Case Report = Спостереження з практики = Наблюдение из практики

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Microsurgical resection of high-flow cerebral arteriovenous malformations after recurrent stroke

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Address for correspondence: Moshiur Rahman, Neurosurgery Department, Holy Family Red Crescent Medical College, 1 Eskaton Garden Rd, Dhaka 1000, Bangladesh, e-mail: dr.tutul@yahoo.com Arteriovenous malformations (AVMs) are tangled lesions that may digress the blood flow particularly the high flow ones and microsurgical resection is challenging. The natural history of AVM is not completely understood and its management is controversial. Microsurgical resection of cerebral arteriovenous malformation is a challenging procedure, particularly for high-flow type. Embolization, microsurgery, or radiotherapy are treatment options. Preoperative planning to control the feeders, arachnoid dissection around the AVM for identification and control of all arterial feeders around the AVM surfaces, lastly control of draining vein is the principal of microsurgery. The goal of surgery is to remove the AVM completely to eliminate the risk of bleeding avoiding neurological deterioration. In this paper, we reviewed a case of high-flow cerebral AVM in recurrent bleeding with successful microsurgical resection.

The patient in this case report significantly improved his neurological condition and demonstrated a good quality of life during long-term follow-up. The results of this study showed that the microsurgical removal of AVMs represents an efficient treatment with good clinical outcomes. In the future, more investigations of the factors that lead to AVM rupture are required for the advancement of effective medical procedures.

Keywords: cerebral arteriovenous malformations; recurrent stroke

Мікрохірургічна резекція високопотокових артеріовенозних мальформацій головного мозку після повторного інсульту

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Moshiur Rahman, Neurosurgery Department, Holy Family Red Crescent Medical College, 1 Eskaton Garden Rd, Dhaka 1000, Bangladesh, e-mail: dr.tutul@yahoo.com Артеріовенозні мальформації (АВМ) являють собою патологічні сплетення артерій і вен, які можуть відхиляти потік крові, зокрема високопотоковий, що істотно ускладнює мікрохірургічну резекцію. Природна динаміка АВМ ще не цілком вивчена, в зв'язку з чим думки щодо ведення хворих з даною патологією носять суперечливий характер. Мікрохірургічна резекція артеріовенозних мальформацій головного мозку є досить складною процедурою, особливо при високопотоковой формі. До можливих варіантів лікування відносять емболізацію, мікрохірургічні втручання та променеву терапію. Доопераційне планування з метою контролю живлячих артерій, диссекція арахноїдальної оболонки навколо АВМ для визначення і контролю живлячих артерій навколо поверхні АВМ і нарешті контроль дренуючої вени становлять базові принципи при проведенні мікрохірургічного втручання. Метою операції є видалення АВМ в повному обсязі, що дозволить скоротити ризик крововиливу і уникнути погіршення неврологічного статусу. У представленій статті розглядається випадок успішної мікрохірургічної резекції високопотоковой АВМ головного мозку при повторному крововиливі.

В описаному випадку у пацієнта достовірно покращилися неврологічний статус, якість життя протягом довгострокового періоду спостереження. Результати даного дослідження підтверджують, що проведення мікрохірургічного видалення АВМ забезпечує ефективне лікування з успішним результатом. Необхідне проведення подальших досліджень факторів, які викликають розрив АВМ, з метою поліпшення методів ефективного ведення даної патології.

Ключові слова: артеріовенозні мальформації головного мозку; повторний інсульт

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Микрохирургическая резекция высокопотоковых артериовенозных мальформаций головного мозга после повторного инсульта

