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Neuroradiology Report

Delayed progressive bilateral supraclinoid internal carotid artery stenosis in a patient with a ruptured basilar artery aneurysm

Mina G. Safain, Adel M. Malek *

Cerebrovascular and Endovascular Division, Department of Neurosurgery, Tufts Medical Center and Tufts University School of Medicine, 800 Washington Street, Proger 7, Boston, MA 02111, USA

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ABSTRACT

Cerebral vasospasm is a common radiographic and clinical diagnosis after subarachnoid hemorrhage. Conventional treatments include medical hypertension, hypervolemia, and modest hemodilution. When medical treatments fail in severe vasospasm cases, intra-arterial vasodilation and balloon angioplasty may be useful. We present a 47-year-old woman with a ruptured basilar artery aneurysm who developed severe bilateral internal carotid artery vasospasm requiring bilateral balloon angioplasty. Prior to discharge, the patient's bilateral stenosis had improved. Three months post-discharge, severe restenosis in her bilateral internal carotid arteries occurred; a rare event. Balloon angioplasty has been demonstrated to histologically tear and stretch collagen fibers in the vessel wall and overexpansion of vessels may lead to a neo-intimal reaction that is similar to the one seen after stent placement in the intracranial circulation. Clinicians should be aware of the possibility of delayed and progressive stenosis in vessels treated with angioplasty. Follow-up vascular imaging is necessary after subarachnoid hemorrhage. Future study is required on the treatment paradigms necessary for this delayed restenosis.

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1. Introduction

Cerebral vasospasm after subarachnoid hemorrhage (SAH) occurs radiographically in up to 70% of angiograms at 7 days after the initial bleed with clinically significant vasospasm occurring in up to 30% of patients [1–3]. It is well known that cerebral vasospasm of the major intracranial vessels is one of the major causes of morbidity and mortality of SAH, with delayed ischemic events resulting in stroke. Vasospasm is treated medically with "triple-H" therapy (hypertension, hypervolemia, and slight hemodilution) and through endovascular means via intra-arterial vasodilators (nicardipine and verapamil) and, in severe cases, balloon angioplasty [4,5]. Although, to our knowledge, there is no prospective clinical trial data to support its use, balloon angioplasty has become a cornerstone of treatment at the majority of centers for focal large vessel vasospasm that is non-responsive to intra-arterial dilation or traditional medical therapy [4,5]. Radiographic improvement after balloon angioplasty is quite impressive but there are conflicting reports regarding use and timing of this treatment modality to augment medical therapy for moderate vasospasm [5–7]. In severe medically refractory vasospasm, endovascular treatment, including balloon angioplasty, can be essential in preventing delayed ischemic complications of vasospasm [8].

Restenosis after balloon angioplasty for atherosclerosis is a well-known phenomenon [9–11], however, its occurrence in a delayed fashion following its use for cerebral vasospasm is rare [12–14]. We report a patient who underwent successful angioplasty for internal carotid artery (ICA) post-SAH vasospasm, who went on to develop delayed progressive severe focal restenosis. We provide a comprehensive review of the literature on this rare event and postulate possible mechanisms for this phenomenon.

2. Case report

A 47-year-old woman developed sudden onset worst headache of her life, nausea, and vomiting. She presented confused with mild right-sided hemiparesis, Hunt and Hess grade 3. A CT scan demonstrated Fisher grade 4 SAH and hydrocephalus. An external ventricular drain was placed and CT angiogram exhibited a 2.5 mm, anteriorly pointing, distal basilar trunk aneurysm (Fig. 1). Cerebral angiography was performed urgently with an uncomplicated coil embolization of the aneurysm (Fig. 2). No other aneurysms, vasospasm, or stenosis were noted in the remainder of the intracranial circulation (Fig. 2). No personal or family history of vasculopathy or collagen vascular diseases was reported.

* Corresponding author. Tel.: +1 617 636 8200; fax: +1 617 636 7587.
E-mail address: amalek@tuftsmedicalcenter.org (A.M. Malek).

