

Accuracy in Identifying the Source of Subarachnoid Hemorrhage in the Setting of Multiple Intracranial Aneurysms

Jennifer L. Orning, MD
 Sophia F. Shakur, MD
 Ali Alaraj, MD
 Mandana Behbahani, MD
 Fady T. Charbel, MD
 Victor A. Aletich, MD
 Sepideh Amin-Hanjani, MD

Department of Neurosurgery, University of Illinois at Chicago, Chicago, Illinois

Correspondence:

Sepideh Amin-Hanjani, MD
 Department of Neurosurgery,
 University of Illinois at Chicago,
 912 South Wood Street, MC-799,
 Room 451N,
 Chicago, IL 60612.
 E-mail: hanjani@uic.edu

Received, November 1, 2016.

Accepted, May 16, 2017.

Published Online, June 26, 2017.

Copyright © 2017 by the
 Congress of Neurological Surgeons

BACKGROUND: Subarachnoid hemorrhage cases with multiple cerebral aneurysms frequently demonstrate a hemorrhage pattern that does not definitively delineate the source aneurysm. In these cases, rupture site is ascertained from angiographic features of the aneurysm such as size, morphology, and location.

OBJECTIVE: To examine the frequency with which such features lead to misidentification of the ruptured aneurysm.

METHODS: Records of patients who underwent surgical clipping of a ruptured aneurysm at our institution between 2004 and 2014 and had multiple aneurysms were retrospectively reviewed. A blinded neuroendovascular surgeon provided the rupture source based on the initial head computed tomography scans and digital subtraction angiography images. Operative reports were then assessed to confirm or refute the imaging-based determination of the rupture source.

RESULTS: One hundred fifty-one patients had multiple aneurysms. Seventy-one patients had definitive hemorrhage patterns on initial computed tomography scans and 80 patients had nondefinitive hemorrhage patterns. Thirteen (16.2%) of the cases with nondefinitive hemorrhage patterns had discordance between the imaging-based determination of the rupture source and intraoperative findings of the true ruptured aneurysm, yielding an imperfect positive predictive value of 83.8%. Of all multiple aneurysm cases with subarachnoid hemorrhage treated by surgical or endovascular means at our institution, 4.3% (13 of 303) were misidentified.

CONCLUSION: Morphological features cannot reliably be used to determine rupture site in cases with nondefinitive subarachnoid hemorrhage patterns. Microsurgical clipping, confirming obliteration of the ruptured lesion, may be preferentially indicated in these patients unless, alternatively, all lesions can be contemporaneously and safely treated with endovascular embolization.