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Moshiur Rahman, Neurosurgery Department, Holy Family Red Crescent Medical College, 1 Eskaton Garden Rd, Dhaka 1000, Bangladesh, e-mail: dr.tutul@yahoo.com Артериовенозные мальформации (АВМ) представляют собой патологические сплетения артерий и вен, которые могут отклонять ток крови, в частности высокопотоковый, что существенно усложняет микрохирургическую резекцию. Естественная динамика АВМ еще не вполне изучена, в связи с чем мнения относительно ведения больных с данной патологией носят противоречивый характер. Микрохирургическая резекция артериовенозных мальформаций головного мозга является достаточно сложной процедурой, особенно при высокопотоковой форме. К возможным вариантам лечения относят эмболизацию, микрохирургические вмешательства и лучевую терапию. Дооперационное планирование с целью контроля питающих артерий, диссекция арахноидальной оболочки вокруг АВМ для определения и контроля питающих артерий вокруг поверхности АВМ и наконец контроль дренирующей вены составляют базовые принципы при проведении микрохирургического вмешательства. Целью операции является удаление АВМ в полном объеме, что позволит сократить риск кровоизлияния и избежать ухудшения неврологического статуса. В представленной статье рассматривается случай успешной микрохирургической резекции высокопотоковой АВМ головного мозга при повторном кровоизлиянии.

В описанном случае у пациента достоверно улучшились неврологический статус, качество жизни в течение долгосрочного периода наблюдения. Результаты данного исследования подтверждают, что проведение микрохирургического удаления АВМ обеспечивает эффективное лечение с благоприятным исходом. Необходимо проведение дальнейших исследований факторов, которые вызывают разрыв АВМ, с целью улучшения методов эфективного ведения данной патологии.

Ключевые слова: артериовенозные мальформации головного мозга; повторный инсульт

Introduction

Arteriovenous malformations (AVMs) are congenital anomalies of the intracranial vessels that comprise a direct communication between the arterial blood vessels and venous systems and come up short on an interceding capillary bed. The absence of obstruction inside the nidus prompts high-flow shunting of blood among blood vessels and venous courses [1]. Hemorrhagic introduction of AVM is an autonomous indicator of future hemorrhage and it is associated with significant morbidity and mortality. Both genders are influenced similarly but it is more common in males. It is a complex disease and, for symptomatic versus asymptomatic, emergency, or elective cases, the treatment approach may vary. Not only neuroimaging with angiographic data, but also the full history, evaluation, and general state of the patient should be incorporated into the management of AVMs. [2]

In low-grade AVM, mean surgical morbidity and mortality are 2.2 % and 0.3 %, respectively, but can exceed 63 % in high-grade AVMs [3, 4]. Cerebral AVMs represent 1.4 % to 2 % of all hemorrhagic strokes [5]. The normal history of asymptomatic cerebral AVMs remains inadequately comprehended.

AVM incorporates the presence of single or numerous direct arteriovenous associations that grant high-flow arteriovenous shunting through little feeding arteries that come up short on a middle arterial layer and the absence of a capillary bed. In an AVM, a rapid and straightforward abnormal blood flow from

arteries to veins exists, bypassing the encompassing tissues. Encompassing brain tissues are hardly able to assimilate oxygen from the high-flowing blood. High-flow AVMs cause harm to the brain or spinal cord by a few mechanisms. The gold standard for the diagnosis of AVM is cerebral angiography.

Case report

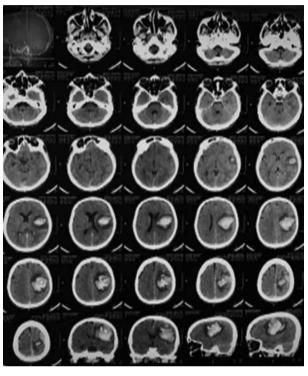
A 20-year old male presented with recurrent hemorrhagic stroke with loss of consciousness in the emergency room. The patient had a similar episode eight months ago and he recovered with conservative treatment over two months without any residual neurological deficit. The examinations revealed the patient's Glasgow Coma Scale (GCS) score E3M5V1 on admission, vital signs (pulse, blood pressure, respiration, and temperature) were stable. He developed rightsided hemiplegia and aphasia. His clinical condition was improved with conservative treatment, although hemiplegia and aphasia were persistent. His computer tomography (CT) scan of the brain revealed a hematoma in the left frontoparietal region (Figure 1). He underwent a CT angiogram of the brain and digital subtraction angiography (DSA) which suggests a high-flow AVM in the relative area causing hematoma formation. The DSA revealed an intranidal aneurysm, venous arterialization, and rapid filling (Figure 2, 3). He was recommended to do a microsurgical resection of AVM with hematoma removal and warned regarding all possible complications. The patient's party agreed and a day later, we performed

This article contains some figures that are displayed in color online but in black and white in the print edition

a left frontoparietal craniotomy for microsurgical removal of AVM which was uneventful. Gradually over 8 weeks, he becomes ambulant and his speech improved over 3 months. At the 2nd year of follow-up, he recovered completely *(Figure 4)*.

