Special Report

A Practical Approach to the Treatment of Vasospasm

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Subarachnoid hemorrhage from a ruptured aneurysm remains a devastating disease (1–8). In as many as one third of survivors, symptomatic vasospasm poses a significant clinical problem that can result in aphasia, hemiparesis, coma, and even death (4, 6, 9). Over the past decade, progress has been made in the treatment of vasospasm through the use of endovascular techniques. Percutaneous transluminal balloon angioplasty and intraarterial papaverine infusion have been effective in some patients (10–19).

The clinical effectiveness of angioplasty has been noted in several published series (10, 11, 13, 15). It can restore neurologic function impaired by vasospasm. A report of patients presenting with proved symptomatic vasospasm and an unclipped but ruptured aneurysm described that urgent surgical obliteration of the aneurysm followed by immediate postoperative angioplasty improved outcome in 80% (20). Other studies in several patients with clipped aneurysms and significant vasospasm recommend early and aggressive angioplasty (12, 21).

Despite these reports, timely angioplasty is an underused technique, perhaps in part because of the reluctance of many neuroradiologists to offer and perform angioplasty for vasospasm.

This paper describes our approach to the endovascular treatment of vasospasm. The specific nature of the description is not meant to imply that it is the only safe and reasonable approach. Rather, it is intended to provide practical and detailed information to those who want to perform these procedures.

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Angioplasty Technique

Typically, one is confronted on the angiography table with a patient in whom vasospasm has been diagnosed in a distribution that correlates with neurologic deficit, and endovascular treatment has been requested. Neurosurgical intensive care treatment including hypertensive, hypervolemic therapy has failed; other causes of new neurologic deficit such as hematoma, cerebral swelling, and hydrocephalus have been excluded; and preprocedure computed tomography (CT) has failed to show an infarct.

Before the diagnostic angiogram, in anticipation of the use of angioplasty for vasospasm, consent from the patient's family is obtained only after fully explaining its 2% to 5% periprocedure risk of stroke or death (12). Although not mandatory, consent is also obtained to intubate and paralyze the patient to allow the use of effective digital roadmapping, which significantly decreases procedure time and risk of technical complication.

The diagnostic catheter in the femoral artery is replaced with a 6F sheath, through which either a 6F Fasguide (Target Therapeutics Corp, Fremont, Calif) or 6F Envoy (Cordis, Miami, Fla) guiding catheter is placed with its tip positioned in the cervical internal carotid artery or dominant proximal vertebral artery, depending on which vascular territory is to be treated. Although the optimal anticoagulation regimen is not well established for this technique, and although debate exists regarding the use of full anticoagulation in patients with an acute subarachnoid hemorrhage who have undergone craniotomy, our tendency is to anticoagulate fully with an initial bolus of 5000 to 7000 U of intravenous heparin followed by an additional 1000 to 2000 U/h, with adequate anticoagulation confirmed by an activated coagulation time greater than 300 seconds. A continuous heparinized saline infusion through the catheter is also started.

A nondetachable silicone balloon is used for these procedures. In the majority of cases, a

4-mm nondetachable low-pressure silicone balloon that is attached to a Tracker (Target Therapeutics) microcatheter (ITC NDSB/8502, 0.2-mL maximum volume, 0.85-mm diameter/ 4.1-mm length deflated, 4.2-mm diameter/ 11.0-mm length inflated, 2F/4.2F coaxial catheter delivery system) is then inflated with a solution of 50% contrast and saline. Any resultant air in the balloon will permeate out through the silicone membrane in the next 5 to 10 minutes. When the balloon is free of air, a 0.010-in guidewire is slowly inserted into the microcatheter until the tip rests just proximal to the end of the balloon. The small size of the wire allows contrast to pass back through the microcatheter without excessive overinflation of the balloon during wire insertion. Once the tip is in position, a torque device is securely tightened on the guidewire at the hub to prevent premature advancement of the tip out the end of the balloon. The balloon and guidewire combination is then placed through a rotating homeostatic valve and attached to the guiding catheter.