KEY WORDS: Cerebral aneurysm, Multiple, Rupture, Subarachnoid hemorrhage

Neurosurgery 83:62–68, 2018

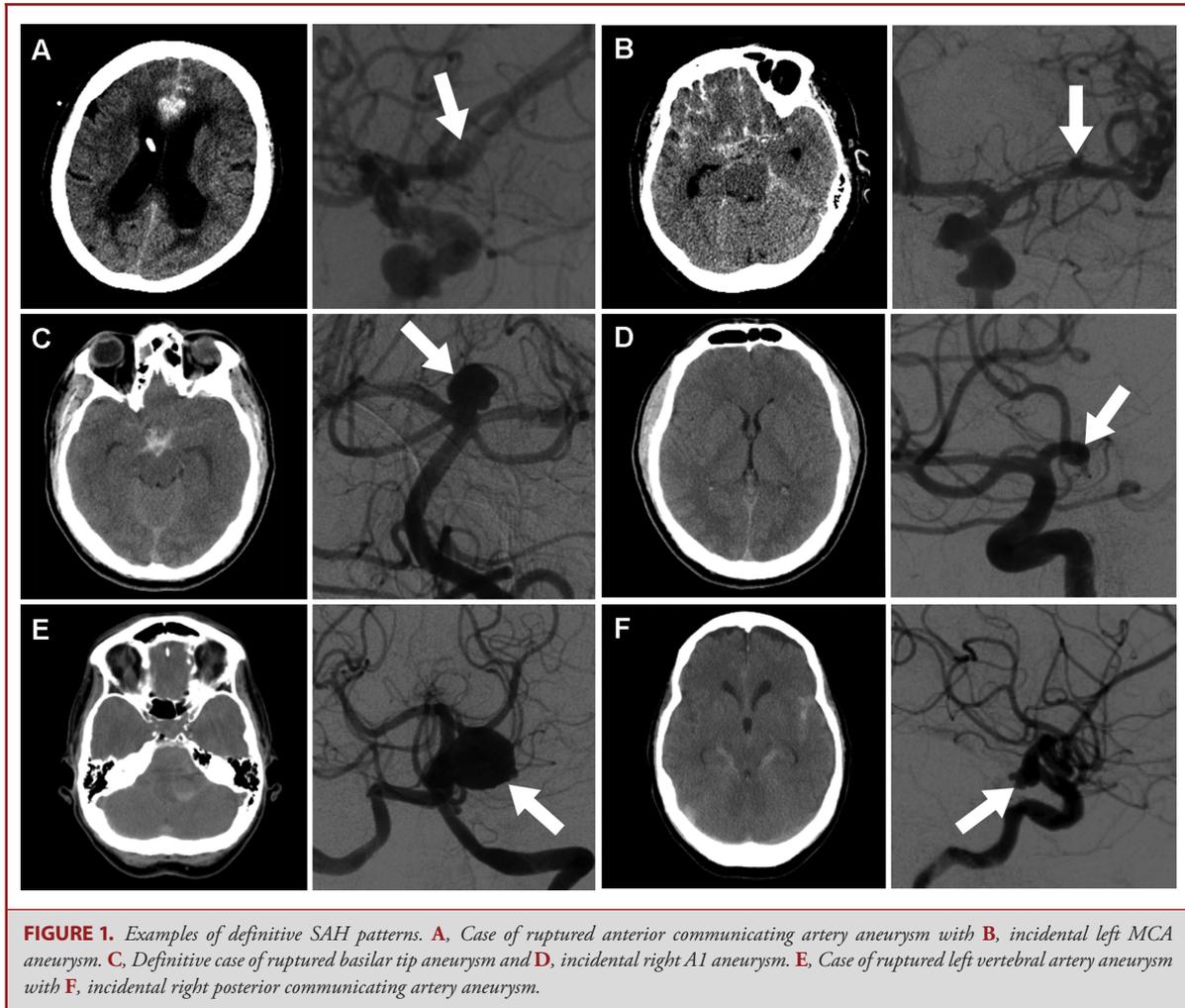
DOI:10.1093/neuros/nyx339

www.neurosurgery-online.com

Intracranial aneurysms are present in approximately 2% to 3% of the population^{1,2} and rupture leads to subarachnoid hemorrhage (SAH), with significant morbidity and mortality. Determining the source of rupture in the patient with SAH is imperative in

order to provide expedient surgical or endovascular treatment and avoid rebleeding. This determination can be more challenging when multiple intracranial aneurysms are present, as seen in 10.7% to 26.4% of patients.^{1,3-5} In this setting, the hemorrhage pattern is generally the primary indicator of the ruptured lesion. When the pattern is not definitive, however, rupture site determination typically relies on angiographic features of the aneurysm such as size, morphology, and location. In this study, we examined the frequency with which such features lead to misidentification of the ruptured lesion,

ABBREVIATIONS: CT, computed tomography; DSA, digital subtraction angiography; IRB, Institutional Review Board; MCA, middle cerebral artery; MRI, magnetic resonance imaging; SAH, subarachnoid hemorrhage



subsequently determined at the time of open microsurgical treatment.

METHODS

Institutional Review Board (IRB) approval was obtained; informed consent was waived by the IRB as this study was comprised of retrospective medical chart review and analysis of existing data. SAH cases that proceeded to craniotomy between January 1, 2004 and August 15, 2014 were reviewed retrospectively, and cases with multiple intracranial aneurysms were identified. The original determination of suspected rupture source was identified as documented in the clinical records at the time of presentation. In addition to the historical determination based on records, the initial head computed tomography (CT) scans and digital subtraction angiography (DSA) images were reviewed by a neuroendovascular surgeon (A.A.) blinded to the surgical findings but aware of aneurysm locations, and the pattern of hemorrhage was designated as “definitive” or “nondefinitive” for source aneurysm. Definitive bleed pattern was defined as that which was clearly lateralizing or of a

location or pattern specific to a particular aneurysm type, ie, interhemispheric predominance in a patient with only 1 anterior cerebral artery territory aneurysm, or predominantly right sided if only 1 aneurysm was located on the right (Figure 1). In those with “nondefinitive” hemorrhage patterns, the blinded reviewer provided their best determination of the rupture source using the combination of angiographic features and CT scan findings. Operative reports were then reviewed to confirm or refute the imaging-based determination of the rupture source.

