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The outcome of treatment for arteriovenous malformations of the brain: A five-year retrospective series from the Philippines

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Abstract

*Background and Objectiv*e: Arteriovenous malformations (AVMs) account for 38% of all intracerebral hemorrhages in patients between 15-45 years. Epidemiologic and treatment data on this disease entity in the Philippines is sorely lacking. This study was undertaken to provide data on the management of these lesions from a long-term series in one institution in the Philippines. *Methods:* All consecutive patients admitted at our institution from January 2001 to December 2005 with an admitting impression of AVM were included in the study. The data was obtained from review of charts and imaging studies. *Results:* There were 83 patients included in the study. Their mean age was 32.8 years. The male: female ratio was 1.7:1. Headache was the most common presentation (50.6%). Majority of patients had a Spetzler-Martin (SM) Grade 2 AVM (34.7%); 28.6% of patients were grade 3, 18.4% were grade 4, 14.3% were grade 1 and 4.1% were grade 5. Surgical morbidity rates of 0%, 8.3% and 0%, respectively were noted for Spetzler-Martin (SM) grades 1, 2 and 3. Surgical mortality rate of 0% was observed for AVM grades 1, 2 and 3. Of 10 patients who underwent embolization, 20% had angiographic obliteration of their AVM. Morbidity and mortality rate for embolization was 0%.
In *conclusion,* the risks of surgery for patients with Spetzler-Martin (SM) grade 1 and 2 AVMs are low. In carefully selected patients, surgery for Spetzler-Martin (SM) grade 3 AVMs also has a low morbidity and mortality rate.

INTRODUCTION

Arteriovenous malformations (AVMs) are abnormalities of intracranial vessels that constitute a fistulous connection between the arterial and venous systems and that lack a normal intervening capillary bed. Typically, these lesions are triangular, with the base toward the meninges and the apex toward the ventricular system. AVMs appear as serpiginous isointense or slightly hyperintense vessels that strongly enhance following contrast administration on computed tomographic scanning. Calcification is identified in 25 to 30% of cases. On magnetic resonance imaging (MRI), the typical AVM appears as a tightly packed "honeycomb" of flow voids on T1 and T2 weighted images, caused by high flow velocity signal loss. Phase contrast magnetic resonance angiography (MRA) can be useful in the depiction of flow, but complete definition of complex lesions and their internal angioarchitecture requires a cerebral angiogram. On cerebral angiography, parenchymal AVMs appear as tightly packed masses of enlarged feeding arteries and dilated tortuous veins with little or no intervening parenchyma within the nidus. Arteriovenous shunting with abnormal early filling of veins that drain the lesion is characteristic of AVM.

AVMs are the most frequently detected symptomatic vascular malformation[1], accounting for 2% of all strokes[2] and 38% of all intracerebral hemorrhages in patients between 15 and 45 years.[3] AVMs are one seventh as common as aneurysms, and the prevalence has been estimated at 0.2% to 0.8% of the general population.[4,5] Data on AVMs in the Philippines are sorely lacking. In the last twenty years, there have only been three published journal articles dealing with AVMs.[6-8] The only series dealing on epidemiology and treatment of AVMs to date was reported by Amor *et al*[8]

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in 1982. They reported on 16 angiographically-verified intracranial AVM patients seen at this same institution.

As the primary tertiary care center for neurosurgery with a catchment area comprised of the island of Luzon with a population of 42.82 million people[9], this study is being undertaken with the goal of providing epidemiological and clinical data on the management of arteriovenous malformations from a long term series in one institution. This consecutive series will also include non-surgically treated patients to allow an understanding of total outcomes of management of arteriovenous malformations.

METHODS

All consecutive patients who were referred or admitted to the Philippine General Hospital (UP-PGH) from January 2001 to December 2005 were included in the study. The data were obtained from review of charts and imaging studies where available, and recorded using an AVM Database Form. The data were recorded into a Microsoft Access Database. The information included demographic characteristics, clinical features before and after surgery, Modified Rankin Scale (MRS) score[10,11] before and after surgery, incidence of hemorrhage, angiographic characteristics, Spetzler-Martin (SM) grade[12], the surgical outcomes, other treatment outcomes, complications and deaths. If a new neurologic deficit due to treatment was present, outcome was recorded as follows: MRS score of 1 (minor deficits not interfering with lifestyle), MRS score of 2 (minor disability but capable of self-care in all aspects of life), MRS score of 3 (moderate disability requiring some help with self-care), MRS score of 4 (moderately severe disability preventing independence but not requiring constant attention) and MRS score of 5 (severe disability requiring constant attention). Outcome was measured according to downgrade of neurological function due to surgery. Downgrade was defined as new permanent neurological deficit after surgery. Significant morbidity was defined as a decrease in MRS score >1 from baseline. Spetzler-Martin (SM) grade[12] was based on an aggregate on the basis of lesion size, location in eloquent area and pattern of venous drainage. One point was assigned to small (<3 cm) AVM, 2 points for medium (3-6 cm) AVM, 3 points for large (>6cm) AVM, one point each for adjacent to eloquent brain and deep venous drainage. Grade VI referred to extremely large and diffuse AVM, dispersed through critical area.