At this point, the image intensifier is placed in the lateral projection and a digital roadmap of the carotid artery is made. It should be stressed that excellent digital roadmapping is crucial to perform angioplasty safely and significantly expedites procedure protocol. Minimizing head and neck movement in an intubated and paralyzed patient should not be difficult in coordination with the anesthesiologist. The procedure should not continue until an adequate digital roadmap is present and maintainable.

Through the guiding catheter and with the guidance of the roadmap, the balloon catheter and wire system is advanced past the cervical portion and into the cavernous segment of the internal carotid artery. Occasionally, the balloon will pass distal to the ophthalmic artery, but it often stops in the horizontal portion of the cavernous carotid just proximal to the ophthalmic artery. At this time, the guidewire is slowly removed as contrast is dripped into the hub to prevent air from entering the microcatheter during guidewire removal.

Next, a 1-mL luer-lock syringe is attached to the hub of the microcatheter and the balloon is slowly test inflated in the horizontal portion of the cavernous segment of the internal carotid artery. Multiple small inflations of the balloon are executed under fluoroscopy to ascertain the responsiveness of the balloon. The microcatheter is advanced with the balloon slightly in-

flated, enabling the balloon to advance beyond the ophthalmic artery into the supraclinoid segment. If this vessel is stenotic from vasospasm, balloon angioplasty is started here.

There are anecdotal reports of rupture of an internal carotid or vertebrobasilar vessel during the first attempt at balloon angioplasty. In most cases, vessel rupture most likely results from overly aggressive full inflation of the balloon during the first dilation. Unlike peripheral vascular angioplasty (a technique most radiologists have learned), in which the balloon is inflated to its near-maximum volume with high pressures to stretch the vessel and crack the atherosclerotic intima, in vasospasm angioplasty the balloon is inflated in relatively more pliable vessels that are stenotic not from atherosclerosis but from intimal and medial thickening (caused by edema, necrosis, proliferation, and later, fibrosis) and adventitial inflammation (22–28).

Although there are no scientific studies to determine whether one long inflation is better than multiple small inflations in mechanically dilating vasospastic cerebral vessels, we espouse a progressive sequence of cautious, gentle, and graduated balloon inflations, on the basis not necessarily of effectiveness in achieving luminal dilation but of safety. Cautious, gentle, and graduated balloon inflations allow the interventionalist to develop a "feel" for a vasospastic vessel, which we believe decreases the risk of catastrophic vessel rupture or occlusion. The vasospasm might be acute and soft, requiring very few dilations to open the vessel, or it might be chronic and more fibrotic, requiring up to an order of magnitude more inflations.

The basic technique of safe and successful intracranial angioplasty centers on a four-step inflation sequence (Fig 1). First, the low-pressure balloon is cautiously inflated so that it barely starts to expand in the spastic vessel. The second balloon inflation is only slightly larger than the first, the third inflation only slightly larger than the second, and the fourth slightly larger than the third. The duration of each inflation is only 1 to 2 seconds, less for the first dilation. The balloon is then advanced to the next segment of narrowing and the sequence repeated.