RESULTS

Patient Characteristics

Five hundred thirty-one cases of aneurysmal SAH subsequently treated microsurgically were identified in the selected 10-yr time frame. Three hundred fifty-five were women (66.9%). One hundred fifty-one had multiple aneurysms found on initial imaging, with a female predominance (81.5%) and a mean of 3.4 (median of 2) aneurysms (range 2-10). A summary of all of the cases is provided in Table 1.

TABLE 1. Summary of All Cases

		Correct site	Incorrect site
Clipped aneurysms			
Total (n)	531		
Multiple aneurysms (n)	151		
Nondefinitive pattern (n)	80	67	13
Definitive pattern (n)	71	71	0
Coiled aneurysms			
Total (n)	494		
Multiple aneurysms (n)	152		
Single aneurysms (n)	342		

Correctly Identified Cases

Of the multiple aneurysm patients, 80 (53%) had nondefinitive hemorrhage patterns on initial CT scan. Of the 71 with definitive bleed patterns, all had the suspected rupture site confirmed to be accurate at the time of surgery. All of the determinations of rupture site by the blinded reviewer agreed with historical determinations from the records, in these definitive bleed pattern cases.

Misidentified Cases

On the other hand, 13 (16.2%) of the cases with nondefinitive hemorrhage patterns on CT had discordance between the intraoperative findings of the true ruptured aneurysm and the suspected rupture source by either the blinded reviewer ($n = 3$), original historical determination ($n = 2$), or both ($n = 8$; Table 2; Figure 2). This yields a positive predictive value of 83.8% in accurately identifying the true source of rupture based on imaging data. Considering only the historical determination of rupture site yields a positive predictive value for accurate identification of the rupture site of 88% (70/80); considering only the blinded review reveals a similar positive predictive value of 86% (69/80).

Illustrative Case

Patient 1 was a 56-yr-old female presenting with Hunt–Hess IV SAH. Her CT showed a diffuse pattern of SAH, and a right frontal craniotomy was placed. She was found on initial DSA to have a 2.5-mm right middle cerebral artery (MCA) aneurysm and a 4 mm × 2.5 mm anterior communicating artery aneurysm (see patient 1 in Table 2 and Figure 2). Due to the location, larger size, and dome irregularity, the anterior communicating artery aneurysm was thought to be the source of hemorrhage. However, the initial hemorrhage pattern had a slightly right-sided dominant hemorrhage pattern and, due to the relative uncertainty, microsurgical clipping was planned in order to treat both aneurysms via a right-sided approach.

The patient was consented for the procedure and a standard pterional craniotomy was performed, and the MCA aneurysm was visualized first due to splitting of the Sylvian fissure in approach to the anterior communicating artery aneurysm. There was SAH evident around the area and fibrin clot adjacent and

adherent to the aneurysm itself, especially at the dome, consistent with the MCA aneurysm being the true source of hemorrhage. This aneurysm was clipped first, and the approach was continued to dissect and clip the anterior communicating aneurysm as well, which showed no evidence of rupture. The patient recovered well overall and has since undergone follow-up DSA demonstrating good obliteration of both aneurysms.

DISCUSSION

Multiple aneurysms are not uncommon, and represented 28.4% of our surgically treated SAH cohort. Definitive treatment of the rupture source is the priority. In our series, a definitive pattern of hemorrhage clearly lateralizing or confined to an aneurysm site was highly accurate in correct identification of the rupture source. However, there was a notable inaccuracy (16.2%) in those cases with nondefinitive bleed patterns. These include a diffuse and symmetric SAH distribution, or simply a localized pattern, but with multiple aneurysms in that particular area, such as adjacent posterior communicating artery and anterior choroidal aneurysms, or multiple anterior cerebral artery aneurysms with an interhemispheric pattern of blood.

