Cerebral arteriovenous malformation case series

2023

Control digital subtraction angiography was arranged during 2021-2022 as part of a new protocol for all AVM patients who were under 21 years of age at the time of their treatment and in whom the treatment had occurred at least five years earlier. Angiography was offered only to patients under 50 years of age at the time of the new protocol. The complete eradication of AVM after the primary treatment had been originally confirmed with DSA in every patient.

A total of 42 patients participated in the late DSA control, and 41 of them were included in this analysis after excluding the patient diagnosed with HHT. The median age at the time of admission for AVM treatment was 14.6 (IQR 12-19, range 7-21 years) years. The median age at the time of the late follow-up DSA was 33.8 years (IQR 29.8-38.6, range 19.4-47.9 years). Two recurrent sporadic AVMs and one recurrent AVM in a patient with hereditary hemorrhagic telangiectasia (HHT) were detected. The recurrence rate was 4.9% for sporadic AVMs and 7.1% if HHT-AVM was included. All the recurrent AVMs had originally bled and been treated microsurgically. The patients with sporadic AVM recurrence had been smoking their whole adult lives.

Conclusions: Pediatric and adolescent patients are prone to develop recurrent AVMs, even after complete AVM obliteration verified by angiography. Therefore, imaging follow-up is recommended [1]

---

150 patients who underwent gamma knife radiosurgery for AVMs between 2002 and 2020; twenty-five underwent further radiosurgical procedures for incompletely obliterated AVMs. We recorded the median margin doses at the first (median, 20 Gy; range, 12-23 Gy; AVM volume, 0.026-31.3 mL) and subsequent procedures (median, 18 Gy; range, 12-23 Gy; AVM volume, 0.048-9.2 mL).

Results: After the first treatment, radiologic radiation-induced changes developed in 48 (32%) patients, eight of whom had symptomatic changes. After repeat gamma knife radiosurgery, 16 of 25 patients achieved complete AVM obliteration (64%). The development of radiation-induced changes after the first treatment was significantly associated with successful obliteration by subsequent radiosurgery (OR = 24.0, 95% CI 1.20-483, P = .007). Radiation-induced changes occurred in only 5 (20%) patients who underwent a second gamma knife radiosurgery, one of whom experienced transient neurologic deficits. Between the first and repeat gamma knife radiosurgery procedures, there was no significant difference in radiologic and symptomatic radiation-induced changes (P = .35 and P = 1.0, respectively).

Conclusions: Radiation-induced changes after the first gamma knife radiosurgery were associated with AVM obliteration after a repeat procedure. The risk of symptomatic radiation-induced changes did not increase with retreatment. When the first procedure fails to achieve complete AVM obliteration, a favorable outcome can be achieved by a repeat gamma knife radiosurgery, even if radiation-induced changes occur after the first treatment [2].

2022

Talaat et al. retrospectively retrieved patients with low-grade BAVMs, either ruptured or unruptured, treated by embolization as first-line treatment in our department between January 2005 and January 2020. The primary endpoint was the total obliteration rate of BAVMs, and the secondary endpoints were hemorrhagic complications and final clinical outcome, assessed through shift of the modified Rankin scale, and mortality rate secondary to BAVM embolization.

Results: A total of 145 patients meeting inclusion criteria and treated by EVT as first-line therapy were included in the study (82 ruptured and 63 unruptured BAVMs). Overall, the complete exclusion of BAVMs was achieved in 110 patients (75.9%); 58 patients (70.7%) with ruptured and 52 (82.5%) unruptured BAVMs, including 37.9% BAVMs excluded by EVT alone (35.5% among ruptured and 44.4% among unruptured BAVMs) and 38% by combined treatment (EVT and surgery or EVT and SRS). There was no BAVM volume cut-off predictive for total obliteration by embolization alone. Early minor hemorrhagic complications were reported in 14 patients (9.6%) and early major hemorrhagic complications were reported in 5 patients (3.4%). No late hemorrhagic complications (0%) occurred; mortality rate was 0.7% (1/145 patients). Improved/unchanged mRS was reported in 137 patients (94.5%).

Endovascular treatment alone or associated with others exclusion techniques, might be safe and effective for the complete exclusion of low-grade brain arteriovenous malformations regardless of the volume [3].

A retrospective cohort study recruited patients diagnosed with AVM admitted to the hospital between 2002 and 2020. The demographic data, clinical presentations, seizure semiology, neuro-imaging findings, modality of treatment, and clinical outcomes were compared between the 2-year seizure-free and non-2-year seizure-free groups. A logistic regression model was applied to determine the significant predictors of a 2-year seizure-free outcome.

