Original Article

Cerebral artery restenosis following transluminal balloon angioplasty for vasospasm after subarachnoid hemorrhage

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Received: 3 September 2010 Accepted: 14 March 2011 Published: 19 April 2011

This article may be cited as: Umeoka K, Kominami S, Mizunari T, Murai Y, Kobayashi S, Teramoto A. Cerebral artery restenosis following transluminal balloon angioplasty for vasospasm after subarachnoid hemorrhage. Surg Neurol Int 2011;2:43.

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Abstract

Background: Although percutaneous transluminal angioplasty (PTA) is a widely used less invasive method to treat coronary artery stenosis, 10% of treated patients experience restenosis. Restenosis also occurs in approximately 5% of patients subjected to carotid artery stenting. Animal and human data suggested that restenosis is a response to injury incurred during PTA. As PTA has come into wide use to manage symptomatic cerebral vasospasm after subarachnoid hemorrhage (SAH) we studied the incidence of restenosis after PTA for cerebral vasospasm.

Methods: Our study population consisted of 32 patients who had undergone PTA. They were followed by cerebral or 3DCT angiography or MRA for 6-126 months post-PTA (mean 48.65 months) to diagnose restenosis of the cerebral artery. We compared the size of the cerebral artery on the PTA and the contralateral side.

Results: All 32 patients underwent successful PTA of 38 vascular territories and all manifested angiographic improvement of vasospasm. None suffered restenosis during the follow up period.

Conclusion: PTA resulted in a significant improvement in the vessel diameter in patients with vasospasm after SAH and they did not suffer restenosis in the course of prolonged follow-up.

Key Words: Percutaneous transluminal angioplasty, restenosis, subarachnoid hemorrhage, vasospasm

INTRODUCTION

Symptomatic cerebral vasospasm is the most common contributor to acute focal ischemia after aneurysmal subarachnoid hemorrhage (SAH) and at least two-thirds of SAH patients present with angiographic evidence of some degree of vessel narrowing between days 4 and 14.[19] As a 1.5 to 3 fold increase in morbidity and mortality during the first 2 weeks after aneurysmal SAH is attributable to cerebral vasospasm,[18,19,20,26] its prompt recognition and treatment may improve treatment outcomes. The first line treatment for cerebral vasospasm is blood pressure elevation, volume expansion, and hemodilution (triple H therapy).[18,19,21] However, up to 40% of patients fail to respond.[2,11] Zubkov et al.[29] first reported performing PTA in patients with cerebral vasospasm. Subsequently,
its safety and efficacy for reversing cerebral vasospasm have been documented.\[3,7,14,23,29\] Although PTA is now widely used as a less invasive method to treat coronary artery stenosis, 10% of patients suffer restenosis.\[12\]

Restenosis also occurs after carotid artery stenting (CAS) in no less than 5% of patients\[16,17,24\] and in 36% of patients who had undergone stenting to treat intracranial atherosclerosis.\[25\] The rate of restenosis after PTA for cerebral vasospasm remains to be investigated. In animal models, atherosclerotic vessels manifested a more severe degree of restenosis\[6,11\] and Tsuruta et al.\[27\] developed a model of post angioplasty stenosis using rats fed a normal diet. Normal arteries may develop cerebral vasospasm, and PTA is the technique used to expand these vessels. We investigated the incidence of restenosis after PTA for cerebral vasospasm.