Morphological features can be used to judge certain aneurysms as being more at risk for hemorrhage, such as size, secondary dilatations, and irregular contours.^{2,6-8} Backes et al² demonstrated that aspect ratio rather than size was most important in their series as correlating with rupture.² Our data, however, reveal that despite consideration of morphological variables, the source of rupture can be misidentified in a substantial minority of cases. Even taken as a percentage of all the multiple aneurysms, 8.6% (13 of 151) were incorrectly assigned based on imaging review alone.

Recent reports indicate that specific magnetic resonance imaging (MRI) sequences can distinguish which of multiple aneurysms is the site of rupture. These include vessel wall imaging using contrast,⁹ susceptibility weighted imaging,¹⁰ or black blood sequences.¹¹ However, the reliability of such imaging is not certain. Studies of aneurysm wall enhancement, for example, have demonstrated that, although the incidence of enhancement was higher in ruptured aneurysms, up to 28.5% of stable unruptured aneurysms also demonstrate enhancement features.^{12,13}

In the setting of SAH and multiple aneurysms, treatment of coincident unruptured lesions is also potentially desirable given natural history data demonstrating higher future rupture risk in the setting of prior SAH.^{14,15} Some small aneurysms, depending on patient and location factors, may be observed and some authors would especially recommend conservative management of unruptured aneurysms in elderly patients ≥ 65 yr old.¹⁶ However, Chien et al¹⁷ demonstrated that multiple aneurysms are more likely to grow over time, especially posterior circulation aneurysms. Huhtakangas et al¹⁸ also demonstrated excess long-term mortality in SAH survivors after their initial recovery

TABLE 2. Misidentified cases: patient demographics and aneurysm characteristics

Patient	Age (years)	Number of aneurysms	Aneurysm locations	Morphology features ^a	Suspected location	Suspected aneurysm size (mm)	True source	True source size (mm)
1	56	2	R MCA bifurcation ACoA	Shape Second dilatation	ACoA	4	R MCA bifurcation	2.5
2	36	2	R MCA bifurcation L ICA terminus	Location	R MCA bifurcation	2.5	L ICA terminus	1.5
3	49	2	R M1 R MCA bifurcation	Size Shape	R M1	5	R MCA bifurcation	3
4	32	2	R MCA bifurcation ACoA	Size Second dilatation	ACoA	9	R MCA bifurcation	6
5	41	9	R ICA cavernous R ophthalmic R M1 ACoA L ICA paraclinoid L AChA L M1 L MCA bifurcation L SCA	Size Shape	L ICA paraclinoid	10	ACoA	2.8
6	51	4	R MCA bifurcation ACoA L M1 L MCA bifurcation	Location	ACoA	3.5	R MCA bifurcation	4
7	35	2	R ophthalmic L ICA paraclinoid	Location	R ophthalmic	3	L ICA paraclinoid	7.6
8	46	5	R AChA R ICA terminus ACoA L PCoA L paraophthalmic	Size	L paraophthalmic	12	ACoA	7
9	50	3	R ICA terminus R MCA bifurcation L MCA bifurcation	Shape	R ICA terminus	3.5	R MCA bifurcation	2.5
10	46	6	R ICA terminus R ICA paraclinoid R MCA bifurcation L ICA terminus L PCoA L ICA paraclinoid	Size	L ICA terminus recurrence (previously coiled)	2	L PCoA	2
11	62	3	R A1-A2 R pericallosal L callosomarginal	Size	L callosomarginal	4	R pericallosal	3
12	38	2	R PCoA L ICA terminus	Second dilatation	L ICA terminus	4.5	R PCoA	6.5
13	69	3	R MCA bifurcation ACoA L SCA	Location Size Shape	L SCA	5	ACoA	4