Of 372 radiologically confirmed patients with cerebral AVM, 105 (28.23%) experienced a seizure and a 2-year seizure-free outcome was achieved in 76.19%. Most seizures presented as the initial symptom. Generalized onset seizure was the most common seizure semiology. A nidus diameter < 3 cm (adjusted odds ratio [aOR] 3.102; 95% CI 1.129-9.683; p = 0.046) was the independent predictor of a 2-year seizure-free period, whereas underlying epilepsy (aOR 0.141; 95% CI 0.010-0.688; p = 0.015) was an independent predictor against a 2-year seizure-free outcome.

A arteriovenous malformation nidus diameter < 3 cm was the independent predictor of a 2-year seizure-free outcome, whereas underlying epilepsy was the factor against a 2-year seizure-free outcome [4].

2020

A retrospective analysis of a prospectively maintained database was performed in children with treated and nontreated pediatric AVMs at the University of California, San Francisco, from 1998 to 2017. Inclusion criteria were age ≤ 18 years at time of diagnosis and an AVM confirmed by a catheter

angiogram.

The authors evaluated 189 pediatric patients with AVMs over the study period, including 119 ruptured (63%) and 70 unruptured (37%) AVMs. The mean age at diagnosis was 11.6 ± 4.3 years. With respect to Spetzler-Martin (SM) grade, there were 38 (20.1%) grade I, 40 (21.2%) grade II, 62 (32.8%) grade III, 40 (21.2%) grade IV, and 9 (4.8%) grade V lesions. Six patients were managed conservatively, and 183 patients underwent treatment, including 120 resections, 82 stereotactic radiosurgery (SRS), and 37 endovascular embolizations. Forty-four of 49 (89.8%) high-grade AVMs (SM grade IV or V) were treated. Multiple treatment modalities were used in 29.5% of low-grade and 27.3% of high-grade AVMs. Complete angiographic obliteration was obtained in 73.4% of low-grade lesions (SM grade I-III) and in 45.2% of high-grade lesions. A periprocedural stroke occurred in a single patient (0.5%), and there was 1 treatment-related death. The mean clinical follow-up for the cohort was 4.1 ± 4.6 years, and 96.6% and 84.3% of patients neurologically improved or remained unchanged in the ruptured and unruptured AVM groups following treatment, respectively. There were 16 bleeding events following initiation of AVM treatment (annual rate: 0.02 events per person-year).

Coordinated multidisciplinary evaluation and individualized planning can result in safe and effective treatment of children with AVMs. In particular, it is possible to treat the majority of high-grade arteriovenous malformations with an acceptable safety profile. Judicious use of multimodality therapy should be limited to appropriately selected patients after thorough team-based discussions to avoid additive morbidity. Future multicenter studies are required to better design predictive models to aid with patient selection for multimodal pediatric care, especially with high-grade AVMs [5].

Data of 191 cerebral arteriovenous malformation patients were evaluated. After a mean follow-up of 80 months (range 37-173), the total obliteration rate after the first GKSR treatment was 66%. Mean dose higher than 22 Gy (P = .019, OR = 2.39, 95% CI 1.15-4.97) and flow rate dichotomized into high vs non-high (P < .001, OR = 0.23, 95% CI 0.11-0.51) resulted to be independent predictors of obliteration. Flow-surrogate angioarchitecture features did not emerge as independent outcome predictors.

Flow rate seems to be associated in predicting outcome after GKSR conferring high-flow AVM a lower occlusion rate. Its role should be considered when planning radiosurgical treatment of AVM, and it could be added to other parameters used in GKRS outcome predicting scales [6].

2017

A study aimed to determine whether functional outcomes at last follow-up (LFU) in patients 60 years or older differed when stratified by age.

Patients 60 years or older (n = 104) who had undergone microsurgical AVM resection (total, n = 72; 60-65 years, n = 35; and > 65 years, n = 37) or observation (n = 32) were identified from a prospective database. Age, sex, Spetzler-Martin (SM) grade, supplemented SM grade, clinical presentation, AVM location, AVM-associated aneurysms, and functional outcome measured using the modified Rankin Scale (mRS score 0-2 [favorable] vs mRS score > 2 [unfavorable]) at LFU were analyzed.