Assessment of performance in activities of daily living by Barthel Index Score

Acute stroke results in functional disability which is measurable using Barthel Index. It is an ordinal scale used to measure performance in activities of daily



 $\textbf{\textit{Figure 1.}} \ \, \text{CT scan of brain showing a left frontal hematoma}$



Figure 2. DSA of left frontoparietal AVM

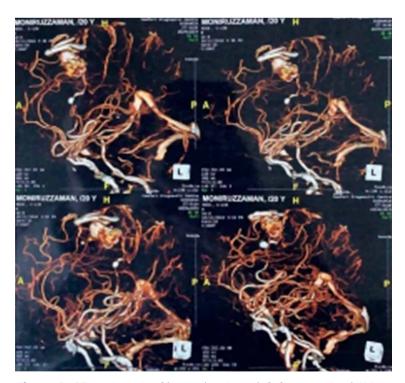


Figure 3. CT angiogram of brain showing a left frontoparietal AVM



Figure 4. Photograph of the patient after 2 years of a surgery

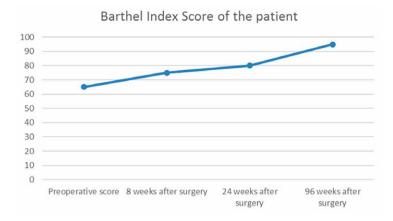


Figure 5. Preoperative and postoperative Barthel Index Score of the patient

living and in most extreme cases the lower the Barthel Index, the worse the performance. In our study, the physicians identified the patient's preoperative and postoperative daily living status using this scale. Scores in the scale range from 0–20 (total dependency) to 100 (no dependency). The patient's preoperative Barthel Index score was 65. There were no neurological deficits, impairment, disability found in the patient and he was considered independent in his daily activities. Thus after 2 months of the surgery, he improved with a score of 75. Gradually after 2 years, he recovered completely, having a score of 95 (*Figure 5*).

Surgical treatment outcome scale (Spetzler Martin Grades, Size, and Eloquence)

The Spetzler Martin Grading Scale appraises the danger of open neurosurgery for a patient with AVM by assessing AVM size, type of venous drainage patterns, and eloquence of brain area. A Grade I AVM would be considered as small, superficial, and situated in a non-eloquent cerebrum, and low risk for a medical procedure. Grade IV or V AVM is huge, deep, and adjacent to the eloquent brain; grade VI AVM is not operable. In this case report, CT angiogram of brain and DSA had revealed a Spetzler Martin grade IV AVM in the left frontoparietal region with feeding arteries from the left posterior cerebral artery, deep drainage into the vein, and superficial drainage through a cortical vein. It showed a decreased size of the AVM nidus (< 6 cm and located in an eloquent area with deep venous drainage). The scale required both DSA and cross-sectional imaging to make the conclusions.

Complete resection rate, procedure time, blood loss, and procedural complications

The time required for surgery was 4 hours. In this case, it was possible to resect AVM completely and there were no intraoperative ruptures as the proximal arterial feeders were anticipated preoperatively. The estimated blood loss was approximately 150 ml. There were no procedural complications nor any new neurological deficit. The hospital stay was 11 days.

Digital subtraction angiography

DSA is the reference standard for the analysis of AVMs. Past examinations have announced a few angioarchitectural indicators of seizure, superficial

venous drainage, shallow area with the outer carotid course or middle cerebral artery feeding, and presence of venous ectasia [6, 7]. Injuries with a little nidus may not be noticeable on CTA or MRA or may not be discernable from typical vessels. Follow-up vascular imaging after the goal of the clots was significant for the patient, contingent upon the clinical circumstance. For this case, DSA demonstrated an intranidal aneurysm along with tangled blood vessels over the left frontoparietal region with deep drainage into the vein and there was the very rapid filling of the shunted vessels (*Figure 2*). Previously a scoring framework dependent on AVM angioarchitecture was proposed and also it approved the AVM stream acquired by DSA with genuine stream estimations from quantitative MRA [8, 9].