RESULTS

There were 129 patients admitted or referred to the UP-PGH from January 2001 to December 2005 with an admitting impression of AVM, as identified by the Records Section of our institution using the ICD classification. Ninety-five charts were available for review. Twelve patients had admitting impressions other than AVMs and were excluded from the study, leaving 83 charts for review and analysis. The mean age of patients was 32.8 years, with a range of 1 to 72 years. There was a male predominance (54, 65%) compared to females (11, 35%). The mean length of hospital stay was 15.3 days (range of 1 to 63 days). For patients who underwent craniotomy and excision of the AVM, the mean length of hospital stay was 25.2 days (range of 7 to 59 days). For patients who underwent embolization, the mean length of hospital stay was only 4.7 days (range of 2 to 8 days).

Clinical presentation

The presenting symptoms are listed in Table 1. As shown, majority of patients presented with headache (50.6%). The second most frequent presentation was seizure (26.5%). Uncommon presenting signs included pulsatile scalp mass, focal weakness, dizziness, eye swelling and loss of consciousness. A patient diagnosed with a vein of Galen malformation presented with prominent scalp veins. The average duration of symptoms was 23.9 months, with a range of 1 day to 26 years. No patient had a family history of AVM.

Four patients had undergone craniotomy and hematoma evacuation at an outside institution before admission at UP-PGH. One patient underwent tube ventriculostomy for intraventricular hemorrhage prior to her admission here. Another patient underwent stereotactic radiosurgery for his diencephalic AVM seven years prior to his admission at our institution. Eight patients had pre-existing hypertension with a mean duration of 4.3 years. Eleven patients had a smoking history ranging from 1 to 60 pack-years.

The clinical signs on admission were: Motor weakness (26 patients -- 31.3%), cranial nerve deficits (12 patients -- 14.5%), sensory abnormalities (5 patients -- 6%), cerebellar signs (3 patients -- 3.6%). Majority of patients had a Glasgow Coma Scale (GCS) score of 15 on admission (66, 79.5%), five patients had a GCS score of 14 (6%), and one each had a score of 13, 11 and 10. Two patients had a GCS score of

Table 1: The presenting symptoms of patients admitted for AVM at the Philippine General Hospital

Clinical presentation	No of Patients	Percent
Headache	42	50.6
Seizure	22	26.5
Pulsatile scalp Mass	4	4.8
Focal weakness	3	3.6
Dizziness	3	3.6
Eye swelling	2	2.4
Loss of consciousness	1	1.2
Prominent scalp veins	1	1.2

12. Two patients presented with a GCS score of 6.

Incidence of hemorrhage

Five patients had undergone surgery at an outside institution for intracranial hemorrhage (6%); 4 underwent craniotomy and evacuation of hematoma, and one underwent tube ventriculostomy. Another 32 patients had cranial CT scan evidence of hemorrhage (38.6%) on admission. The location of hematoma was cortical in 18 patients, basal ganglia in 5 patients, thalamus in 4 patients and cerebellum in 3 patients. Intraventricular hemorrhage was also noted in 11 patients; 4 patients had subdural hematomas, and 3 patients bled in the subarachnoid space. Thus, hemorrhage occurred in 37 of 83 patients (44.6%).

Angiographic characteristics

The angiographic plates of 67 patients were available for review. On angiography, majority of AVMs had feeders from the anterior circulation (23 of 67 patients, 34.3%); 7 patients had AVMs with feeders from the posterior circulation (10.4%). Fourteen patients had feeders from both anterior and posterior circulations (20.9%). There were 5 patients identified who also had feeders from the external carotid circulation (mixed pial-dural AVMs, 7.5%).

Deep venous drainage was noted in 18 patients (26.9%). Seven patients had both superficial and deep venous drainage (10.4%); the rest of the patients had superficial venous drainage of their AVMs (21, 31.3%). There were 8 associated aneurysms documented on angiography in this series (11.9%); 5 were intranidal, 2 were flow-related proximal aneurysms, and one was located at the proximal draining vein. Cerebral steal phenomenon was noted in 4 patients (6%).