Dural reflections allow subarachnoid hemorrhage to pool about the supraclinoid carotid artery and the distal vertebral artery near the origin of the posterior inferior cerebellar artery
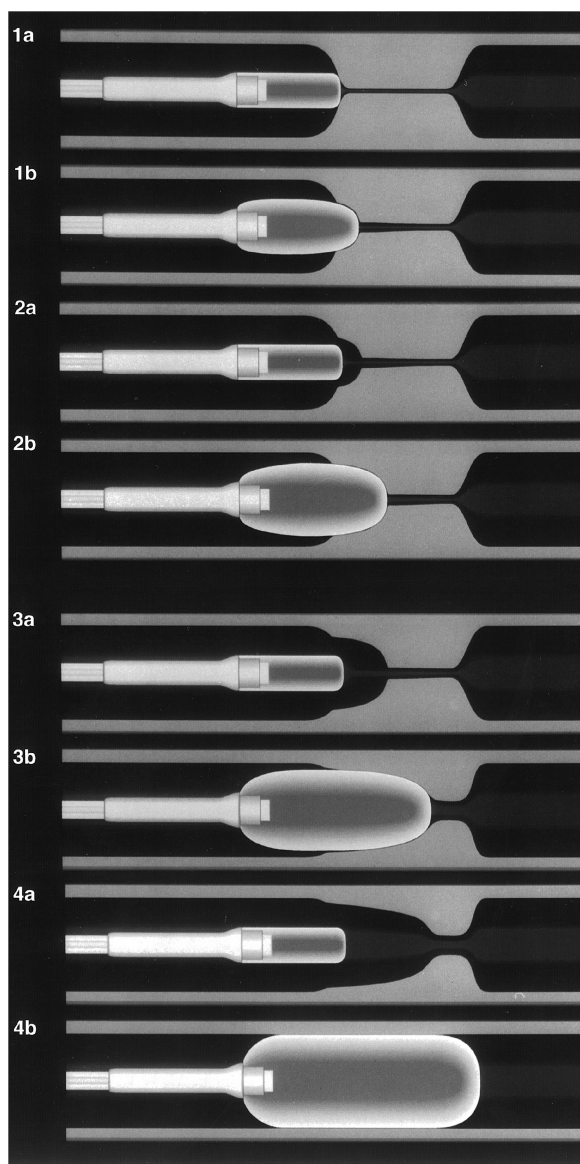
Fig 1. Angioplasty of vasospasm should be performed in a progressive manner to avoid overdilation and risk of vessel rupture. *1a* and *b* show the balloon 25% inflated; *2a* and *b*, 50% inflated; *3a* and *b*, 75% inflated; and *4a* and *b* show full balloon inflation. The balloon is then advanced to the edge of narrowing and the sequence is repeated.

(PICA), increasing the severity of vasospasm at these locations (29–31). Consequently, the supraclinoid segment of the carotid artery will often be one of the most difficult areas to do angioplasty. With patience and extreme caution, the spastic supraclinoid segment will usually dilate, but it can require up to 40 or 50 small gradual inflations. If the low-pressure silicone balloon fails to open the narrowed supraclinoid carotid, a higher-pressure balloon could be needed (Sub-4, Meditech, Watertown, Mass;

outside diameter 3.0 mm, length 5 mm, accepts 0.018-in guidewire, up to 10 atm) but should be used with caution.

Once the supraclinoid segment is open, the balloon is advanced into the proximal middle cerebral artery (MCA). At this point, a digital roadmap is repeated but in the anterior projection. If vasospasm is present in the proximal MCA, it is dilated with an identical technique, using repetitions of the low-pressure four-step inflation sequence (Fig 2). In the MCA, it is wise to stop at the M2 division. Once the balloon passes beyond this segment, its size begins to exceed that of the vessel, significantly increasing the chance of rupture (32).

It is usually (less than 10% of the time in our experience [unpublished data, May 1996]) not possible to perform angioplasty in the A1 segment of the anterior cerebral artery (ACA) if it is stenotic (12, 13, 33). Fortunately, opening the supraclinoid carotid artery and MCA usually improves flow through the ACA despite the persistent narrowing in the A1 segment. However, if the A1 segment remains significantly narrowed and the microcatheter cannot be securely positioned into the proximal ACA, the balloon can be temporarily inflated in the MCA and papaverine infused in the internal carotid artery via the guiding catheter in an attempt to drive all the papaverine into the ACA territory (Fig 3) (12). If the initial diagnostic angiogram in the workup of subarachnoid hemorrhage shows a generous prespasm A1 segment, a low-profile over-the-wire balloon can be used with a steerable microguidewire (Stealth Dilatation System/ 120502, Target Therapeutics; 2.5-mm diameter, 10-mm length) for angioplasty in vasospastic A1 segments in selected patients.