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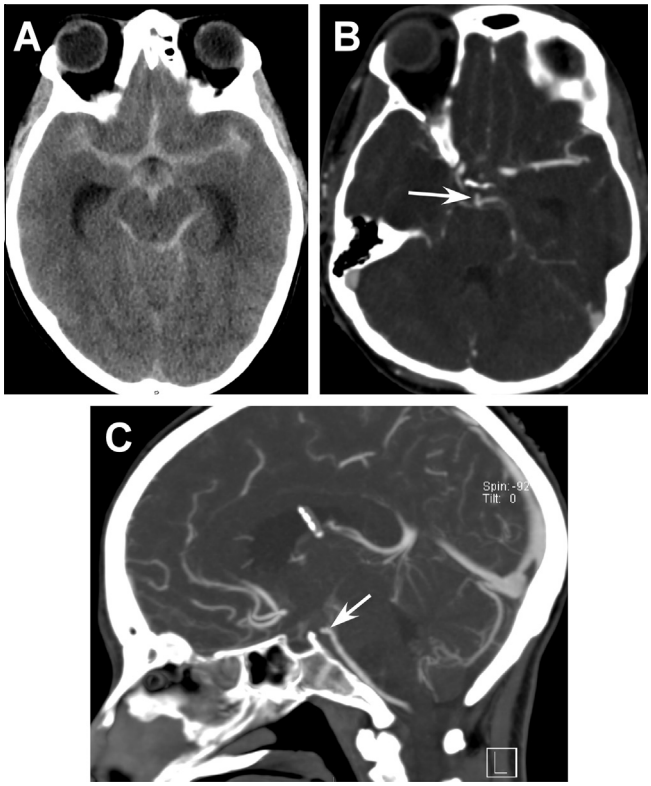


Fig. 1. (A) Initial axial CT scan demonstrating diffuse subarachnoid hemorrhage and hydrocephalus. (B) Axial CT angiography demonstrating a 2.5 mm basilar artery aneurysm (white arrow). (C) Sagittal CT angiography demonstrating a 2.5 mm basilar artery aneurysm (white arrow).

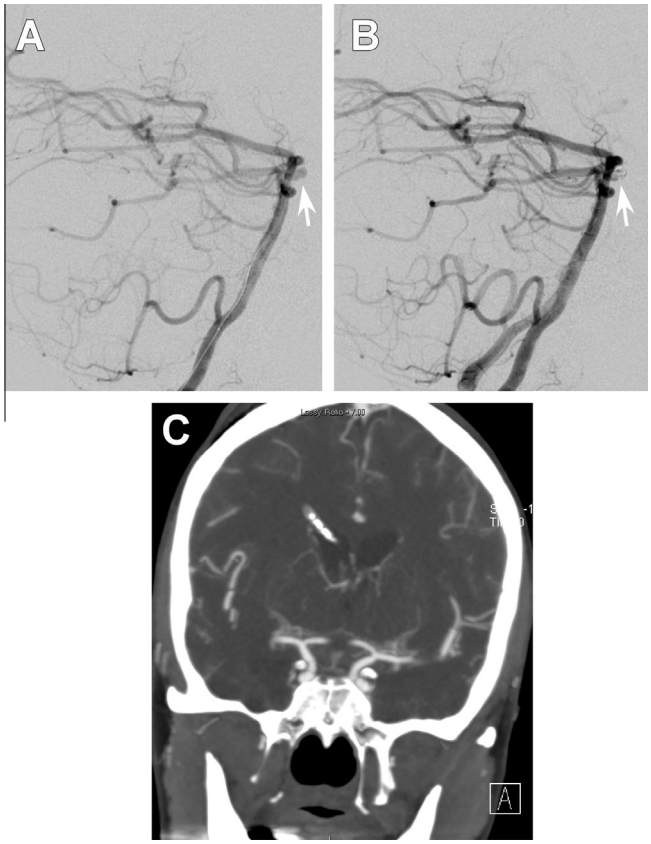


Fig. 2. (A) Lateral cerebral angiography, vertebral artery injection pre-coil embolization of basilar aneurysm (white arrow). (B) Lateral cerebral angiography, vertebral artery injection post-coil embolization of basilar aneurysm (white arrow). (C) Coronal CT angiography demonstrating no other aneurysm or stenosis in the anterior circulation.