Spetzler-Martin (SM) grade

There were 50 patients whose hospital records and/or angiograms were available for review as to size of the AVM. There were 31 patients (62%) with small AVMs (size less than 3 cm), 14 patients (28%) with moderate-sized AVM (between 3-6 cm), and 5 patients (10%) with large AVM (>6 cm). There were 32 patients with AVMs located adjacent to eloquent cortex (64%). Twenty-eight patients had deep draining veins (56%).

There were 49 patients whose hospital records and/or angiograms were available for classification as to the Spetzler-Martin grade of their AVM. There were 7 patients with grade 1 AVMs (14.3%), 17 patients with grade 2 AVMs (34.7%), 14 with grade 3 AVMs (28.6%), 9 with grade 4 AVMs (18.4%), and 2 patients with grade 5 AVMs (4.1%).

Treatment and outcome

Twenty patients underwent craniotomy and excision of AVM (24.1%). Of these patients, 5 were Spetzler-Martin (SM) grade 1 (25%), 12 were grade 2 (60%), and 3 patients were grade 3 (15%). Ten patients underwent embolization. Eight patients underwent the procedure with the intent of palliation and as part of a combination of therapy with surgery or focused radiation. One patient had a Spetzler-Martin (SM) grade of 4, and another one had a grade of 5. No patient underwent focused radiation as primary treatment for his AVM.

Of the 5 patients with Spetzler-Martin (SM) Grade 1 who underwent excision, 2 developed

seizures post-operatively; these were easily controlled with anti-epileptic drugs. The rest of the patients had no complications and were discharged with no neurologic deficits. MRS score for all patients was 0. Surgical morbidity rate was 0%. There was no surgical mortality.

Of the 12 patients with a Spetzler-Martin (SM) Grade 2, 8 were discharged with a MRS score of 0. Of these 8 patients, one had a seizure postoperatively, but this was controlled with medication. Two patients had a MRS score of 1; one had a homonymous hemianopsia after excision of his occipital AVM, and another had a Medical Research Council (MRC) Grade 4+/5 weakness of her left extremities after excision of her parietal parasagittal AVM (which bled prior to surgery). These patients had neurologic downgrades from their admission MRS scores of 0 (16.7%). One patient was admitted with a poor neurologic grade (GCS 6: E1V1M4), and had intra-operative rupture of his flow-related left posterior cerebral artery aneurysm while undergoing excision. His post-operative course was stormy, with pneumonia and surgical site infection. He was discharged with a MRS score of 4 (improved compared to his admission MRS score). Another patient rebled 4 hours post-excision of her frontal AVM and underwent re-opening, evacuation of hematoma. A retained nidus was noted. This patient also developed pneumonia during her stay. She was discharged with a MRS score of 4. For Spetzler-Martin (SM) Grade 2 patients, surgical morbidity was 8.3%, and there was no surgical mortality.

Two of the three patients with Spetzler-Martin (SM) grade 3 who underwent excision had some neurologic deficits post-operatively, with a MRS score of 1. Both had Medical Research Council (MRC) Grade 4 to 4+/5 weakness of unilateral extremities after excision of their AVM. The percentage of patients with Spetzler-Martin (SM) grade 3 who had neurologic downgrades was 66.7%. The third patient had a MRC Grade 2/5 weakness of his left extremities on admission; he had a right thalamic bleed secondary to his Grade 3 posterior temporal AVM, which had some perforator-type feeders. Post-excision, his weakness had improved to MRC Grade 3, although an infarct of the anterior choroidal artery perforator territory was documented by computed tomography. His MRS score was 4. For Spetzler-Martin (SM) Grade 3 patients, the surgical morbidity was 0% and there was no surgical mortality.

Of the 10 patients who underwent embolization, 2 patients (20%) had successful embolization of their AVM, with no angiographic evidence of early venous filling after embolization. Of the 8 patients underwent the procedure with the intent of palliation and as part of a combination of therapy with surgery or focused radiation, one patient had Spetzler-Martin (SM) grade 4, and another patient was grade 5. The other patients had no angiograms available for review. Partial diminution of flow into the AVM was achieved in all but one patient, who had intra-procedural rupture of her AVM. In this patient, the embolization was aborted. She had a MRS score of 1 with no downgrade in neurologic deficit from the procedure. The rest had a MRS score of 0. Embolization morbidity and mortality rates were 0%.