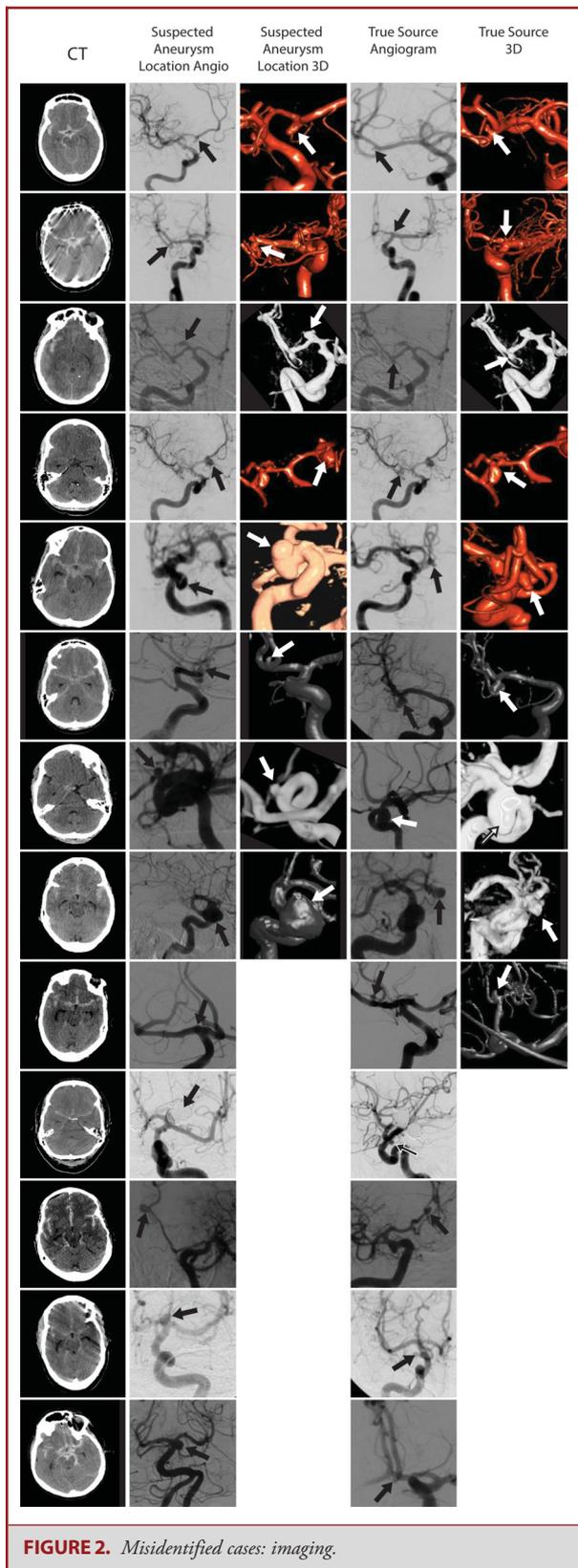
^aAneurysm features that influenced the suspected location.

R, right; L, left; ACoA, anterior communicating artery; MCA, middle cerebral artery; ICA, internal carotid artery; AChA, anterior choroidal artery; SCA, superior cerebellar artery; PCoA, posterior communicating artery.

compared to the general population, with the highest mortality in those with multiple aneurysms.

The timing of the treatment for coincident lesions can be debated. As far as surgical treatment, Nemoto et al¹⁹ demon-

strated that multiple surgical approaches during the acute stage after SAH lead to poorer outcomes. Alternatively, however, multiple aneurysms have been shown to be effectively treated in the initial surgery through the same approach²⁰⁻²⁹ including



priori to treatment is still significant and comprises 4.3% (13 of 303) of all multiple aneurysm cases with SAH treated at our institution.

CONCLUSION

SAH cases with multiple aneurysms frequently demonstrate a hemorrhage pattern that does not definitively delineate the source aneurysm. Morphological features cannot reliably be used to determine rupture site in these cases. Microsurgical clipping, confirming obliteration of the ruptured lesion, may be preferentially warranted in this setting, unless alternatively, all lesions can be contemporaneously and safely treated with endovascular embolization.

Disclosures

Dr Alaraj has a research grant from NIC and is a consultant for Cordis-Codman. Dr Aletich has a research grant from Micrus and is a consultant for Cordis-Codman. Dr Charbel has ownership interest in VasSol Inc and is a consultant for Transonic. The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES

