Angioarchitectural Risk Factors for Hemorrhage and Clinical Long-Term Outcome in Pediatric Patients with Cerebral Arteriovenous Malformations

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BACKGROUND: **Intracranial arteriovenous malformation (AVM) in children is a rare diagnosis. Little is known about factors determining AVM rupture and appropriate treatment strategies to prevent hemorrhage and associated disability. Available data suggest that children are subject to an increased risk for AVM rupture compared with adults.**

METHODS: **In 46 pediatric patients with AVM, demographic factors, clinical presentation, angioarchitectural features, and treatment regimens as well as clinical and radiologic outcomes were retrospectively analyzed. First-line treatment option was microsurgical resection of the disease, with or without preoperative embolization.**

RESULTS: **Twenty-four boys (52.2%) and 22 girls (47.8%) with a mean age on admission of 12.4 years (4—18 years) were included. Mean follow-up was 4 years (median, 1.5; range, 0.1—16.4). Thirty-one children presented with intracerebral hemorrhage (67.4%). Small AVMs (<3 cm) ruptured in 83.3% ($n = 25$) and were shown to be more prone to hemorrhage than larger ones ($P < 0.01$). Small AVM size ($P < 0.01$; odds ratio [OR], 0.12; 95% confidence interval [CI] 0.02—0.59) and exclusive deep venous drainage ($P < 0.01$; OR, 29.74; 95% CI, 2.45—4445.34) were independent risk factors for hemorrhage in the presented cohort. Good long-term outcome was associated with a high score on the Glasgow Coma Scale on admittance ($P < 0.05$; OR, 0.148; 95% CI, 0.03—0.73).**

CONCLUSIONS: **Two-thirds of children with AVM are admitted with intracerebral hemorrhage. Microsurgical resection was successful as confirmed by radiologic studies in 95%, and 79.5% of patients presented in a good clinical condition on follow-up (modified Rankin Scale 0 or 1). Microsurgical treatment is recommended if the lesion is accessible and angioarchitectural risk factors favor definitive treatment.**

INTRODUCTION

Cerebral arteriovenous malformations (AVMs) in children are a congenital disease but rarely become symptomatic during childhood other than with hemorrhage.[1,2] The prevalence in the pediatric population is estimated at 0.0014%—0.028%.[3] In adults, 30%—50% of patients with cerebral AVM initially present with intracerebral hemorrhage (ICH), but AVM rupture in the pediatric population is more common and ICHs are seen in 58%—77% on admission.[2-4] The annual risk for hemorrhage is estimated to be between 2% and 4% for the entire AVM group, depending on the method of calculation, but is reported to reach 10% during the pediatric age period,[1-3] putting these patients at higher risk compared with elderly patients.[5] The greater regenerative capacity and plasticity of a child's brain enables better recovery from hemorrhage and possible adverse treatment events, thus justifying an aggressive treatment approach.[6] We analyzed possible angioarchitectural risk factors for AVM rupture in children to add more substantial data on treatment planning and to identify factors determining clinical long-term outcome in a pediatric cohort predominantly treated by microsurgery in our institution.

Key words
- Angioarchitecture
- AVM
- Clinical outcome
- Pediatric arteriovenous malformations

Abbreviations and Acronyms
AVM: Arteriovenous malformation
CI: Confidence interval
GCS: Glasgow Coma Scale
ICH: Intracerebral hemorrhage
mRS: Modified Rankin Scale
OR: Odds ratio
SM grading: Spetzler-Martin grading

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METHODS

Patients younger than 18 years with an intracerebral AVM admitted between 1992 and 2015 at a single center were included. The study group ($n = 46$) was extracted out of a total number of 560 patients from an AVM database (8.2%) (local ethics committee registry number: PV4342).

Demographic factors and clinical symptoms on admission and on long-term follow-up were retrospectively analyzed. The severity of neurologic symptoms on admission was assessed according to the Glasgow Coma Scale (GCS) and subdivided into 3 groups: severe neurologic deterioration with a GCS 3–8, moderate neurologic impairment with a GCS 9–12, and minor neurologic symptoms with a GCS 13–15.[7]

General treatment strategy in pediatric patients is shown in Figure 1. AVMs were classified according to the Spetzler-Martin grading (SM grading) scale.[8] AVM size was classified as small (<3 cm), intermediate (3–6 cm), or large (>6 cm). Angioarchitectural features of AVMs were assigned per radiologic reports and review of pre- and postoperative angiographic images. Location of the AVM, nidus size, venous drainage pattern and anomalies, AVM-associated aneurysms (flow-associated/intranidal), arterial territorial blood supply, and the number of arterial feeders were assessed and univariately analyzed.