Discussion

Treatment of cerebral AVMs is a major challenge, particularly high-flow grade IV–V AVMs are a major problem in the field of cerebrovascular microneurosurgery. In most cases, surgical developments involve rapid disposal of the AVM and a reduced risk of potential hemorrhage [10]. Previously promising results for surgical management in patients with AVM have been observed. The patient of this study had high-flow cerebral AVMs after a recurrent hemorrhagic stroke and had 100% successful microsurgical resection without any neurological deficits. In a study, microsurgery in just 4.6 percent of patients resulted in death or permanent neurological defects [11].

In any case, early data showed that evaluation scales can be applied reliably to most AVMs with great understanding among observers [12]. In this analysis, we used the Barthel Index Score and Spetzler Martin Grades to assess the patient's case and postoperative recovery. The patient's postoperative improvements were measured on the Barthel Index Score. He recovered well, became ambulant, and independent in his daily activities over 2 months which helped him to increase the Barthel Index score gradually.

The Spetzler Martin Grading Scale can be extended reliably to most AVMs by developing the most appropriate and efficient grading scale for AVMs. The cautious grimness associated with microsurgery for AVMs may involve hemorrhagic brain injury and its auxiliary impacts. Touchy proportions of clinical outcomes are bound to show minor changes in patients with no

preoperative side effects at first [13]. We assessed the complete resection of AVM in our grade IV patient using this scale. There was a 12% mortality rate in the Humphreys [14] series of 105 surgically treated AVM patients, all of whom were grade IV or V at the time of preoperative assessment [14]. Thirty-one consecutive high-grade AVM cases performed by Spetzler, 27 % for Grade IV and 31 % for Grade V, had a minor or major deficit, respectively, after surgery [15].

The size of AVM, deep position, exclusive deep vein drainage, and the occurrence of arterial aneurysms are correlated with the hemorrhagic presentation of brain AVMs. It is recognized that the AVM size and such lesions are an acceptable contender for microsurgical management. Stüer and colleagues have shown that complex autoregulatory work is by all accounts, unblemished in the perioperative cerebrovascular bed in patients with small and medium-sized AVMs [16]. Also, larger AVMs are bound to have all the more depleting veins that have been shown to place a patient at risk for complications of postoperative progression. In the treatment of high-flow AVMs, the safeguarding of substantial passage and perfusion of the brain tissue adjacent to the nidus is important.

Radiosurgery is an alternative to microsurgery for AVMs in eloquent and deep areas. Stereotactic radiosurgery (SRS), a high-dose radiation fraction that is stereotactically guided, induces gradual vessel obliteration over 2-3 years. Tu et al. demonstrated in a histopathological analysis that radiotherapy imparts permanent damage to endothelial cells and causes contraction in myofibroblasts adjacent to the elastic layer of vessel walls of the AVM [17]. This contraction narrows the lumen of the vessel, leading to vasoocclusion. A comparison of three treatment modalities microsurgery, embolization, and radiosurgery —was performed in a previous paper, and there the conclusion was that "microsurgery for small AVMs is superior to radiosurgery or interventional neuroradiology because of its high efficacy rate and low permanent morbidity rate and because in the vast majority of patients with AVMs, the immediate cure can be obtained" [18]. The drawbacks of radiosurgical treatments compared to microsurgery were illustrated in a recent statement by Lawton et al. [13]. A multicenter study of 1,255 patients undergoing radiotherapy identified a neurological deficiency in 102 (8 %) patients after radiosurgery [19]. Other drawbacks of radiosurgery include the 1 to 2-year delay risk of bleeding, cognitive deficits from natural brain tissue edema, and necrosis; which is not found in the microsurgery of our studied patient.

