Massive Cerebral Microemboli after Protected Carotid Artery Angioplasty and Stenting Using a Distal Filter Embolic Protection Device for a Vulnerable Plaque with a Lipid Rich Necrotic Core and Intraplaque Hemorrhage: A Case Report

Hae-Jung Kim, MD, Myung-Ho Rho, MD*
Department of Radiology, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea

A major concern associated with carotid artery angioplasty and stenting (CAS) is a peri-procedural distal cerebral embolization. To prevent distal embolization, embolic protection devices (EPDs) have been developed. However, the risk of cerebral embolism after protected CAS in patients with a vulnerable plaque is controversial and either a silent or a symptomatic stroke can occur despite the use of EPDs. Here, we report a case of a massive cerebral microemboli after a protected CAS using a distal filter EPD for a vulnerable plaque with a lipid rich necrotic core and intraplaque hemorrhage.

Index terms Cerebral Embolism; Carotid Arteries; Angioplasty; Stents; Embolic Protection Device; Plaque, Atherosclerotic
INTRODUCTION

Although a carotid endarterectomy (CEA) is the standard treatment for carotid artery stenosis, carotid artery stenting (CAS) has emerged as an effective alternative to CEA (1). However, the major concern associated with CAS is the potential for distal embolization of particles from the treatment site during endovascular manipulation (1, 2). To prevent distal embolization, cerebral embolic protection devices (EPDs) have been developed. However, the risk of a cerebral embolism after protected CAS in patients with vulnerable plaque is controversial and either silent or symptomatic strokes may occur despite the use of EPDs. To the best of our knowledge, there have been no case reports of severe cerebral microemboli after CAS with a distal filter type EPD. Here, we report a case of massive cerebral microemboli presented as ipsilateral multiple cortical infarctions and bilateral border zone infarctions after protected CAS using a distal filter EPD for a vulnerable plaque with a lipid rich necrotic core (LRNC) and intraplaque hemorrhage (IPH).

CASE REPORT

An 83-year-old man was admitted to our emergency room with left-sided weakness which started one day before. He had no specific medical history. On neurologic examination, the patient demonstrated dysarthria and left hemiparesis but was mentally alert. Diffusion-weighted imaging (DWI) was performed and showed multifocal small acute infarctions in the right frontoparietal cortex and right corona radiata (Fig. 1A). CT angiography demonstrated long segmental severe stenosis of the right proximal internal carotid artery (ICA) (Fig. 1B). The atherosclerotic carotid plaque had an attenuation of < 60 Hounsfield unit, suggesting LRNC (3). A small ulceration was also noted as a depression at the distal portion of the plaque surface. Magnetic resonance angiography (MRA) was performed and revealed an IPH on the source images and maximum intensity projection images from time-of-flight MRA as a high signal intensity in the plaque (Fig. 1C). At seven days after the symptom onset, CAS procedures were performed by an interventional neuroradiologist with 20 years of experience. Under local anesthesia, a 6F 90 cm-long Shuttle® guiding sheath (Cook Medical, Bloomington, IN, USA) was positioned in the distal common carotid artery via the percutaneous transfemoral route and a 3-vessel cerebral angiography was performed before treatment to evaluate collateral flow. The right carotid angiogram showed a long segmental severe stenosis of the right proximal ICA, measuring about 80% at the most stenotic portion using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria (Fig. 1D, 1st panel). Systemic anticoagulation was initiated with a 3000 I.U. bolus of intravenous heparin followed by a 1000 I.U./h infusion. The SpiderFx (ev3, Plymouth, MN, USA), distal filter type EPD, was deployed at the distal cervical ICA through the stenotic portion with aid of a Traxcess 14 guide-wire (Microvention, Aliso Viejo, CA, USA). Predilatation was performed using an Aviator Plus 5 mm × 30 mm (Cordis, Bridgewater Township, NJ, USA). The ipsilateral carotid angiogram after the angioplasty revealed the contrast medium oozed and pooled into the plaque that was ruptured by balloon dilatation (Fig. 1D, 2nd panel). A self-expandable Protege RX® carotid stent (ev3) with a diameter of 10/7 mm (proximal/distal) and a length of 40 mm was deployed.
Fig. 1. Massive cerebral microemboli after protected CAS using a distal filter EPD for a vulnerable plaque with a LRNC and IPH in an 83-year-old men. 
A. Axial DWI at admission shows multiple small hyperintense embolic infarctions in the right frontoparietal cortex and right corona radiata. 
B. Axial (left panel) and sagittal multiplanar reconstruction (right panel) CT angiography images demonstrate a long segmental severe stenosis of the right proximal ICA (black arrow) with a small ulceration (arrowhead). The atherosclerotic carotid plaque has an attenuation of < 60 Hounsfield unit, suggesting a LRNC (white arrow). 
C. Maximum intensity projection image (left panel) and axial source image (right panel) of time-of-flight MR angiography show high signal intensity IPH (arrows) in the eccentric right carotid plaque, which surrounds the lumen of the ICA with severe stenosis. IPH is identified as a hyperintense signal compared with the adjacent neck muscle. 
CAS = carotid artery angioplasty and stenting, DWI = diffusion-weighted imaging, EPD = embolic protection device, ICA = internal carotid artery, IPH = intraplaque hemorrhage, LRNC = lipid rich necrotic core
Massive Cerebral Microemboli after Protected CAS