AVM location was determined as superficial (parenchymal/cortical), deep (basal ganglia, thalamus, corpus callosum), or infratentorial. Venous drainage was classified as superficial or deep and the number of draining veins was assessed. Territorial blood supply was assigned to the anterior, middle, posterior cerebral artery, or the vertebrobasilar complex.

Microsurgical resection alone or in combination with preoperative embolization was considered as the first-line treatment option.[2,9-11] Definitive embolization was chosen if the complete endovascular exclusion of the AVM seemed to be promising (single feeder, deeply located AVM); palliative embolization was reserved for the cases in which reduction of arteriovenous shunting seemed to be advisable to prevent recurrent hemorrhage. Radiosurgery or conservative therapy ("wait and scan") were considered if none of the aforementioned options promised to be successful.

Treatment success was verified by postoperative digital subtraction angiography on follow-up at 3–6 months after treatment. Patient outcome was assessed either with a neurologic examination in a routine outpatient visit or via telephone interview using the modified Rankin Scale (mRS). Good outcome was defined as an mRS of 0 or 1 according to Darsaut et al.[12]

Descriptive statistics were used to characterize the study population. A Student t test was used to compare means of metric variables and the likelihood-ratio χ^2 test for categorial variables was used whenever appropriate. Univariate logistic regression analysis was used to identify potential independent associations of angiographic factors and hemorrhagic presentation as well as factors influencing clinical outcome. Selected variables that have previously been shown in the literature to be associated with a hemorrhagic presentation were analyzed in a multivariate regression model. We used Firth's method for exact logistic regression to calculate odds ratios (ORs) and corresponding confidence intervals (CIs). Statistical significance was set at $P < 0.05$. All statistics were performed using SPSS R 2.15.2 (IBM, Armonk, New York, USA).[13]

RESULTS

Twenty-four males (52.2%) and 22 females (47.8%) with a mean age on admission of 12.4 years (median, 13 years; minimum, 4; maximum, 17) were included. The study population comprised 3 patients aged 0–5 years (6.5%), 12 children aged 6–11 years (26.1%) and a majority of young adolescents between the ages of 12 and 18 years (67.4%, $n = 31$). Mean follow-up was 4.0 years (median 1.5 years; minimum, 0.1; maximum, 16.4).

Clinical Presentation

Neurologic symptoms, initial GCS, and rates of hemorrhage on presentation are shown in Table 1. Hemorrhage was seen in the youngest group in 66.6% ($n = 2$), in the group from 6 to 11 years in 75% ($n = 9$), and in the oldest group in 55% ($n = 20$) of patients. Statistical analysis did not show a correlation between age and the rate of hemorrhage ($P = 0.74$; OR, 0.667; CI, 0.124–3.003) in our cohort. Nonhemorrhagic presentations mostly occurred as a result of incidental findings of the AVM on MRI scans (eg, as a result of imaging initiated because of fever convulsions or trauma).

Hemorrhage

In 67.4% ($n = 31$) of pediatric patients, a hemorrhagic event led to admission. Of these, 93.5% ($n = 29$) showed a parenchymal ICH, 22.6% ($n = 7$) of whom had in addition intraventricular hemorrhage. All patients with intraventricular hemorrhage were immediately treated by placement of an external ventricular drainage. In 4 patients (12.9%), the intracerebral hematoma was evacuated as an emergency procedure without approaching the AVM itself, which was consequently approached electively at a later stage. In 2 cases (6.5%), the hematoma and the underlying AVM were surgically removed simultaneously. In these cases, the AVM had been assessed by angiography, yet the size of the ICH and threatening intracranial pressure called for an earlier rather than delayed intervention.

AVM Size and Grading

Figure 2 shows the distribution of AVMs according to the SM grading. AVM nidus size was smaller than 3 cm in 65.2% ($n = 30$) followed by an intermediate size of 3–6 cm in 28.3% ($n = 13$), and AVMs larger than 6 cm were found in 6.5% ($n = 3$) of cases. When comparing the nidus size in AVMs less than 3 cm with those larger than 3 cm, univariate analysis showed that small AVMs were more likely to rupture than larger ones ($P < 0.01$; OR, 0.128; CI, 0.023–0.583) (Figure 3) in the presented cohort.

Location

Superficially located AVMs (cortical) were identified in 73.9% ($n = 34$), deeply located AVMs (thalamic/basal ganglia) were found in 17.4% ($n = 8$), and infratentorial AVMs were found in 8.7% ($n = 4$) of patients. All patients with infratentorial AVM presented with cerebellar hemorrhages on admission, although this was not shown to be a significant risk factor for rupture on univariate analysis ($P = 0.288$) (Figure 4).