The dominant vertebral artery in vasospasm should also be treated with angioplasty when at all possible. The technique in the vertebrobasilar system is the same (Fig 4). Again, a 4-mm nondetachable silicone balloon is typically used. Vasospasm usually starts in the distal vertebral artery just below the origin of the PICA. Much like the supraclinoid segment of the carotid, this segment of the distal vertebral artery is difficult for angioplasty. Once the distal vertebral artery has been opened, as with the supraclinoid carotid, subsequent dilations become easier.

Again, with the aid of digital roadmapping in the anterior projection, the balloon is gradually inflated and deflated with multiple successive

Fig 2. *A*, Left internal carotid artery angiogram, anterior projection, of a hemiplegic patient shows severe vasospasm of the supraclinoid carotid artery, proximal ACA, and MCA (*arrows*).

B, Postangioplasty angiogram shows return to normal caliber of the supraclinoid carotid, proximal ACA, and MCA, resulting in the resolution of the patient's hemiparesis within the next 24 hours.
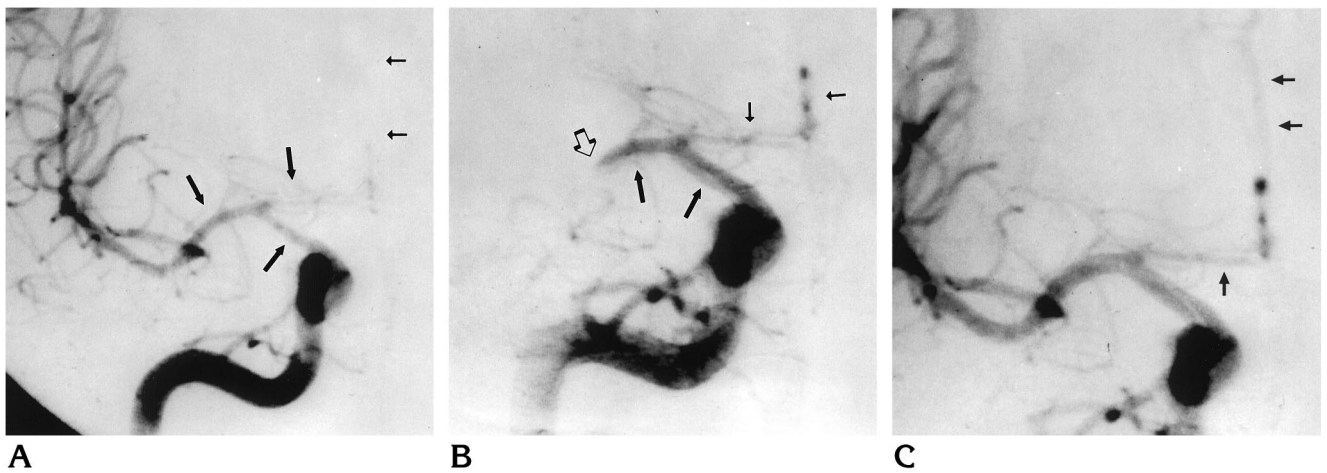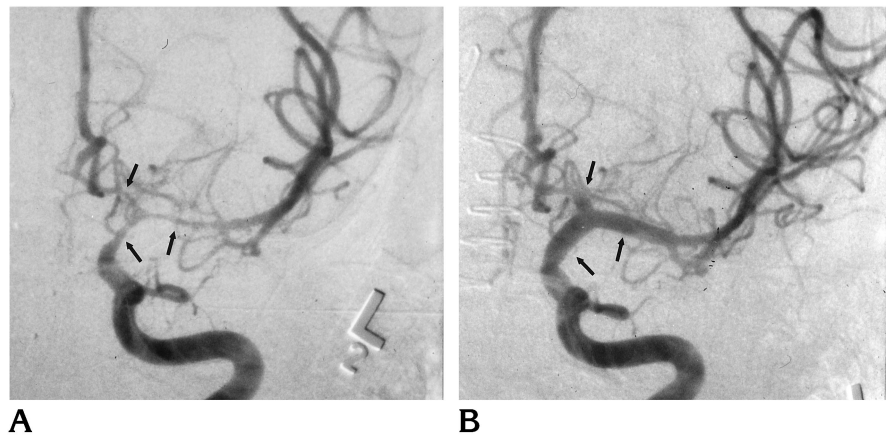