**MATERIALS AND METHODS**

We reviewed 32 patients with aneurysmal SAH who suffered symptomatic cerebral vasospasm and were treated with PTA between 1995 and 2009. All underwent aneurysmal clipping within 2 days of rupture. Clinically suspected symptomatic vasospasm was considered an indication for diagnostic four vessel cerebral angiography. Diagnostic angiograms were obtained to confirm the adequacy of aneurysmal clipping and the presence of vasospasm. Vasospasm was considered severe when there was angiographic evidence of narrowing of the arterial lumen by more than 50% of the normal caliber. Patients with angiographically confirmed vasospasm and patients in whom the distribution explained the deficit underwent PTA. Arterial access was gained via a 90 cm 6Fr sheath (Envoy, MPC, Cordis, Johnson and Johnson, Tokyo, Japan) placed percutaneously in the femoral artery. A 2.5 to 5.0 mm 0.08 mL PTA catheter (model TRANVAS, MAVI balloon, Kaneka Medix, Osaka, Japan) was advanced coaxially through a guide catheter. Subsequently, mechanical dilation by PTA was performed to treat proximal vasospasm. Angioplasty balloons were inflated for 2 s to the vessel diameter; the procedure was usually performed segmentally from distal to proximal points. All angioplasty balloon manipulations were under systemic heparinization (5000 U) performed immediately before balloon introduction and not reversed after the procedure. A postangioplasty angiogram was obtained in all cases to evaluate changes in the vessel caliber and to identify any vessel damage. No arteries were expanded beyond their normal diameter during angioplasty, and no balloon ruptures occurred. After their return to the neurosurgical intensive care unit the patients received standard medical management for vasospasm. After intensive care we performed 3DCTA, angiography, or MRA to diagnose aneurysmal recurrence and arterial restenosis.

**RESULTS**

Our study included 32 patients (12 men and 20 women, mean age 51.7 years, range 27-80 years) with aneurysms in the anterior circulation. PTA was used successfully to treat 38 vascular territories in the 32 patients with post SAH vasospasm. The patient characteristics are shown in Table 1. All patients manifested angiographic improvement of vasospasm. Follow up was by cerebral or 3DCT angiography or MRA and ranged from 6 to 126 months (mean 12 months) to diagnose restenosis of the cerebral artery. Comparison of the size of the cerebral artery on the PTA and the contralateral side indicated that none of the 32 patients suffered restenosis.

### Table 1: Characteristics of our 32 patients with percutaneous transluminal angioplasty for cerebral vasospasm

| Case | Age/Sex | Site of PTA | Duration of follow-up (months) |
|------|---------|-------------|-------------------------------|
| 1    | 80/F    | bil M1      | 50                            |
| 2    | 59/M    | Lt M1       | 22                            |
| 3    | 36/F    | bil M1      | 50                            |
| 4    | 36/F    | Lt M1       | 16                            |
| 5    | 55/F    | Rt M1       | 9                             |
| 6    | 40/F    | bil M1      | 126                           |
| 7    | 42/F    | bil M1      | 120                           |
| 8    | 59/F    | Rt M1       | 116                           |
| 9    | 51/F    | Lt A1 M1    | 107                           |
| 10   | 44/M    | bil M1      | 37                            |
| 11   | 58/M    | Lt A1       | 90                            |
| 12   | 51/F    | bil IC M1   | 26                            |
| 13   | 51/M    | Lt M1 A1    | 32                            |
| 14   | 51/M    | Rt IC M1 A1 | 91                            |
| 15   | 51/M    | Lt M1 A1    | 91                            |
| 16   | 55/M    | bil A1 M1   | 93                            |
| 17   | 45/F    | bil IC M1   | 84                            |
| 18   | 38/M    | Lt M1       | 51                            |
| 19   | 76/F    | Lt M1       | 6                             |
| 20   | 54/F    | Rt M1       | 8                             |
| 21   | 36/M    | Lt M1       | 15                            |
| 22   | 44/F    | bil M1      | 9                             |
| 23   | 65/F    | Lt A1 M1    | 20                            |
| 24   | 54/M    | Rt M1       | 33                            |
| 25   | 27/M    | Lt M1       | 10                            |
| 26   | 67/M    | Rt M1       | 110                           |
| 27   | 73/F    | Rt M1       | 31                            |
| 28   | 55/F    | bil M1      | 37                            |
| 29   | 63/F    | Rt M1       | 18                            |
| 30   | 43/F    | bil A1 M1   | 22                            |
| 31   | 62/F    | bil M1      | 20                            |
| 32   | 36/M    | Lt IC       | 7                             |