- Ahmed O, Kalakoti P, Hefner M, Cuellar H, Guthikonda B. Seven intracranial aneurysms in one patient: treatment and review of literature. *J Cerebrovasc Endovasc Neurosurg*. 2015;17(2):113-119.
- Backes D, Vergouwen MD, Velthuis BK, et al. Difference in aneurysm characteristics between ruptured and unruptured aneurysms in patients with multiple intracranial aneurysms. *Stroke*. 2014;45(5):1299-1303.
- Inagawa T. Incidence and risk factors for multiple intracranial saccular aneurysms in patients with subarachnoid hemorrhage in Izumo City, Japan. *Acta Neurochir (Wien)*. 2009;151(12):1623-1630.
- Shen X, Xu T, Ding X, Wang W, Liu Z, Qin H. Multiple intracranial aneurysms: endovascular treatment and complications. *Interv Neuroradiol*. 2014;20(4):442-447.
- Xu Y, Chen SD, Lei B, Zhang WH, Wang WY. One-stage operation for rare multiple mirror intracranial aneurysms: a case report and literature review. *Turk Neurosurg*. 2014;24(4):598-601.
- Liu J, Xiang J, Zhang Y, et al. Morphologic and hemodynamic analysis of paraclinoid aneurysms: ruptured versus unruptured. *J Neurointerv Surg*. 2014;6(9):658-663.
- Duan G, Lv N, Yin J, et al. Morphological and hemodynamic analysis of posterior communicating artery aneurysms prone to rupture: a matched case-control study. *J Neurointerv Surg*. 2016;8(1):47-51.
- Lin N, Ho A, Gross BA, et al. Differences in simple morphological variables in ruptured and unruptured middle cerebral artery aneurysms. *J Neurosurg*. 2012;117(5):913-919.
- Kondo R, Yamaki T, Mouri W, et al. Magnetic resonance vessel wall imaging reveals rupture site in subarachnoid hemorrhage with multiple cerebral aneurysms. *No Shinkei Geka*. 2014;42(12):1147-1150.
- Kheireddin AS, Pronin IN, Kornienko VN, Belousova OB. Diagnosis of the source of bleeding in multiple cerebral aneurysms by susceptibility-weighted imaging. *Vestn Rentgenol Radiol*. 2012;4(1):4-9.
- Matouk CC, Mandell DM, Gunel M, et al. Vessel wall magnetic resonance imaging identifies the site of rupture in patients with multiple intracranial aneurysms: proof of principle. *Neurosurgery*. 2013;72(3):492-496.
- Nagahata S, Nagahata M, Obara M, et al. Wall enhancement of the intracranial aneurysms revealed by magnetic resonance vessel wall imaging using three-dimensional turbo spin-echo sequence with motion-sensitized driven-equilibrium: a sign of ruptured aneurysm? *Clin Neuroradiol*. 2016;26(3):277-283.
- Edjlali M, Gentric JC, Regent-Rodriguez C, et al. Does aneurysmal wall enhancement on vessel wall MRI help to distinguish stable from unstable intracranial aneurysms? *Stroke*. 2014;45(12):3704-3706.
- Ishibashi T, Murayama Y, Urashima M, et al. Unruptured intracranial aneurysms: incidence of rupture and risk factors. *Stroke*. 2009;40(1):313-316.
- Wiebers DO, Whisnant JP, Huston J, 3rd, et al. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. *Lancet*. 2003;362(9378):103-110.
- Garbossa D, Panciani PP, Fornaro R, et al. Subarachnoid hemorrhage in elderly: advantages of the endovascular treatment. *Geriatr Gerontol Int*. 2012;12(1):46-49.
- Chien A, Liang F, Sayre J, Salamon N, Villablanca P, Vinuela F. Enlargement of small, asymptomatic, unruptured intracranial aneurysms in patients with no history of subarachnoid hemorrhage: the different factors related to the growth of single and multiple aneurysms. *J Neurosurg*. 2013;119(1):190-197.
- Huhtakangas J, Lehto H, Seppa K, et al. Long-term excess mortality after aneurysmal subarachnoid hemorrhage: patients with multiple aneurysms at risk. *Stroke*. 2015;46(7):1813-1818.
- Nemoto M, Yasui N, Suzuki A, Sayama I. [Problems of surgical treatment for multiple intracranial aneurysms]. *Neurol Med Chir (Tokyo)*. 1991;31(13):892-898.
- Chandela S, Chakraborty S, Ghobrial GM, Jeddiss A, Sen C, Langer DJ. Contralateral mini-craniotomy for clipping of bilateral ophthalmic artery aneurysms using unilateral proximal carotid control and Sugita head frame. *World Neurosurg*. 2011;75(1):78-82.