Fig 3. *A*, Right internal carotid artery angiogram, anterior projection, shows moderate vasospasm in the supraclinoid carotid artery and MCA (*large arrows*) and severe narrowing in the proximal ACA (*small arrows*). Note minimal distal ACA vessel filling.

B, After the supraclinoid carotid artery and MCA were dilated with angioplasty (*large arrows*), the balloon was temporarily inflated in the MCA (*open arrow*) and 360 mg of intraarterial papaverine was infused into the internal carotid artery through the guiding catheter to direct the papaverine into the proximal ACA segment (*small arrows*).

C, Postprocedure angiogram shows normal caliber of the supraclinoid carotid artery, MCA, and proximal ACA with improved filling of the distal ACA branches (*arrows*).

expansions up through the vertebral artery and then to the basilar artery. Usually, angioplasty is stopped at the tip of the basilar artery. But if it is definitely known from previous angiograms that the P1 segments of the posterior cerebral arteries (PCA) are not hypoplastic and quite large, then the origins of the PCAs can sometimes be safely dilated. However, it is not essential that the balloon be passed into the proximal PCA segments. Moreover, just as the balloon should not be advanced past the M2 division of the MCA, it should not be advanced beyond the P1 segment of the PCA, as the risk of vessel rupture becomes exceedingly high. Most of the time it is unnecessary to dilate both distal vertebral arteries. Angioplasty of one distal vertebral artery and the basilar artery will usually suffice.

Patient Selection

In our institution, angioplasty has been used early and often to treat symptomatic vasospasm in over 150 patients (more than 400 vessel segments) since 1988. We treat angiographically documented vasospasm in any patient with an unexplained neurologic deficit. Every effort is made to treat these patients within a few hours of symptom onset. The best results occur when the patients are treated within 12 to 18 hours of the onset of symptoms that are attributable to vasospasm. Although less common, delayed recovery does occur, with some patients completely recovering after experiencing symptomatic vasospasm for 72 hours before angioplasty.
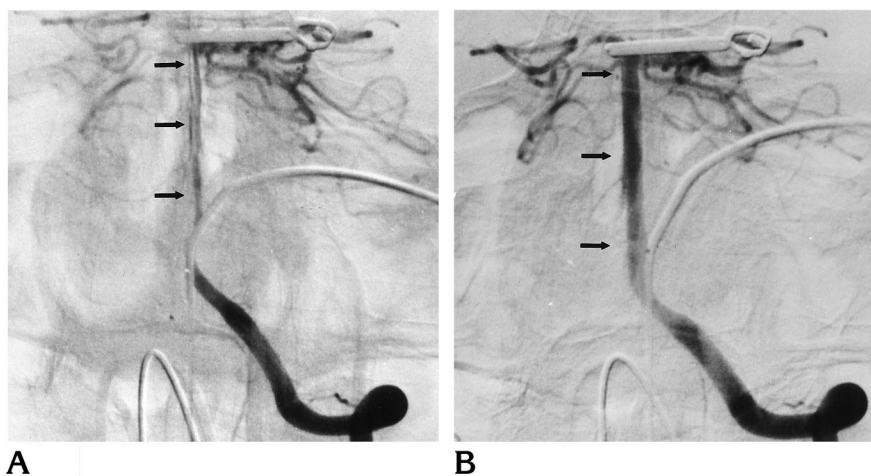
Fig 4. *A*, Left vertebral artery angiogram, anterior projection, shows severe vasospasm of the distal left vertebral artery and proximal basilar artery (*arrows*). Four hours before angioplasty, the patient was comatose and had respiratory arrest.