In this study, we did not notice any postoperative neurological problems in the patient and after a few months of surgery, the patient gradually recovered a lot. Previously it has been observed that complications may occur and postoperative deterioration may mainly be due to occlusion of arteries, re-bleeding from the retained AVM nidus, or small coagulated feeding vessels at the time of the postoperative seizure, normal perfusion. During the late stage of surgery or after surgery, microsurgical removal of large high-flow cerebral AVMs is often impeded by massive brain swelling and uncontrollable hemorrhage. Though this study only focused on one patient, using this method successful

management can be done in selected patients based on AVM anatomy, clinical presentation, course of treatment, etc. The status of this treatment modality should be familiar to neurosurgeons who operate on AVMs under a surgical microscope.

Conclusion

The main purpose of surgery in AVM management is to prevent recurrent hemorrhages, controlling seizures, and to restrain the progressive neurological deficit. The patient in this case report significantly improved his neurological condition and demonstrated a good quality of life during long-term follow-up. The results of this study showed that the microsurgical removal of AVMs in well-experienced hands represents an efficient treatment with good clinical outcomes. In the future, more investigations of the factors that lead to AVM rupture are required for the advancement of effective medical procedures.

Disclosure

Conflict of Interest

There is no potential conflict of interest relevant to this case report.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Patient Consent

This study obtained patient consent directly from the patient.

Financial Disclosure

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References

- Morshed RA, Winkler EA, Kim H, Braunstein S, Cooke DL, Hetts SW, Abla AA, Fullerton HJ, Gupta N. High-Flow Vascular Malformations in Children. Semin Neurol. 2020 Jun;40(3):303-314. doi: 10.1055/s-0040-1708869. PMID: 32252098.
- Kato Y, Dong VH, Chaddad F, Takizawa K, Izumo T, Fukuda H, Hara T, Kikuta K, Nakai Y, Endo T, Kurita H, Xu B, Beneš V, Christian R, Pavesi G, Hodaie M, Sharma RK, Agarwal H, Mohan K, Liew BS. Expert Consensus on the Management of Brain Arteriovenous Malformations. Asian J Neurosurg. 2019 Nov 25;14(4):1074-1081. doi: 10.4103/ajns.AJNS_234_19. PMID: 31903343; PMCID: PMC6896626.
- Potts MB, Lau D, Abla AA, Kim H, Young WL, Lawton MT; UCSF Brain AVM Study Project. Current surgical results with lowgrade brain arteriovenous malformations. J Neurosurg. 2015 Apr;122(4):912-20. doi: 10.3171/2014.12.JNS14938. PMID: 25658789; PMCID: PMC4422639.
- Ding D, Ilyas A, Sheehan JP. Contemporary Management of High-Grade Brain Arteriovenous Malformations. Neurosurgery. 2018 Sep 1;65(CN_suppl_1):24-33. doi: 10.1093/neuros/nyy107. PMID: 31076783.
- Stapf C, Labovitz DL, Sciacca RR, Mast H, Mohr JP, Sacco RL. Incidence of adult brain arteriovenous malformation hemorrhage in a prospective population-based stroke survey. Cerebrovasc Dis. 2002;13(1):43-6. doi: 10.1159/000047745. PMID: 11810010.
- Cordero-Tous N, Jorques-Infante AM, Santos-Martin L, Alcazar-Romero PP, Fandiño-Benito E, Martin-Linares JM, Olivares-Granados G, Horcajadas-Almansa A. Angiographic characteristics of epileptogenic arteriovenous malformations and effectiveness in the seizure control after treatment with radiosurgery. J Radiosurg SBRT. 2014;3(2):103-110. PMID: 29296391; PMCID: PMC5675482.