During the stent deployment, the patient exhibited a stuporous mental state with right eyeball deviation and bilateral limb spastic paralysis. The ipsilateral intracranial angiogram obtained after the CAS showed intact cerebral blood flow without evidence of distal embolization and the carotid angiogram showed minimal residual stenosis at the origin site of the right ICA and no in-stent thrombosis of the right proximal ICA (Fig. 1D, 3rd panel). A large amount of lipid-rich atherosclerotic plaque particles was captured in a filter type distal EPD (4th panel).

Fig. 1. Massive cerebral microemboli after protected CAS using a distal filter EPD for a vulnerable plaque with a LRNC and IPH in an 83-year-old man.

D. Lateral projection of the right carotid angiogram (1st panel) shows a long segmental severe stenosis of the right proximal ICA, measuring about 80% at the most stenotic portion (arrow). The right carotid angiogram after balloon angioplasty (2nd panel) reveals the contrast medium oozed and pooled into the plaque (arrow) that was ruptured by balloon dilatation. The post-carotid artery stent placement angiogram (3rd panel) shows minimal residual stenosis at the origin site of the right ICA. A large amount of lipid-rich atherosclerotic plaque particles was captured in a filter type distal EPD (4th panel).

E. DWI at eight-hours after the CAS shows massive new ischemic lesions in the right middle cerebral artery territory and bilateral border zone regions.

CAS = carotid artery angioplasty and stenting, DWI = diffusion-weighted imaging, EPD = embolic protection device, ICA = internal carotid artery, IPH = intraplaque hemorrhage, LRNC = lipid rich necrotic core

During the stent deployment, the patient exhibited a stuporous mental state with right eyeball deviation and bilateral limb spastic paralysis. The ipsilateral intracranial angiogram obtained after the CAS showed intact cerebral blood flow without evidence of distal embolization and the carotid angiogram showed minimal residual stenosis at the origin site of the right ICA and no in-stent thrombosis of the right proximal ICA (Fig. 1D, 3rd panel). A large amount of lipid-rich atherosclerotic plaque particles was captured in the EPD (Fig. 1D, 4rd panel) and the procedure was ended. An immediate postprocedural DWI showed multifocal new ischemic lesions in the ipsilateral middle cerebral artery and vascular watershed territories of bilateral cerebral hemispheres. Contralateral lesions were from collateral circulation through the anterior communicating artery. DWI, performed eight-hours after the CAS, showed additional bright hyperintensities of the new ischemic lesions in bilateral cerebral hemispheres (Fig. 1E). We concluded a distal massive microemboli due to a ruptured lipid rich, hemorrhagic plaque during balloon angioplasty despite the distal fil-
DISCUSSION