She was managed in the intensive care unit for vasospasm with frequent detailed neurologic examination, hypertension, hypervolemia, nimodipine, fludrocortisone, and daily transcranial ultrasonography (TCD). On hospital day 5, TCD revealed increasing velocities in the ICA without clinical deficit. Cerebral angiography demonstrated severe vasospasm in both ICA with greater spasm in the right (Fig. 3). Verapamil 10 mg was injected into both ICA and 4 mg into both vertebral arteries (VA). The following day she developed transient left arm numbness and weakness with further increase in TCD velocities. Repeat angiography revealed increasing bilateral vasospasm which was treated with additional bilateral ICA and VA verapamil as well as angioplasty of the bilateral supraclinoid ICA (Fig. 4, 5). Prior to proceeding to angioplasty we performed a 10–15 minute follow-up angiogram after verapamil injection to assess for continued severe stenosis. At our center, we usually perform all balloon angioplasties with the compliant Hyperform Balloon Catheter (eV3, Irvine, CA, USA) initially, gently proceeding from proximal to distal to avoid skip areas and avoid the common watermelon seed phenomenon. This technique was successful with a 4 mm × 7 mm Hyperform balloon catheter in the left ICA. During angioplasty of the right ICA there was difficulty in steering the 0.010" X-Pedion wire (eV3) which had already been pre-bent across the stenosis atraumatically. Accordingly we elected to use a Synchro-wire based 4 mm × 7 mm Transform super compliant balloon (Stryker Neurovascular, Fremont, CA, USA) which was used in similar fashion as the Hyperform. There was no significant force or severe manipulation during this attempt. Once the Synchro wire was advanced across the vasospastic segment, the Transform super compliant balloon catheter was passed with ease from proximal to distal. Inflation of both balloons was controlled by visual feedback rather than by a set volume. Angiography 1 week following ICA angioplasty demonstrated improved stenosis in the bilateral supraclinoid ICA segments although with some apparent restenosis (Fig. 4C, 4G, 5C, 5G). The patient required ventriculoperitoneal shunting and was discharged home on hospital day 35 with minimal headache and normal motor strength.

Routine clinical follow-up at 1 week and 1 month were unremarkable with only mild headache. MRI and magnetic resonance angiography (MRA) were obtained at 3 months post-discharge demonstrating progressive restenosis of the bilateral proximal supraclinoid ICA. Angiography was therefore performed which demonstrated severe focal stenosis of both supraclinoid ICA; the left was worse than the right. She was treated with aspirin 81 mg and verapamil 180 mg daily with repeat MRI/MRA obtained 1 month later. This demonstrated continued progressive stenosis. She was therefore taken to angiography which demonstrated stable but severe bilateral ICA stenosis (Fig. 4, 5). A MRI perfusion scan was obtained and demonstrated mild asymmetric prolonged mean transit time in the right cerebral hemisphere without perfusion mismatch. Clopidogrel 75 mg daily was added to her regimen and she remains at her neurologic baseline with a repeat MRI/MRA scheduled 1 month from her most recent discharge.

3. Discussion

Restenosis after angioplasty for both intracranial and coronary atherosclerosis has been reported to occur in 30–50% [15–18] of cases but reports of it occurring in a delayed fashion after cerebral vasospasm are uncommon [12–14]. Although balloon angioplasty has become established in the treatment of medically and