B, Postangioplasty angiogram shows normal flow through the distal left vertebral and basilar arteries (*arrows*). During the next 12 hours, the patient was extubated and awoke without neurologic deficit.

Treating vasospasm in the presence of infarcts is controversial. For many years, we were reluctant to perform angioplasty if there was any CT evidence of ischemia because of the fear of reperfusion hemorrhage. Over time, we did perform angioplasty in patients who were *in extremis* and found that reperfusion hemorrhage did not develop. Gradually, our reluctance was overcome and now these patients are also treated aggressively. Nonetheless, if a large ischemic area is present in the MCA distribution, it would probably be unwise to proceed with angioplasty. If small areas of low density are present on head CT, they may represent not ischemia but edema from surgical retraction. In this situation, it is probably wiser to proceed with angioplasty, since the risk of hemiparesis from vasospasm outweighs the risk of a small reperfusion hemorrhage.

Early Diagnosis

In the past, the extent of vessel narrowing could be determined only with conventional angiography, an imaging modality obviously not suitable as a serial monitoring technique because of its invasiveness and the need for patient transport away from the neurosurgical intensive care unit. The recent development of transcranial Doppler (TCD) ultrasonography has made possible the noninvasive diagnosis of vasospasm in its earliest stages and at the bedside (34–36). Systolic, diastolic, and mean velocities of basal intracranial vessels can be recorded using a 2-MHz ultrasonic frequency, which allows penetration of the thin portions of the cranial vault. TCD is technically feasible in nearly all cases and is directed toward the prox-

imal basal segments of major intracranial arteries where vasospasm is most likely to occur (37). Any lesion, such as vasospasm, that results in stenosis is expected to increase blood flow velocity through the stenotic area in proportion to the reduction in cross-sectional area. A close correlation between blood flow velocities and the degree of angiographic narrowing has been shown (43).

The normal blood flow velocity range for the proximal middle cerebral artery is 30 to 80 cm/s with an average of 62 cm/s (34). Mild to moderate arterial spasm of the MCA correlates with a TCD velocity of greater than 120 cm/s, with a velocity greater than 200 cm/s indicative of severe vasospasm. The ratio of the proximal MCA or distal internal carotid artery velocities to the cervical internal carotid artery—the Lindegaard ratio—is calculated to differentiate generalized increased blood flow (hyperemia) from vasospasm, with a ratio greater than 3 indicative of vasospasm (38). The sensitivity and specificity of TCD in showing MCA vasospasm are approximately 85% and 90%, respectively (39–42). Although specific velocity levels that correspond to the degree of vasospasm have not been firmly established for the posterior circulation vessels, a trend of increasing blood flow velocities in the basilar and distal vertebral arteries suggests vasospasm.

When TCD velocities are significantly higher, it is an indication that vasospasm is developing. Because vasospasm can occur in a patient not experiencing clinical deterioration, once TCD documents vasospasm, hypertensive and hypervolemic medical therapy is added to the patient's calcium channel-blocker regimen. Therefore, at the earliest sign of asymptomatic vaso-

spasm, the patient is given maximum medical therapy. If the patient progresses to symptomatic vasospasm in the next 2 or 3 days, the trial of maximum medical therapy has failed, and angioplasty is immediately pursued.

In addition to TCD, single-photon emission CT (SPECT) is valuable in assessing patients with poor grades who cannot be easily evaluated for clinical deterioration (43). In these patients, a regional cerebral perfusion defect on SPECT and evidence of vasospasm on TCD indicate that angioplasty should be urgently pursued to prevent impending cerebral infarction.

Unfortunately, in many institutions TCD is not available. Therefore, aggressive medical therapy is not started until the patient has become symptomatic from vasospasm, with the tendency to wait 24 hours or longer to determine whether the medical therapy will reverse the symptoms. It almost never does, and then angioplasty is tried. As a result, at least 24 hours have been lost and the chances of the vasospasm's improving clinical outcome are drastically reduced. The patient must be treated early in the disease to have a good chance of recovery; therefore, the availability of TCD is instrumental to the success of angioplasty of vasospasm.

