, mainly hydration, 4 patients recovered completely within several days, while the other 2 patients showed some improvement, although the deficit remained. Thus, a persistent symptomatic thromboembolic event occurred in 2 cases among the 163 (1.2%).

Case illustrations of thromboembolic events

Case 1

A 55-year-old female presented an unruptured aneurysm in the cavernous portion of the right internal carotid artery on a diagnostic cerebral angiography (Fig. 3A). During 125 minutes, 17 coils were used for the embolization, resulting in the obliteration of the aneurysm sac (Fig. 3B). Although

Table 2. Six patients who showed neurological deficits after coil embolization (n=6)

Sex/Age (years)	Aneurysm presentation	Symptoms	Outcomes
F/58	Right ICA cavernous	Left arm monoparesis	Full recovery after 3 days
F/61	Left PCA P2 segment	Right hemiparesis	Improved on next day
F/58	Left P-coA (ruptured) Left SCA (unruptured)	Left arm monoparesis	Full recovery after 2 days
F/69	A-coA	Left leg monoplegia	Improved on next day
M/48	A-coA	Left leg monoparesis	Full recovery after a week
F/72	A-coA	Left arm monoparesis	Full recovery after 3 days

ICA : internal carotid artery, PCA : posterior cerebral artery, P-coA : posterior communicating artery, SCA : superior cerebellar artery, A-coA : anterior communicating artery

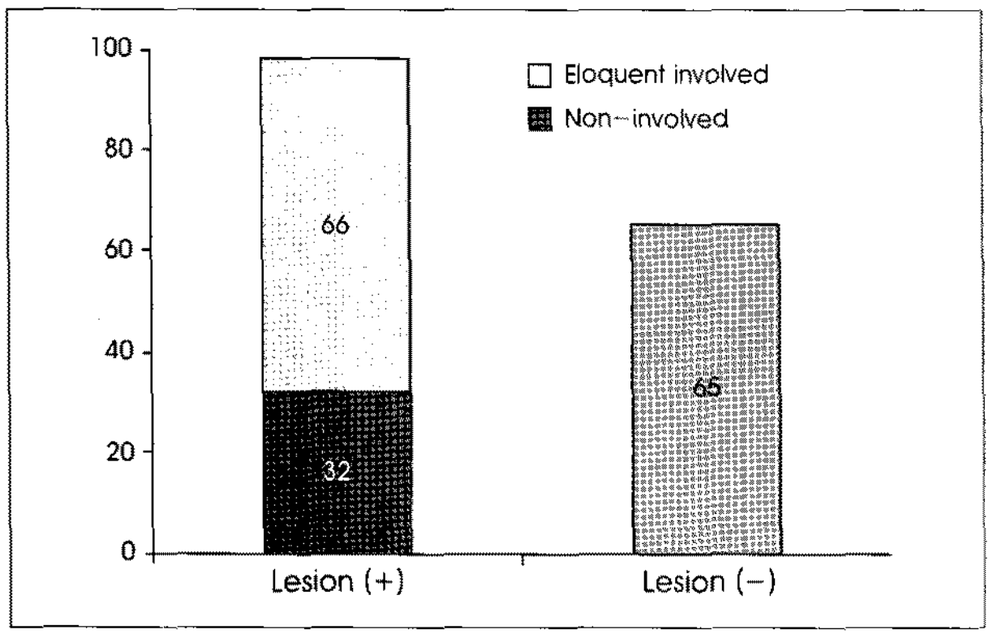

Fig. 1. Diffusion-weighted magnetic resonance (DW-MR) imaging follow-up after coil embolization.