AVM patients undergoing microsurgical resection were younger, had lower AVM grades, and were more likely to present with rupture. Overall outcome in the surgical group was favorable in 71% of the

patients and was statistically significantly better in patients 60-65 years old (p = 0.039). In patients older than 65 years, outcome was dependent on SM grade and level of preexisting functional dependence. Patients with supplemented SM grades of greater than 6 points had favorable outcomes that were age dependent (p = 0.029). This difference was not observed in patients with lower supplemented SM grades or in those with low or high preoperative SM grades (SM grade ≤ 2 and grade ≥ 4, respectively).

This study demonstrates that favorable outcomes can be achieved with microsurgical resection of AVMs in elderly patients, with careful patient selection. Outcomes in more elderly patients (> 65 years of age) are more dependent on preoperative SM and supplemented SM grading than those in younger cohorts [7].

Yang et al. recruited 890 patients with BAVMs: 72 had FA(s) and 818 did not. Several factors were assessed including patient's age, gender, BAVM volume and location, and Spetzler-Martin grade.

The 890 patients with BAVM had a mean age of 30 years (range: 2-84), mean BAVM volume of 10.6 mL (range: 0.13-91.4). BAVMs were ruptured in 42% of patients. Compared to BAVM patients without FAs, the 72 patients with FAs had older age (mean 41 yrs vs 31 yrs, p < 0.001); larger average BAVM volume (39.6 mL vs 16.1 mL, p < 0.001). No statistical significance in Spetzler-Martin grades ($\chi 2$ value = 8.687 and p = 0.122) was found in terms of formation of FA. FA demonstrated similar gender distribution and BAVM location distribution (the $\chi 2$-value was 0.242 and 0.812, respectively).

Patients with older age and large BAVM volume are more prone to FA. Gender, BAVM location, and BAVM grade are not statistically significant predisposing factors for FA [8].

2016

A total of 6527 patients were hospitalized from 2009-2013 with brain AVM (Q28.2) as the principal diagnosis. Age-specific admission rate during the first year of life was high with 19.0/100,000 during the 5-year study period, corresponding to a yearly admission rate of 3.8 per 100,000 babies. Apart from the high admission rate during the first year of life, the admission rate was low, but steadily increasing during first decades of life reaching a plateau with 11.1/100,000 in the age group 30-34 years, corresponding to an annual admission rate of 2.2/100,000. After the age of 30-34 years, admission rates decreased continuously, reaching 0 in the age group 90-95 years. The lifetime risk of admission in terms of admission per 100,000 age-matched people was calculated by retrograde integration of the admission rates. At the age of 1 year, the cumulative number of future admissions for AVM during lifetime amounted to 131.3/100,000 children. For the older age groups, the chance of future admission for AVM decreased as expected, reaching 43.8/100,000 by the age of 50 and 0 by the age of 90.

Despite some open issues, the current data suggests that achieving old age with an untreated brain AVM is unlikely. Furthermore, the data support the concept that most brain AVMs are not necessarily a congenital entity but develop during the first decades of life [9].

Six patients (mean age, 44 years, male-to-female ratio, 5) presented an angiographic diagnosis of cerebral arteriovenous malformation mAVMs. Only one of them was known to have a hereditary hemorrhagic telangiectasia (HHT). Five patients presented two cerebral AVMs and one patient had three. Three AVMs (23.1 %) presented bleeding at admission. Three patients had supratentorial mAVMs only and the three others had supra and infratentorial AVMs. Only one patient suffered from bleeding of more than one of his mAVMs with an interval of 23 years.

For asymptomatic AVMs discovered incidentally without angiographic bleeding risk, Robert et al propose a therapeutic abstention. In case of AVM rupture and bleeding, the other "associated" AVMs (discovered through a complete angiographic assessment) should also be treated if they are not located in an eloquent area and if the treatment does not present technical difficulties. AVMs with a history of bleeding or associated to angiographic risks have to be treated more aggressively [10].

2014

Kim et al. harmonized data from Kaiser Permanente of Northern California (n = 856), University of California San Francisco (n = 787), Columbia University (n = 672), and the Scottish Intracranial Vascular Malformation Study (n = 210). We censored patients at first treatment, death, last visit, or 10-year follow-up, and performed stratified Cox regression analysis of time-to-hemorrhage after evaluating hemorrhagic presentation, sex, age at diagnosis, deep venous drainage, and AVM size as predictors. Multiple imputation was performed to assess impact of missing data.