Papaverine

Overall, the clinical results of intraarterial papaverine for the treatment of vasospasm have been disappointing, with clinical response rates as low as 25% (17–19). There is no question that intraarterial injections of papaverine can dilate the arteries as documented by angiography. Unfortunately, the vasodilatory effect lasts only a short time, and there is no strong evidence of sustained clinical improvement in patients treated only with papaverine for symptomatic vasospasm. It appears that the durability and reliability of dilatory effects of intraarterial papaverine are less than typical with angioplasty (44).

Although papaverine has failed to replace angioplasty as the primary treatment for symptomatic vasospasm, it is useful in some situations. For example, papaverine is routinely used to treat distal vasospasm (distal to the M2 division of the MCA and P1 segment of the PCA) after angioplasty of the proximal vessels. As

with angioplasty, papaverine is more likely to be effective in early vasospasm (45).

A typical dose of papaverine is 300 mg/100 mL saline infused over 30 to 60 minutes (19, 46). The spectrum of adverse effects of papaverine is broad and includes drug precipitation, transient neurologic dysfunction, and paradoxical aggravation of vasospasm (47–50). Another concern of papaverine infusion is its tendency to increase intracranial pressure (ICP) (46). The infusion of papaverine can easily double the ICP. From a technical standpoint during slow hand infusion of papaverine, ICP is vigilantly monitored. As the ICP increases, the rate of papaverine infusion is decreased. The increase in ICP associated with papaverine infusion makes it imperative that the patient be intubated and well ventilated. A dangerous situation can result when a patient is not intubated and sedation is given to limit patient motion. This can result in a decrease in respiratory rate, which will increase P_{CO_2}, increasing the ICP, and if papaverine is infused, the ICP can skyrocket, placing the patient at high risk for an intracranial hemorrhage or infarct.

Clinical Results

In our institution, based on an analysis of the first 50 patients (now more than 150) who underwent angioplasty (170 vessel segments: 114 anterior circulation; 46 posterior circulation) for symptomatic vasospasm, 60% showed a significant and sustained neurologic improvement— defined as a two-level increase in motor strength or a two-point increase in the Glasgow Coma Scale (GCS) score (51, 52); an increase in GCS of one plus complete clearance of a previously clouded sensorium; or resolution of mild weakness or focal neurologic impairment such as homonymous hemianopsia—within 72 hours of angioplasty (unpublished data, August 1995). Thirty-two (64%) were treated within 12 hours of symptom onset; 46 (92%) within 18 hours. Fifteen (30%) patients did not objectively improve within 72 hours of angioplasty, although angiographic dilatation did occur. Two of the first 50 patients died from vessel rupture during angioplasty (4% procedure-related mortality). In one patient, transient mild right arm weakness developed 6 weeks after angioplasty. In this patient, a high-pressure balloon ruptured in a middle cerebral branch without adverse sequelae at the time of the immediate postan-

gioplasty angiogram. Repeat angiography at the time of this delayed deficit showed that this branch had become occluded. None of the other first 50 patients showed any permanent or temporary deficits with long-term follow-up, indirect supportive evidence that there is no long-term vessel damage after angioplasty. In a 10-year review of 224 good-grade patients treated for aneurysmal subarachnoid hemorrhage at our institution, 39 (17.4%) patients experienced symptomatic vasospasm, 22 treated with angioplasty, 17 treated without (not available before 1988). Comparing these two groups of good-grade patients, of those treated with angioplasty 95.5% had a favorable outcome, whereas of those not treated 76.5% had a favorable outcome (21).

Conclusion

Despite maximum medical treatment, some patients with symptomatic vasospasm will continue to deteriorate. In these patients, the judicious use of angioplasty and, in selected cases, intraarterial papaverine infusion can be effective in reversing delayed ischemic deficit caused by vasospasm. The 2% to 5% mortality rate of angioplasty should not dissuade us from treating these patients by endovascular techniques.

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