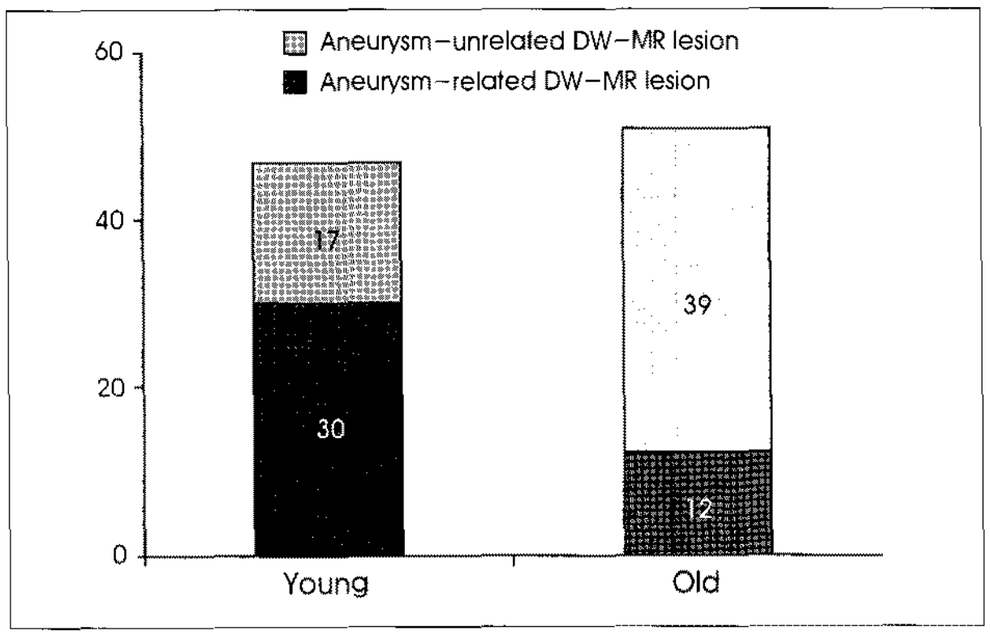

Fig. 2. Correlation between MR lesion territory and aneurysm location.

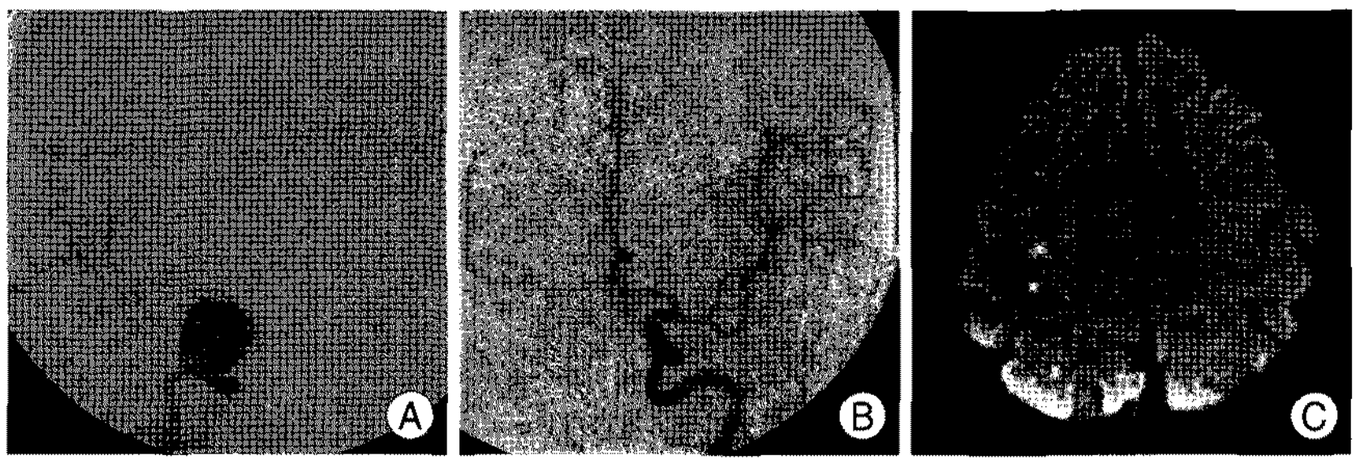

Fig. 3. A 55-year-old female (Case 1). A : Right internal carotid artery angiogram showing a giant aneurysm in cavernous portion of the internal cerebral artery. B : Post-embolization angiogram showing total obliteration of the aneurysm sac using internal trapping. C : DW-MR revealing multiple high-signal-intensity lesions in the motor cortex.