A total of 141 hemorrhage events occurred during 6,074 patient-years of follow-up (annual rate of 2.3%, 95% confidence interval [CI] 2.0%-2.7%), higher for ruptured (4.8%, 3.9%-5.9%) than unruptured (1.3%, 1.0%-1.7%) AVMs at presentation. Hemorrhagic presentation (hazard ratio 3.86, 95% CI 2.42-6.14) and increasing age (1.34 per decade, 1.17-1.53) independently predicted hemorrhage and remained significant predictors in the imputed dataset. Female sex (1.49, 95% CI 0.96-2.30) and exclusively deep venous drainage (1.60, 0.95-2.68, p = 0.02 in imputed dataset) may be additional predictors. AVM size was not associated with intracerebral hemorrhage in multivariable models (p > 0.5).

This large, individual patient data meta-analysis identified hemorrhagic presentation and increasing age as independent predictors of hemorrhage during follow-up. Additional AVM cohort data may further improve precision of estimates, identify new risk factors, and allow validation of prediction models [11]

Hemorrhage led to hospital admission in 58.2% patients; 35.5% were admitted with epileptic seizures and 24.5% of patients reported chronic headaches. On the Spetzler-Martin scale, 26.0% were grade 1, 38% grade 2, 25% grade 3, and 11% grade 4. Preoperative embolization was performed in 43.6%. Treatment-associated new neurological deficits at the time of discharge from the hospital occurred in 25.5%. At the time of follow-up, 94.2% of the patients were completely independent (Barthel index of 100). 64.7% of the patients with preoperative epilepsy were free of disabling seizures or rarely have disabling seizures (Engel class 1 and 2), 16.7% reported no significant change, and 17.6% reported worsening. A total of 17.6% patients in whom epilepsy was not known at the time of AVM treatment reported new seizures after therapy, all but one had hemorrhage. 38.5% of patients with preoperative chronic headache reported improvement, 53.8% no change, and 7.7% deterioration. Regarding SF-36 QoL scores, a statistically significant difference from the age-matched German norm values was found in the dimensions Bodily Pain (p = 0.03) and Emotional Role Function (p = 0.04). There was a trend for

lower physical and mental sum scores in patients undergoing emergency surgery.

A series of 110 patients with cerebral AVM, surgically treated between 1994 and 2009, were analyzed. Epidemiological, sociodemographic, and disease-related characteristics were extracted from the patient records. A detailed follow-up interview was possible with 51 patients after a median of 7 ± 5 years after surgery. A structured telephone interview using the Short Form (SF)-36 for QoL assessment was performed. In addition, specific questions regarding epilepsy and seizure outcome as well as independence and professional activity were asked. Results Hemorrhage led to hospital admission in 58.2% patients; 35.5% were admitted with epileptic seizures and 24.5% of patients reported chronic headaches. On the Spetzler-Martin scale, 26.0% were grade 1, 38% grade 2, 25% grade 3, and 11% grade 4. Preoperative embolization was performed in 43.6%. Treatment-associated new neurological deficits at the time of discharge from the hospital occurred in 25.5%. At the time of follow-up, 94.2% of the patients were completely independent (Barthel index of 100). 64.7% of the patients with preoperative epilepsy were free of disabling seizures or rarely have disabling seizures (Engel class 1 and 2), 16.7% reported no significant change, and 17.6% reported worsening. A total of 17.6% patients in whom epilepsy was not known at the time of AVM treatment reported new seizures after therapy, all but one had hemorrhage. 38.5% of patients with preoperative chronic headache reported improvement, 53.8% no change, and 7.7% deterioration. Regarding SF-36 QoL scores, a statistically significant difference from the age-matched German norm values was found in the dimensions Bodily Pain (p = 0.03) and Emotional Role Function (p = 0.04). There was a trend for lower physical and mental sum scores in patients undergoing emergency surgery.

SF-36-based QoL scores after treatment of AVM differ little from the age-matched German averages. The long-term results regarding chronic epilepsy and chronic headache need further analysis [12].

[1)
Oulasvirta E, Koroknay-Pál P, Numminen J, Hafez A, Raj R, Jahromi BR, Niemelä M, Laakso A. Recurrence of brain arteriovenous malformations in pediatric patients: a long-term follow-up study. Acta Neurochir (Wien). 2023 May 4. doi: 10.1007/s00701-023-05612-8. Epub ahead of print. PMID: 37140647.

[2)
Sasagasako T, Mori H, Hattori EY, Ikedo T, Hamano E, Shimonaga K, Kushi Y, Iihara K, Kataoka H. Radiation-Induced Changes Associated with Obliteration of Brain AVMs after Repeat Radiosurgery. AJNR Am J Neuroradiol. 2023 Feb;44(2):143-149. doi: 10.3174/ajnr.A7772. Epub 2023 Jan 26. PMID: 36702500; PMCID: PMC9891338.