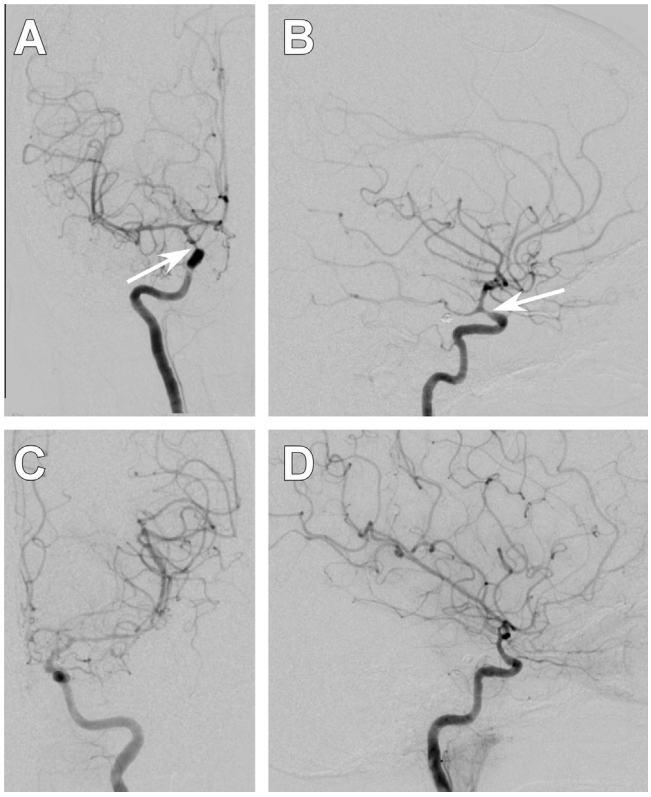


Fig. 3. Five days post-hemorrhage. Right internal carotid artery (ICA) anteroposterior (A) and lateral (B) digital subtraction angiography demonstrating severe stenosis of the supraclinoid ICA (white arrow). Left anteroposterior (C) and lateral (D) digital subtraction angiography demonstrating minimal supraclinoid ICA stenosis.

pharmacologically refractory vasospasm, it is not a benign procedure. Complications of balloon angioplasty can include vessel rupture, arterial dissection, reperfusion hemorrhage, and thromboembolic stroke [19,20]. In a case series of 75 patients who underwent 85 balloon angioplasties, Terry et al. [21] reported no vessel rupture or perforation, but a 4.7% rate of thromboembolic stroke. This current patient, however, suggests that there may be more than the well-known acute complications of angioplasty and that the long-term and delayed effects of this therapy must be monitored. In our patient, angioplasty restored vessel caliber that remained stable 1 week after treatment. However, 3 months after angioplasty a significant restenosis occurred that continued to progress 4 months after angioplasty. At this time, we are continuing antiplatelet therapy but future endovascular or surgical recanalization may be necessary.

3.1. Pathophysiology of balloon angioplasty

Yamamoto et al. [22] compared both normal and balloon angioplastied middle cerebral arteries from humans and described that the collagen fibers in angioplasty specimens were torn and stretched when compared to controls. These changes returned to normal in 7 days. Similarly, another group [23] histologically studied canine basilar arteries that had a 30% dilation via balloon angioplasty. They demonstrated denudation of endothelial cells, significant deposition of fibrin, and like Yamamoto et al. [22] a stretching and focal dehiscence of the internal elastic lamina and altered myocytes in the media. Finally, Honma et al. [24] replicated the aforementioned histologic findings in two postmortem SAH patients who received balloon angioplasty for severe vasospasm. They demonstrated heterogeneously extended walls and dilated lumina as well as increased stretched and torn collagen fibers. Interestingly, the vessel wall of one patient contained atheromatous