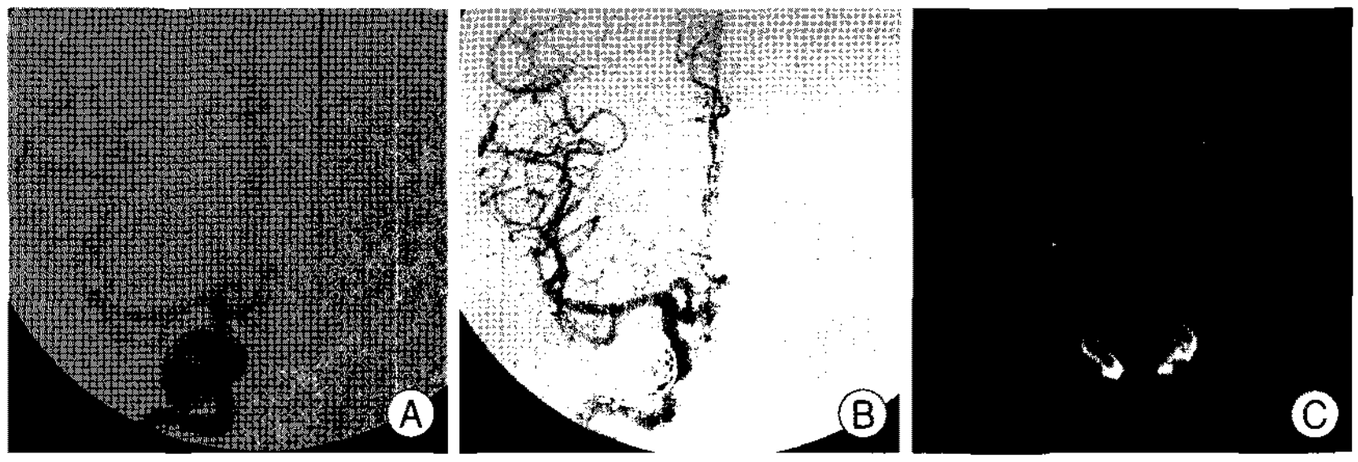

Fig. 4. A 58-year-old female (Case 2). A : Right internal carotid artery angiogram showing a giant aneurysm in cavernous portion of the internal carotid artery. B : Post-embolization angiogram showing obliteration of the aneurysm. C : DW-MR revealing high-signal-intensity lesions in the right precentral gyrus.