One patient died secondary to basal ganglia hemorrhage from a ruptured AVM. She arrived in poor neurologic condition (GCS 6: E1V1M4) with anisocoria. No consent for surgery was granted.

DISCUSSION

There has been an increase in the number of patients with AVM admitted in our institution. A comparison with a 5-year retrospective review done in 1982 in this same institution[8] showed an almost three-fold increase in angiographically-verified cases. The mean age of patients in this series was 32.8 years, whereas it was common in the 11-30 age group in the previous series. These probably partly reflect improving diagnostic facilities and increasing age of general population The male: female ratio is 1.8:1 in the present study; it was 1.7:1 in 1982.

The most common clinical presentation in this series was headache, whereas it was subarachnoid hemorrhage in the previous series. The incidence of hemorrhage in the present study was 44.6%, with a mortality rate of 2.7%. This was lower than the estimated mortality rate of 10-29% associated with AVM hemorrhage in previous reports.[13,14] The improved mortality rate may have been partly due to timely evacuation of hematoma.

The mortality rate for Spetzler-Martin (SM) Grade 1 to 3 AVMs in this series was 0%, which was in agreement with the report of Hamilton & Spetzler.[15] This was a major improvement when compared with the 1982 series reported by Amor et al from this center[8], which had a surgical mortality rate of 14.3%. The low surgical morbidity rate for Spetzler-Martin (SM) Grade 1 AVMs of 0% is also in agreement with the series of Hamilton & Spetzler.[15] Minor complications occurred in 2 patients; they developed seizures post-operatively, which were easily controlled with medications.

All patients had no neurological deficits post-operatively.

For patients with Spetzler-Martin (SM) Grade 2 AVMs, the morbidity rate was higher (8.3%). One patient sustained a rebleed post-excision due to a retained nidus. She had a decrease in MRS score from 0 to 4, resulting in the lone surgical morbidity. Two other patients had a downgrade of MRS score from 0 to 1 with homonymous hemianopsia and mild limb weakness. These morbidities were not clinically significant downgrades. Another patient developed seizures post-operatively, but this was also easily controlled with medications.

For Spetzler-Martin (SM) Grade 3 AVM patients, the low morbidity rate of 0% was also concurrent with that in the report by Hamilton and Spetzler[15], although it is possible that case selection has contributed to the excellent result. It has been shown that Spetzler-Martin (SM) Grade 3 AVMs with deep perforating arteries have a similar complication rate to that of Grade 4 to 5 AVMs.[16] The rates of new permanent neurologic deficit leading to a downgrade in quality of life in Grade 4-5 AVMs are 44-57%.[15,17] Two of the three patients with Spetzler-Martin (SM) Grade 3 AVM in the present series had a downgrade of MRC scores from 0 to 1 with mild limb weakness after excision of AVM. These morbidities were not clinically significant. The third patient had MRS score of 4 from residual limb weakness. However, the muscle weakness preceded the surgical excision and improved after the operation.

Endovascular embolization may be used as a sole mode of treatment if the complete obliteration of the malformation is accomplished with a permanent agent, or as palliative treatment with targeted embolization of areas of weakness in the angioarchitecture of the AVM. Embolization may also be used as a pre-treatment adjunct before microsurgical resection or focused radiation. In this series, angiographic cure was achieved in two patients (20%). In other reports, the complete cure rate for AVMs by embolization alone varies between 10% and 40%.[18] An early series from 1992-1994 detailing morbidity & mortality rates from embolization document a permanent morbidity rate of 2% and a mortality rate of 0.5%.[19] The present series shows a morbidity & mortality rate of 0% for embolization; however, the number of patients is too low to make any generalizations.

The lone mortality in this series (1.2%) is lower than the mortality associated with initial symptomatic hemorrhage of 6-29%.[4,20] This may be due to referral bias as patients with poor neurological grades may not be referred to our institution. Although many studies report complete recovery or mild disability in more than 50% of patients after an initial hemorrhage[21,22], the risk of death from an initial bleed should not be taken lightly.

In conclusion, the risks of surgery for patients with Spetzler-Martin (SM) grade 1 & 2 AVMs are low. As surgery immediately negates the risk of hemorrhage from the lesion after excision, we believe these low-grade AVMs are best treated with microsurgical resection. Patients with Spetzler-Martin (SM) grade 3 AVMs may undergo microsurgical resection, as surgical morbidity & mortality rates are also low. However, patient selection, skill and experience of the surgical team are important factors in achieving these low rates. Endovascular embolization may be used as sole treatment, as part of combination therapy, or to eliminate angioarchitectural weaknesses in a patient's AVM.

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