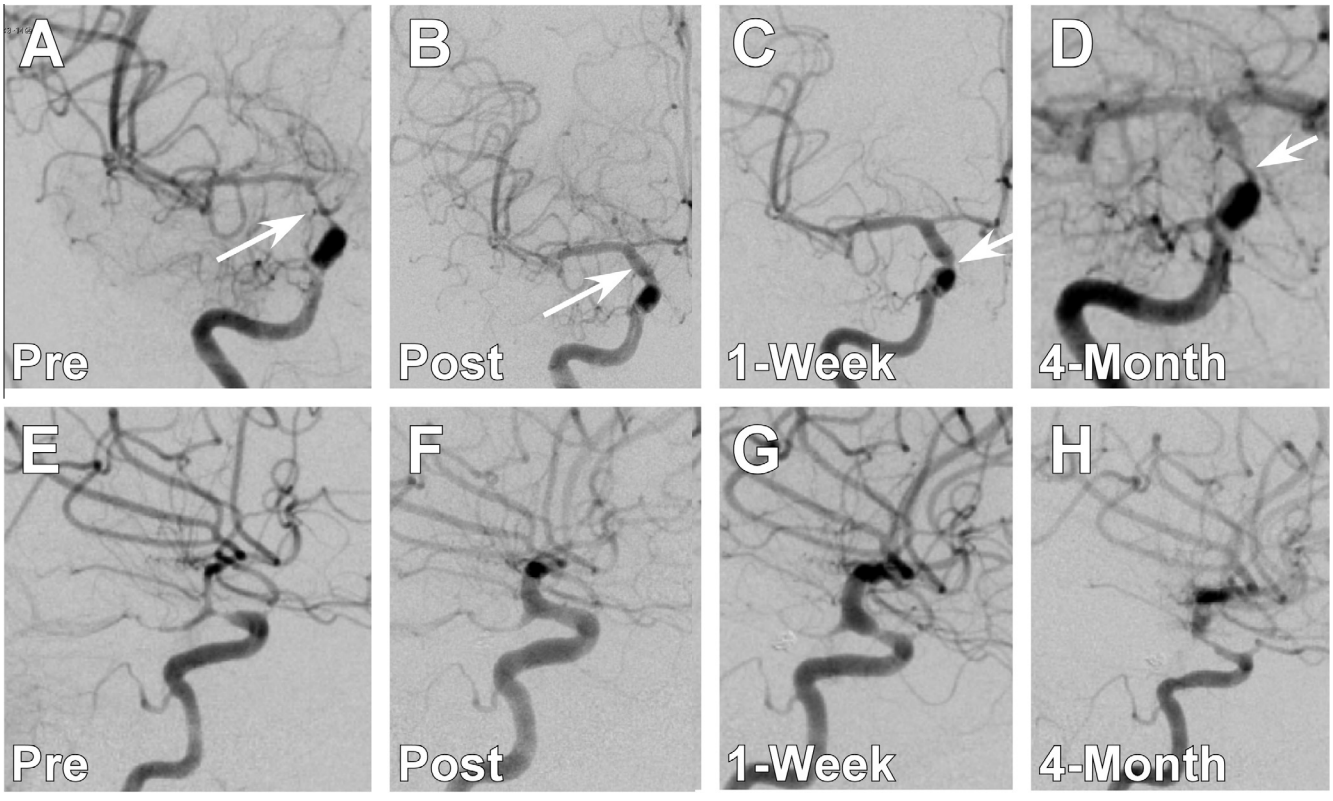


Fig. 4. Right internal carotid artery (ICA) angiography. Top row: anteroposterior digital subtraction angiography (DSA). Bottom row: lateral DSA. (A, E) Pre-angioplasty demonstrating severe right ICA stenosis (white arrow). (B, F) Post-angioplasty demonstrating treated stenosis (white arrow). (C, G) One week post-angioplasty demonstrating minimal proximal ICA stenosis (white arrow). (D, H) Four months post-angioplasty demonstrating severe proximal ICA stenosis (white arrow).