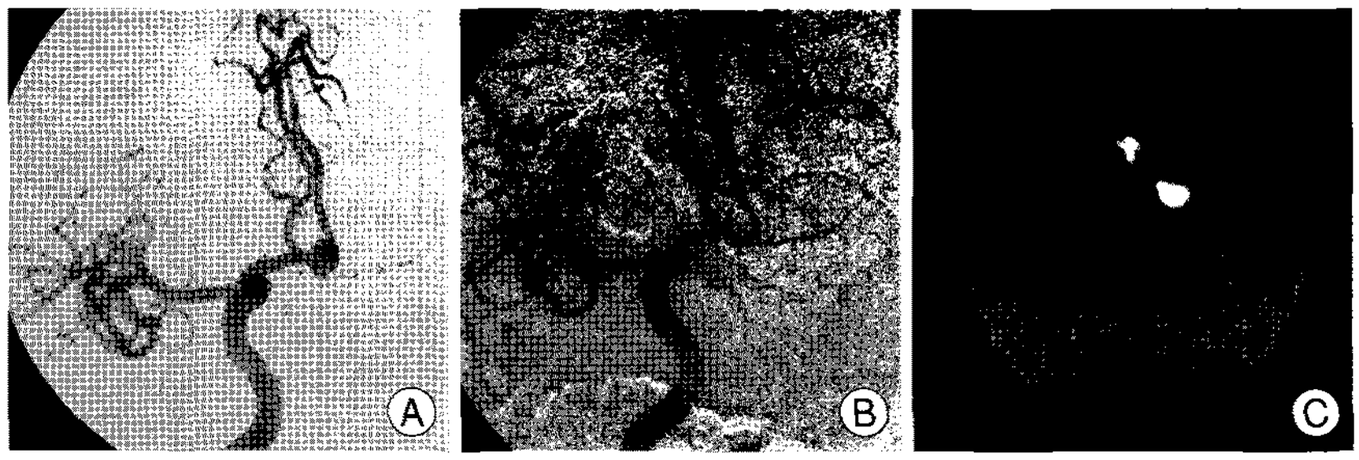

Fig. 5. A 32-year-old male (Case 3) A : Right internal carotid artery angiogram showing an aneurysm in the anterior communicating artery. B : Post-embolization angiogram showing obliteration of the aneurysm. C : DW-MR revealing high-signal-intensity lesion in the left basal ganglia.

the patient did not exhibit any neurological symptoms, a routine follow-up DW-MR image revealed 29 high-signal spots in the eloquent area (Fig. 3). The patient was discharged without any neurological symptoms.

Case 2

A 58-year-old female presented an unruptured aneurysm in the cavernous portion of the right internal carotid artery on an MRI. The patient did not suffer from any underlying disease, such as hypertension or diabetes mellitus, and no neurological symptoms were presented. A diagnostic cerebral angiogram confirmed a 20-mm aneurysm and excluded any additional cerebral aneurysm (Fig. 4A). The patient was given 5000 U of heparin intravenously for procedural embolic prophylaxis. During 192 minutes, 17 coils were used for embolization, resulting in a subtotal obliteration of the aneurysm sac without any compli cations (Fig. 4B). After the coil embolization, the patient was sent to the neurosurgical intensive care unit and monoparesis (grade IV) was observed in the left arm. Immediate DW-MR imaging showed high-signal spots in the right precentral gyrus, and other spots in the right frontal base and right occipital area (Fig. 4C). No other neurological symptoms were reported. Aggressive hydration therapy under central venous pressure monitoring was performed and the patient's weakness was recovered completely after 3 days.

Case 3

A 32-year-old male presented a ruptured anterior communicating artery aneurysm with a subarachnoid hemorrhage (Fig. 5A). During 72 minutes, 3 coils were used for the embolization. With the third coil attempt, the aneurysm sac was ruptured and immediately secured (Fig. 5B). Following the procedure, the patient did not show any neurological deterioration, although a follow-up DW-MR image showed a large high-signal-intensity lesion in the left basal ganglia (Fig. 5C). The patient was discharged without any neurological deficit or weakness on the right side.

Case 4

A 48-year-old male presented a ruptured anterior communicating artery aneurysm with a subarachnoid hemorrhage (Fig. 6A). During 76 minutes, 7 coils were used for the embolization (Fig. 6B). In the immediate post-embolization neurological examination, the patient showed left leg monoparesis (grade III). Occlusion of the right anterior cerebral artery was observed in a follow-up cerebral angiogram and a DW-MR image showed a high signal intensity lesion in the right medial frontal lobule. A perfusion MRI showed hypoperfusion in the right anterior cerebral artery territory. After aggressive 3-H therapy, the weakness improved to grade IV on the next day, and the patient had completely recovered by following week. A