Although a CEA is the standard treatment for carotid artery stenosis, it has limitations, particularly patients’ comorbidities (1). CAS has emerged as an effective alternative to CEA in high-risk patients (1). However, the major concern associated with CAS is the potential for distal embolization of particles from the treatment site during endovascular manipulation (1, 2). To prevent distal embolization, cerebral EPDs have been developed and their usage has become a common practice during CAS. However, the risk of a periprocedural cerebral embolism during protected CAS in patients with vulnerable plaque is controversial. It has been reported that plaque instability such as IPH is associated with a high risk of cerebral embolism during protected CAS (4). However, Chung et al. (5) suggested that IPH is not a significant risk factor for cerebral embolism during CAS and protected CAS is safe in patients with severe carotid stenosis and IPH. Despite the controversy, our patient showed massive symptomatic embolic infarctions as a periprocedural complication after protected CAS for a vulnerable plaque that was unable to guarantee the safety of EPD.

Distal filter type cerebral EPDs have some pitfalls. Selective protection is one of them (6). The average filter has 100-μm pores; therefore, embolic particles sized < 100-μm will escape through the filter’s pores and microembolization may occur with the use of all currently available filters (6). We used SpiderFx with pore sizes ranging from 70-μm to 200-μm, with the largest and smallest pores located at the proximal and distal ends of the basket, respectively. Siewiorek et al. (7) compared the performance in vitro of 6 distal filter type EPDs and reported that Spider had the lowest capture efficiency (143-μm: 1.50%; 200-μm: 19.34%, (p < 0.0005), likely due to the design of the device and relatively larger pore size. As occlusion of vessels in the 50 to 300 μm diameter range is associated with “border zone” infarctions (8), a relatively large number of particles of 200 μm or less might have escaped through the filter’s pores and contributed to the distal cerebral embolization of our patient. If we used an EPD filter with smaller pores, such as FilterWire EZ (Boston Scientific, Marlborough, MA, USA) which has 110 μm pores, we also could not have prevented microemboli less than 110 μm. Another pitfall of filter type EPD is filter occlusion or flow stagnation (6). In our patient, a large amount of lipid-rich atherosclerotic plaque particles were captured in the filter after the rupture of the vulnerable plaque. This large embolic load probably overwhelmed the capacity of the filter and may have caused a significant reduction in antegrade flow in the ICA, proximal to the filter device, which is referred to as “slow-flow” phenomena (6). This is consistent with a previous study by Casserly et al. (9) that shows “slow-flow” during carotid interventions with EPDs is associated with a higher risk of periprocedural stroke and the embolization of vulnerable plaque elements may play a pathogenic role. Rosenkranz et al. (2) reported that the frequency of procedure-related silent cerebral lesions is independent of the number of solid cerebral microemboli during the CAS procedure. They also showed that most cerebral microemboli that occur during CAS are gaseous and < 15% of microemboli are solid. However, in case of vulnerable plaques which are prone to rupture, like in our patient, there may be an association between the number of solid microemboli during the CAS...
Massive Cerebral Microemboli after Protected CAS

There are several studies comparing the outcomes between proximal EPDs and distal filter type EPDs for CAS. A recent systematic review and meta-analysis by Texakalidis et al. (10) reported that proximal EPDs can reduce distal embolization phenomena which result in ischemic lesions when compared to distal filter type EPDs based on the results from real-world studies. However, proximal EPDs were not superior in regard to risk of periprocedural stroke, transient ischemic attack, and death. Further studies are needed to provide a clear answer to this debate. In the case of a high-risk vulnerable plaque, such as in our patient, a proximal EPD could be a better neuroprotection strategy than a distal filter type EPD during CAS.

In conclusion, radiologists and clinicians should always keep in mind that an ‘embolic shower’ could occur as a complication of protected CAS in the case of a vulnerable plaque, and the safety of distal EPD cannot be guaranteed. Plaque vulnerability could be accurately and noninvasively predicted using multimodality imaging due to technological improvements and therefore preoperative radiologic assessment of such plaques is beneficial and necessary to reduce the rate of complications after CAS. If a carotid plaque has a LRNC and hemorrhage, the CEA or proximal EPD could be better treatment methods to prevent massive cerebral microemboli.