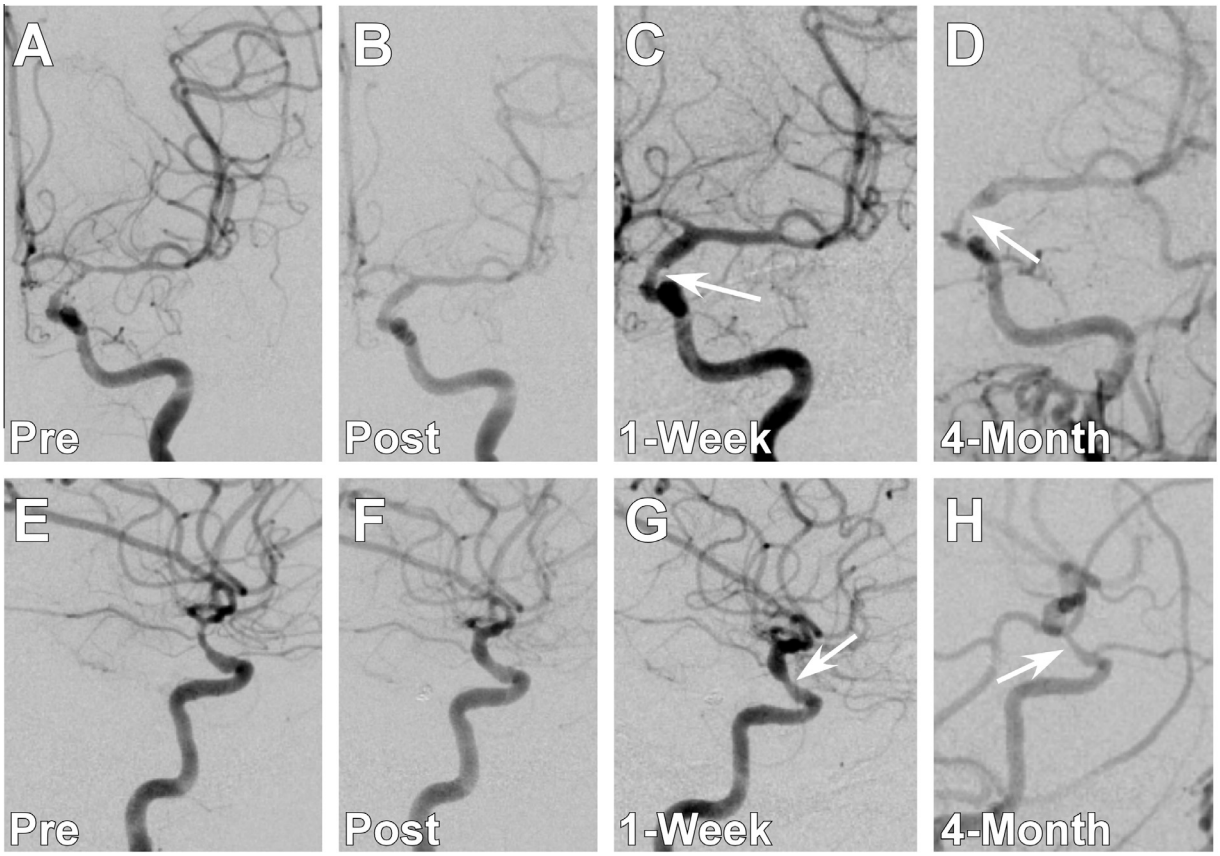


Fig. 5. Left internal carotid artery (ICA) angiography. Top row: anteroposterior digital subtraction angiography (DSA). Bottom row: lateral DSA. (A, E) Pre-angioplasty demonstrating severe moderate left ICA stenosis. (B, F) Post-angioplasty demonstrating treated stenosis. (C, G) One week post-angioplasty demonstrating minimal proximal ICA stenosis (white arrow). (D, H) Four months post-angioplasty demonstrating severe ICA stenosis (white arrow).

plaque in portions where the vessel wall was not stretched and these collagen changes were not found. This may be one reason to explain why restenosis is so common in balloon angioplasty performed for intracranial atherosclerosis and the relative rarity of restenosis in vasospasm-associated balloon angioplasty. Another important finding in this study was that smooth muscle cells did not have an intricate attachment to the extracellular matrix and collagen suggesting that vasospastic vessels may actually lose some of their contractile activity and therefore provide a secondary reason for the rarity of restenosis in balloon angioplasty for vasospasm.