M1: M1 portion of the MCA, A1: A1 portion of the ACA, ICA: Internal carotid artery, PTA: Percutaneous transluminal angioplasty
ILLUSTRATIVE CASE

A 36 year old woman presented with massive SAH due to a dorsal aneurysm at the left internal carotid artery (Hunt and Hess grade III, Fisher group 3). She underwent trapping of the left internal carotid artery and a radial artery external carotid artery bypass involving the M2 portion of the MCA. Although she responded well to verbal commands after the operation, one week later she developed consciousness disturbance; the mean TCD velocity was increased to 140 cm/s. Emergent angiography demonstrated severe spasms of the M1 portion of the MCA and the A1 portion of the ACA [Figure 1a]. Immediate PTA to the M1 portion of the MCA resulted in normalization of the vessel size [Figure 1b]; her consciousness disturbance improved and the mean TCD velocity was 80 cm/sec. She was discharged 1 month later without neurological deficit. She was followed at regular intervals and 3DCTA obtained 50 months after PTA yielded no evidence of MCA restenosis [Figure 1c].

DISCUSSION

Our assessment of the incidence of restenosis after PTA for post SAH vasospasm documented no restenosis in the course of prolonged follow up.

Suggested mechanisms underlying the occurrence of restenosis include intimal hyperplasia[4,5,28] attributable to the migration and proliferation of vascular smooth muscle cells and the migration and myofibroblastic transformation of adventitia cells.[9,28] Platelets and inflammatory cells such as macrophages and lymphocytes accumulate after endothelial and medial injury.[4]

Wound healing after PTA is dominated by smooth muscle cells.[28] Wall lacerations that occur during PTA expose smooth muscle cells to blood, an event that initiates an excessive fibrocellular tissue response.[9]

PTA restenosis is usually related to atherosclerotic lesions in extracranial and intracranial vessels and not normal endothelialization. We posit that in our patients, the absence of restenosis after intracranial angioplasty for vasospasm was attributable to the absence of atherosclerosis in the vessel wall.

Transmission electron micrographs of arterial walls after PTA showed flattening of endothelial cells, straightening and thinning of the internal elastic lamina, and straightening and crowding of the smooth muscle cells in the tunica media without evidence of frank rupture. These observations suggest that cellular and subcellular mechanical disruption may result in the post PTA impairment of smooth muscle function.[1,23] Mechanical injury to the arterial wall during PTA may produce hyperplasia and result in restenosis of the treated arterial segment. Andersen et al.[1] who developed a stenotic model using an oversized chain encircled angioplasty balloon produced a circumferential deep vessel wall injury in pigs by inflating and withdrawing the balloon in the coronary artery. They hypothesized that in their model, deep vessel wall injury induced an exuberant circumferential healing response thereby increasing the risk for stenosis.

In a canine model of cerebral vasospasms, histological evaluation of the PTA segments immediately after PTA showed denuding of endothelial cells and stretching of the internal elastic lamina without disruption of the muscle layer.[22] These histological changes are different from the vascular changes usually observed after PTA for atherosclerotic arteries such as destruction of the vascular structure, desquamation, and splitting of the media or internal elastic layer.[20]
In our patients the angioplasty balloons were inflated to the vessel diameter and no arteries were expanded beyond their normal diameter during the procedure. Consequently, there was no mechanical injury to the arterial wall and there were no restenotic sequelae in any of the 32 patients. PTA should only be performed by expert operators, taking care that there is no damage to the vascular endothelium.

**CONCLUSION**

PTA is a less invasive method to treat cerebral vasospasm after aneurysmal SAH. Mechanical injury to the arterial wall during PTA may result in post-PTA restenosis. Only expert operators should perform PTA and damage to the vascular endothelium must be avoided.

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