[3)
Talaat M, Shotar E, Premat K, Boch AL, Delaitre M, Borius PY, Nouet A, Lenck S, Talbi A, Bessar A, Taema M, Bessar A, Hassan F, Elserafy TS, Lefevre E, Degos V, Sourour N, Clarençon F. Safety and Effectiveness of First-line Endovascular Management of Low-Grade Brain Arteriovenous Malformations : Single Center Experience in 145 Patients. Clin Neuroradiol. 2022 Dec;32(4):1019-1029. doi: 10.1007/s00062-022-01176-9. Epub 2022 May 13. PMID: 35551419.

[4)
Khumtong R, Katawatee K, Amornpojnimman T, Riabroi K, Sungkaro K, Korathanakhun P. Predictors of seizure control in patients with cerebral arteriovenous malformation. Epilepsy Behav. 2022 Feb 2;128:108575. doi: 10.1016/j.yebeh.2022.108575. Epub ahead of print. PMID: 35123239.

[5)
Winkler EA, Lu A, Morshed RA, Yue JK, Rutledge WC, Burkhardt JK, Patel AB, Ammanuel SG, Braunstein S, Fox CK, Fullerton HJ, Kim H, Cooke D, Hetts SW, Lawton MT, Abla AA, Gupta N. Bringing high-grade arteriovenous malformations under control: clinical outcomes following multimodality treatment in children. J Neurosurg Pediatr. 2020 Apr 10:1-10. doi: 10.3171/2020.1.PEDS19487. Epub ahead of print. PMID: 32276243.

6)

Panni P, Gallotti AL, Gigliotti CR, Shehata AB, Albano L, da Passano CF, Barzaghi RLA, Capitanio JF, Righi C, Simionato F, Scomazzoni F, Del Vecchio A, Falini A, Mortini P. Impact of flow and angioarchitecture on brain arteriovenous malformation outcome after gamma knife radiosurgery: the role of hemodynamics and morphology in obliteration. Acta Neurochir (Wien). 2020 Apr 26. doi: 10.1007/s00701-020-04351-4. [Epub ahead of print] PubMed PMID: 32335814.

7)

Burkhardt JK, Lasker GF, Winkler EA, Kim H, Lawton MT. Microsurgical resection of brain arteriovenous malformations in the elderly: outcomes analysis and risk stratification. J Neurosurg. 2017 Dec 22:1-7. doi: 10.3171/2017.6.JNS17392. [Epub ahead of print] PubMed PMID: 29271715.

8)

Yang WY, Luo CB, Tsuei YS, Guo WY, Wu HM, Chung WY. A single-institution study of predisposing factors of patients with BAVMs to flow-related aneurysm. J Formos Med Assoc. 2018 Sep 5. pii: S0929-6646(18)30334-6. doi: 10.1016/j.jfma.2018.08.016. [Epub ahead of print] PubMed PMID: 30195970.

9)

Petridis AK, Fischer I, Cornelius JF, Kamp MA, Ringel F, Tortora A, Steiger HJ. Demographic distribution of hospital admissions for brain arteriovenous malformations in Germany-estimation of the natural course with the big-data approach. Acta Neurochir (Wien). 2016 Feb 13. [Epub ahead of print] PubMed PMID: 26873715.

10)

Robert T, Blanc R, Botta D, Ciccio G, Smajda S, Redjem H, Fahed R, Piotin M. Management of multiple cerebral arteriovenous malformations in a non-pediatric population. Acta Neurochir (Wien). 2016 Jun;158(6):1019-25. doi: 10.1007/s00701-016-2785-5. Epub 2016 Apr 6. PubMed PMID: 27052512.

11)

Kim H, Al-Shahi Salman R, McCulloch CE, Stapf C, Young WL; MARS Coinvestigators. Untreated brain arteriovenous malformation: patient-level meta-analysis of hemorrhage predictors. Neurology. 2014 Aug 12;83(7):590-7. doi: 10.1212/WNL.0000000000000688. Epub 2014 Jul 11. PMID: 25015366; PMCID: PMC4141996.

12)

Rohn B, Haenggi D, Etminan N, Kunz M, Turowski B, Steiger HJ. Epilepsy, Headache, and Quality of Life after Resection of Cerebral Arteriovenous Malformations. J Neurol Surg A Cent Eur Neurosurg. 2014 Mar 12. [Epub ahead of print] PubMed PMID: 24623000.