Author Contributions
Conceptualization, all authors; investigation, all authors; project administration, all authors; resources, all authors; supervision, R.M.; visualization, all authors; writing—original draft, K.H.; and writing—review & editing, all authors.

Conflicts of Interest
The authors have no potential conflicts of interest to disclose.

REFERENCES
1. Noiphithak R, Liengudom A. Recent update on carotid endarterectomy versus carotid artery stenting. Cerebrovasc Dis 2017;43:68-75
2. Rosenkranz M, Fiehler J, Niesen W, Waiblinger C, Eckert B, Wittkugel O, et al. The amount of solid cerebral microemboli during carotid stenting does not relate to the frequency of silent ischemic lesions. AJNR Am J Neuroradiol 2006;27:157-161
3. Saba L, Sanfilippo R, Sannia S, Anzidei M, Montisci R, Mallarini G, et al. Association between carotid artery plaque volume, composition, and ulceration: a retrospective assessment with MDCT. AJR Am J Roentgenol 2012;199:151-156
4. Yoshimura S, Yamada K, Kawasaki M, Asano T, Kanematsu M, Takamatsu M, et al. High-intensity signal on time-of-flight magnetic resonance angiography indicates carotid plaques at high risk for cerebral embolism during stenting. Stroke 2011;42:3132-3137
5. Chung GH, Jeong JY, Kwak HS, Hwang SB. Associations between cerebral embolism and carotid intra-plaque hemorrhage during protected carotid artery stenting. AJNR Am J Neuroradiol 2016;37:686-691
6. Mousa AY, Campbell JE, Aburahma AF, Bates MC. Current update of cerebral embolic protection devices. J Vasc Surg 2012;56:1429-1437
7. Siewiorek GM, Wholey MH, Finol EA. A comparative analysis of bench-top performance assessment of distal protection filters in transient flow conditions. J Endovasc Ther 2012;19:249-260
8. Masuda J, Yutani C, Ogata J, Kurijama Y, Yamaguchi T. Atheromatous embolism in the brain: a clinicopathologic analysis of 15 autopsy cases. Neurology 1994;44:1231-1237
9. Casserly IP, Abou-Chebl A, Fathi RB, Lee DS, Saw J, Exaire JE, et al. Slow-flow phenomenon during carotid artery intervention with embolic protection devices: predictors and clinical outcome. J Am Coll Cardiol
취약한 죽상경화반의 원위 필터형 색전예방장치를 이용한 내경동맥의 스텐트 시술 후 발생한 다량의 뇌 미세혈전: 증례 보고

김혜정 · 노명호*  

경동맥 혈관성형술 및 스텸트삽입술과 관련된 주요 합병증은 시술 도중 발생하는 원위부 뇌 색전증으로 이를 방지하기 위해 색전예방장치가 개발되었다. 그러나 취약한 죽상경화반을 가진 환자의 경우 색전예방장치를 사용한 경동맥 혈관성형술 및 스텸트삽입술 후 뇌 색전증의 위험은 논란의 여지가 있으며, 색전예방장치의 사용에도 불구하고 무증상 또는 증상이 없는 뇌졸중이 발생한다. 저자들은 지방이 풍부한 괴사성 핵과 경화반 내 출혈이 있는 취약한 죽상경화반의 원위 필터형 색전예방장치를 이용한 내경동맥의 스텸트 시술 후 발생한 다량의 뇌 미세혈전의 증례를 보고하고자 한다.

성균관대학교 의과대학 강북삼성병원 영상의학과

2005;46:1466-1472

10. Texakalidis P, Letsos A, Kokkinidis DG, Schizas D, Karaolanis G, Giannopoulos S, et al. Proximal embolic protection versus distal filter protection versus combined protection in carotid artery stenting: a systematic review and meta-analysis. Cardiovasc Revasc Med 2018;19:545-552