- Rajesh A, Praveen A, Purohit AK, Sahu BP. Unilateral craniotomy for bilateral cerebral aneurysms. *J Clin Neurosci*. 2010;17(10):1294-1297.
- Mizoi K, Suzuki J, Yoshimoto T. Surgical treatment of multiple aneurysms: review of experience with 372 cases. *Acta Neurochir (Wien)*. 1989;96(1-2):8-14.
- de Sousa AA, Filho MA, Jr, Faglioni W, Carvalho GT. Unilateral pterional approach to bilateral aneurysms of the middle cerebral artery. *Surg Neurol*. 2005;63(suppl 1):S1-S7.
- Hage ZA, Charbel FT. Clipping of bilateral MCA aneurysms and a coiled ACOM aneurysm through a modified lateral supraorbital craniotomy. *Neurosurg Focus*. 2015;38(Video Suppl 1): Video19.
- Orz Y, Osawa M, Tanaka Y, Kyoshima K, Kobayashi S. Surgical outcome for multiple intracranial aneurysms. *Acta Neurochir (Wien)*. 1996;138(4):411-417.
- Jeon P, Kim BM, Kim DJ, Kim DI, Suh SH. Treatment of multiple intracranial aneurysms with 1-stage coiling. *AJNR Am J Neuroradiol*. 2014;35(6):1170-1173.
- Santana Pereira RS, Casulari LA. Surgical treatment of bilateral multiple intracranial aneurysms. Review of a personal experience in 69 cases. *J Neurosurg Sci* 2006;50(1):1-8.
- Wachter D, Kreitschmann-Andermahr I, Gilsbach JM, Rohde V. Early surgery of multiple versus single aneurysms after subarachnoid hemorrhage: an increased risk for cerebral vasospasm? *J Neurosurg*. 2011;114(4):935-941.
- Inagawa T. Surgical treatment of multiple intracranial aneurysms. *Acta Neurochir (Wien)*. 1991;108(1-2):22-29.
- Chalouhi N, Jabbour P, Singhal S, et al. Stent-assisted coiling of intracranial aneurysms: predictors of complications, recanalization, and outcome in 508 cases. *Stroke*. 2013;44(5):1348-1353.
- Reynolds MR, Buckley RT, Indrakanti SS, et al. The safety of vasopressor-induced hypertension in subarachnoid hemorrhage patients with coexisting unruptured, unprotected intracranial aneurysms. *J Neurosurg*. 2015;123(4):862-871.
- Swift DM, Solomon RA. Unruptured aneurysms and postoperative volume expansion. *J Neurosurg*. 1992;77(6):908-910.
- Hoh BL, Carter BS, Ogilvy CS. Risk of hemorrhage from unsecured, unruptured aneurysms during and after hypertensive hypervolemic therapy. *Neurosurgery*. 2002;50(6):1207-1211.
- Vajda J. Multiple intracranial aneurysms: a high risk condition. *Acta Neurochir (Wien)*. 1992;118(1-2):59-75.

Acknowledgment

The authors would like to thank Ms Christa Wellman for her help with the graphics.

COMMENT

The authors describe a cohort of patients who underwent surgery for subarachnoid hemorrhage at their institution over a 10-year

interval. They found that 151 patients had multiple aneurysms. Seventy-one of these patients had definitive hemorrhage patterns on initial computed tomography scans and 80 patients had non-definitive hemorrhage patterns. In 13 (16.2%) of the cases with non-definitive hemorrhage patterns, there was discordance between the image space determination of the rupture source and intraoperative findings of the true ruptured aneurysm. They found that 13 of 303 patients treated surgically or with endovascular techniques had a misidentified source of hemorrhage, giving an overall rate of 4.3% (13 of 303). As demonstrated by the authors and observed by others, the source of hemor-

rhage in patients with multiple aneurysms can be elusive. The obvious concern is that patients treated with endovascular techniques without direct surgical visualization of the lesion would be at higher risk for obliteration of the offending lesion. This fact met strong consideration in patients with non-definitive hemorrhage patterns and an aggressive approach to complete surgical or endovascular obliteration of all lesions in these patients. This manuscript strongly reiterates this point. The authors are to be commended.

Christopher S. Ogilvy
Boston, Massachusetts