- Garcin B, Houdart E, Porcher R, Manchon E, Saint-Maurice JP, Bresson D, Stapf C. Epileptic seizures at initial presentation in patients with brain arteriovenous malformation. Neurology. 2012 Feb 28;78(9):626-31. doi: 10.1212/ WNL.0b013e3182494d40. PMID: 22345217.
- Shakur SF, Brunozzi D, Hussein AE, Linninger A, Hsu CY, Charbel FT, Alaraj A. Validation of cerebral arteriovenous malformation hemodynamics assessed by DSA using quantitative magnetic resonance angiography: preliminary study. J Neurointerv Surg. 2018 Feb;10(2):156-161. doi: 10.1136/neurintsurg-2017-012991. PMID: 28235955.
- Shankar JJ, Menezes RJ, Pohlmann-Eden B, Wallace C, terBrugge K, Krings T. Angioarchitecture of brain AVM determines the presentation with seizures: proposed scoring system. AJNR Am J Neuroradiol. 2013 May;34(5):1028-34. doi: 10.3174/ajnr.A3361. PMID: 23179653.
- Davies JM, Yanamadala V, Lawton MT. Comparative effectiveness of treatments for cerebral arteriovenous malformations: trends in nationwide outcomes from 2000 to 2009. Neurosurg Focus. 2012 Jul;33(1):E11. doi: 10.3171/2012.5.FOCUS12107. PMID: 22746228.
- 11. Soldozy S, Norat P, Yağmurlu K, Sokolowski JD, Sharifi KA, Tvrdik P, Park MS, Kalani MYS. Arteriovenous malformation presenting with epilepsy: a multimodal approach to diagnosis and treatment. Neurosurg Focus. 2020 Apr 1;48(4):E17. doi: 10.3171/2020.1.FOCUS19899. PMID: 32234990.
- Du R, Dowd CF, Johnston SC, Young WL, Lawton MT. Interobserver variability in grading of brain arteriovenous malformations using the Spetzler-Martin system. Neurosurgery. 2005 Oct;57(4):668-75; discussion 668-75. doi: 10.1227/01.neu.0000175548.23140.12. PMID: 16239878.
- Lawton MT, Du R, Tran MN, Achrol AS, McCulloch CE, Johnston SC, Quinnine NJ, Young WL. Effect of presenting hemorrhage on outcome after microsurgical resection of brain arteriovenous malformations. Neurosurgery. 2005 Mar;56(3):485-93; discussion 485-93. doi: 10.1227/01. neu.0000153924.67360.ea. PMID: 15730573.

- 14. Irikura K, Morii S, Miyasaka Y, Yamada M, Tokiwa K, Yada K. Impaired autoregulation in an experimental model of chronic cerebral hypoperfusion in rats. Stroke. 1996 Aug;27(8):1399-404. doi: 10.1161/01.str.27.8.1399. PMID: 8711809.
- Spetzler RF, Wilson CB, Weinstein P, Mehdorn M, Townsend J, Telles D. Normal perfusion pressure breakthrough theory. Clin Neurosurg. 1978;25:651-72. doi: 10.1093/ neurosurgery/25.cn_suppl_1.651. PMID: 710017.
- Stüer C, Ikeda T, Stoffel M, Schaller C, Meyer B. Dynamic Autoregulation Testing Does Not Indicate Changes of Cerebral Blood Flow Before and After Resection of Small- and Medium-Sized Cerebral AVM. Transl Stroke Res. 2011 Mar;2(1):60-6. doi: 10.1007/s12975-010-0031-7. PMID: 24323585.
- Tu J, Stoodley MA, Morgan MK, Storer KP. Responses of arteriovenous malformations to radiosurgery: ultrastructural changes. Neurosurgery. 2006 Apr;58(4):749-58; discussion 749-58. doi: 10.1227/01.NEU.0000192360.87083.90. PMID: 16575339.
- Schaller C, Schramm J. Microsurgical results for small arteriovenous malformations accessible for radiosurgical or embolization treatment. Neurosurgery. 1997 Apr;40(4):664-72; discussion 672-4. doi: 10.1097/00006123-199704000-00003. PMID: 9092839.
- Flickinger JC, Kondziolka D, Lunsford LD, Pollock BE, Yamamoto M, Gorman DA, Schomberg PJ, Sneed P, Larson D, Smith V, McDermott MW, Miyawaki L, Chilton J, Morantz RA, Young B, Jokura H, Liscak R. A multi-institutional analysis of complication outcomes after arteriovenous malformation radiosurgery. Int J Radiat Oncol Biol Phys. 1999 Apr 1;44(1):67-74. doi: 10.1016/s0360-3016(98)00518-5. PMID: 10219796.