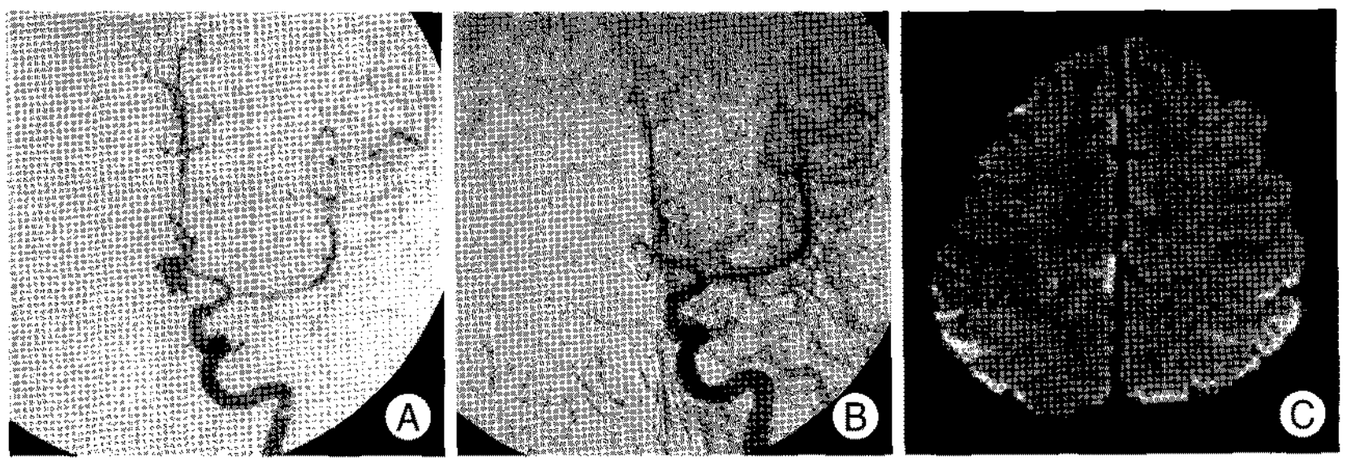

Fig. 6. A 48-year-old male (Case 4). A : Left internal carotid artery angiogram showing an aneurysm in the anterior communicating artery. B : Post-embolization angiogram showing obliteration of the aneurysm. C : One-week DW-MR follow-up revealing high-signal-intensity lesions in the right anterior cerebral artery territories.

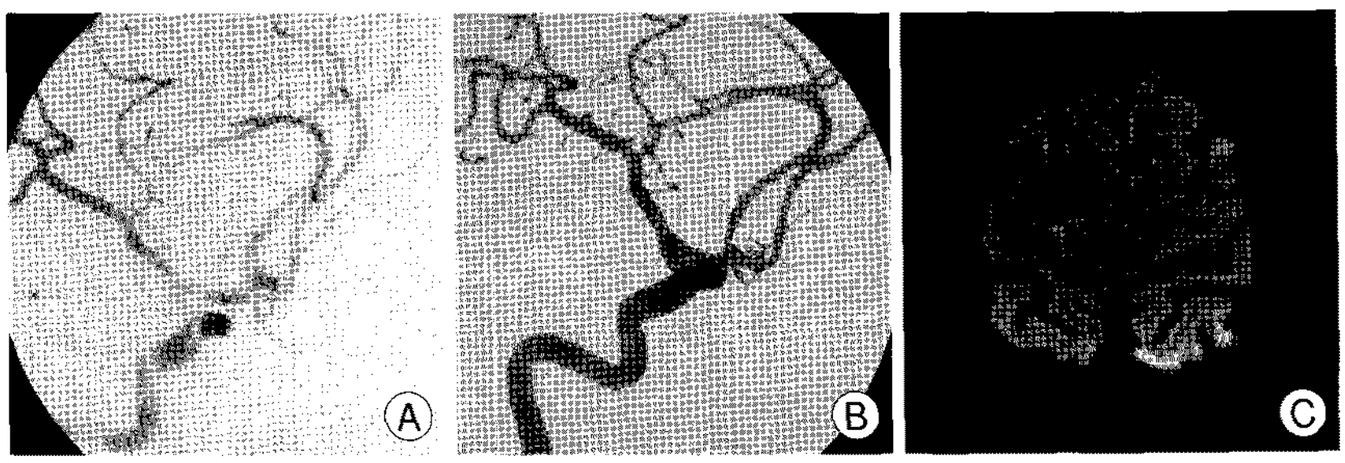

Fig. 7. A 72-year-old female (Case 5). A : Left internal carotid artery angiogram showing a bilobulated aneurysm in the anterior communicating artery. B : Post-embolization angiogram showing obliteration of the aneurysm. C : DW-MR revealing high signal intensity lesions in the right precentral gyrus.

follow-up cerebral angiogram showed a patent right anterior cerebral artery, while a follow-up DW-MR image showed high-signal-intensity lesions in the right anterior cerebral artery territories (Fig. 6C).