3.2. Possible causes of restenosis after vasospasm-associated balloon angioplasty

As mentioned previously, restenosis after vasospasm-associated balloon angioplasty is quite rare and this report, to our knowledge, serves as the fourth [12–14]. We tried to find similarities between these reports to further our understanding of this phenomenon (Table 1). Although numbers are small, all patients were young women with an age range of 24–58 years. Irrespective of aneurysm location, there seems to be a predilection for delayed stenosis in the supraclinoid ICA with all occurrences in this location. In a different patient population with intracranial atherosclerosis, Turk et al. [25] demonstrated that younger patients ($\leqslant$55 years) were two-fold more likely to develop in-stent restenosis than patients older than 55. In addition, the supraclinoid ICA was much more likely than any other location to have a propensity for developing a greater degree of restenosis. Interestingly, in the report by Hsu et al. [13], delayed stenosis occurred in a supraclinoid ICA that did not undergo balloon angioplasty, suggesting that delayed stenosis may or may not be directly linked to balloon angioplasty and that the supraclinoid ICA may have a significant underlying propensity for restenosis. Finally, in all cases (Table 1), compliant and softer balloons were used for treatment. These balloons are designed to inflate to between 3 and 5 mm in diameter, which may cause overexpansion of smaller sized or vasospastic vessels. As reported in the aforementioned histologic studies, balloon angioplasty seems to disrupt smooth muscle cells and collagen and it may be that overexpansion in certain cases can lead to endothelial damage and produce the inflammatory reaction and neointimal hyperplasia seen in in-stent stenosis [26–28]. This may suggest that noncompliant balloons ought to be used in smaller or severely vasospastic vessels but these balloons, in our experience and the experience of others, are harder to navigate through tortuous vessels and multiple size balloons may be needed to treat differing vessel diameters [19]. It may, therefore, be worthwhile to use compliant balloons with less aggressive expansion in patients with severe vasospasm-associated stenosis in order to prevent possible delayed progressive restenosis.

This report aims to provide an additional case report of delayed and progressive restenosis in two balloon angioplastied arteries in addition to reviewing the previously reported patients. This serves to suggest the need for patients treated with balloon angioplasty for SAH-induced vasospasm to undergo surveillance imaging because of the possibility of delayed stenosis and ischemic deficits. There should also be a higher index of suspicion in younger patients who require angioplasty for severe vasospasm. Treatment paradigms are hard to determine from a few case reports but antiplatelet agents are a reasonable initial strategy and stenting or bypass may be required in flow-limiting stenosis.

Table 1
Patients with delayed restenosis after balloon angioplasty reported in the literature

Study	Age	Sex	Aneurysm location and treatment	Balloon angioplasty used to treat vasospasm and location?	Type of device used	Location of delayed stenosis and treatment	Time after angioplasty stenosis occurred
Hsu et al. 2009 [13]	24	F	AcomA, clipping	No	N/A	Supraclinoid ICA, angioplasty	6 weeks, progressed at 10 weeks
Merchant et al. 2009 [14]	53	F	PcoA, clipping	Yes, bilateral ICA and MCA	Hyperglide[a] for ICA and Maveric[b] for MCA	Supraclinoid ICA, considering stenting or bypass	6 months, stable at 9 months
Sedat et al. 2009 [12]	58	F	AcomA, coiling	Yes, right A1, M1, left A1	Hyperform[a] 4 × 7 mm	Communicating ICA, aspirin 100 mg daily	5 months
Current report	47	F	Basilar artery, coiling	Yes, right ICA	Hyperform[a] 4 × 7 mm and Transform Super Compliant[c] 4 × 7 mm	Bilateral supraclinoid ICA, aspirin 81 mg, clopidogrel 75 mg	3 months, progressed at 4 months

[a] eV3, Irvine, CA, USA.
[b] Boston Scientific, Boston, MA, USA.
[c] Stryker Neurovascular, Fremont, CA, USA.
A1 = segment 1 of the anterior cerebral artery, AcomA = anterior communicating artery, F = female, ICA = internal carotid artery, M1 = segment 1 of the middle cerebral artery, MCA = middle cerebral artery, N/A = not applicable, PcoA = posterior communicating artery.

4. Conclusion

Delayed progressive vasospasm associated stenosis can occur in vessels that have had balloon angioplasty for severe vasospasm. A higher degree of suspicion may be necessary in younger female patients who undergo aggressive balloon angioplasty. Clinicians should be aware of this and consider follow-up vascular imaging in post-SAH balloon angioplastied vasospasm. Future study is required on the pathophysiology and treatment paradigms necessary for this delayed restenosis.

Conflicts of Interest/Disclosures

The senior author (A.M. Malek) has received research funding from Stryker Neurovascular and Siemens Inc. for research that is unrelated to the submitted work. The other author reports no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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