Case 5

A 72-year-old female presented an unruptured anterior communicating artery aneurysm (Fig. 7A). During 81 minutes, 5 coils were used for the embolization (Fig. 7B). An immediate post-embolization neurological examination revealed left arm monoparesis (grade I), while immediate DW-MR imaging showed multiple high-signal spots in the right precentral gyrus (Fig. 7C). No other neurological symptoms were noted. Aggressive hydration therapy under central venous pressure monitoring was performed and the weakness was completely gone within 3 days.

DISCUSSION

After the advent of the Guglielmi detachable coil (GDC) in 1991 (Boston Scientific, Fremont, CA) and its FDA approval in 1995, embolization of intracranial aneurysms has been increasingly used due to its reliability and convenience. However, despite the many advantages, the most frequent and serious complication related to this technique is thromboembolic events, including a transient ischemic attack and stroke, which can not be ignored. The prevalence of thromboembolic complications has already been reported as ranging from 2.5% and 28%[2,4-8,11-17,20,22,23]. None of these studies included routine follow-up imaging yet, and the thromboembolic events were only recorded in the event of neurological deterioration. Thus, measures are needed for the early detection of thromboembolic events to enable proper management to start earlier and provide better neurological outcomes. Several experimental and clinical studies have revealed that DW-MR imaging enables the early detection of cerebral ischemic lesions[1]. Soeda, et al. [20] reported on the incidence and appearance of thromboembolic events associated with coil embolization in DW-MR images, and their study showed high-signal-intensities in 60.6% of the DW-MR images. Of these presumed thromboembolic events, 40% were symptomatic. In the present study, high-signal-intensities were found in 60.1% of the DW-MR images, which corresponded with other studies. However, the symptomatic thromboembolic event rate was only 3.6%. Although 67% of the cases with DW-MR findings involved the eloquent area of the brain, 90.9% of them did not present any focal neurological symptoms correlated to the lesions. Moreover, most of them were transient and improved by conservative management. While a lower incidence of total aneurysmal obliteration and the possibility of long-term recanalization remain as problems to be solved, various modifications to the standard coils, such as biologically active surfaces, radioactive components, and coils coated with hydrogels, foreshadow better outcomes for the endovascular treatment of cerebral aneurysms.

It is already known that thromboembolic events related to a coil embolization are more common in a wide-necked or large aneurysm, in association with balloon-assisted techniques, or in case of a lengthy precedure[5,15,20,21]. In the present study, among the 4 balloon-assisted procedures, only one post-embolization DW-MR image showed an abnormal lesion and no neurological symptoms developed. Meanwhile, among the 16 cases that involved an intraluminal stent-assist technique, only 8 cases showed high-signal lesions in the DW-MR images after the coil embolization procedure, and none of the patients showed any

neurological deficit. Thus, the assisted technique, whether stent or balloon, did not increase the incidence of DW-MR lesions or neurological deficit. However, the size of the population was too small and larger scaled study is needed. Also, the size of the aneurysm and length of the procedure time did not show any significant association with the incidence of DW-MR lesions (p=0.68, 0.17).

We assumed that more atherosclerotic changes in the cerebral artery were present in older patients, and that these patients were more vulnerable to thromboembolic events in aneurysm-unrelated territories as a result of routine procedures, such as the use of a guiding catheter. For the younger patients, the incidence of thromboembolic events related to the coil embolization procedure, as revealed by DW-MR imaging, was 62.2%, which was far higher than that for the older ones (24.5%). Conversely, for the older patients, the incidence of aneurysm-unrelated thromboembolic events was higher and the statistical difference was significant (p=0.0003, odd's ratio=5.078), indicating that thromboembolic events related to a coil embolization are unpredictable, especially in the case of older patients.

CONCLUSION

This prospective study revealed that the incidence of symptomatic thromboembolic attacks after a coil embolization of the cerebral aneurysm was less frequent than that previously reported. While DW-MR imaging revealed a higher number of thromboembolic events, most of them were clinically silent. Even in the clinically non-silent group, most of them were transient and improved by conservative management. The incidence of DW-MR abnormalities was found to be higher in older patients, along with unpredictable thromboembolic events. Thus, to enable adequate and timely treatment and minimize neurological sequelae, DW-MR imaging follow-up might be helpful after a coil embolization of cerebral aneurysms, especially in the case of older patients.

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