

Radiologic Characteristics and High Risk of Seizures in Infants with Ruptured Intracranial Aneurysms: Case Report and Review of the Literature

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■ **OBJECTIVE:** To evaluate the parameters related to the high risk of preoperative seizures in infants (1 year or younger) with ruptured intracranial aneurysms.

■ **METHODS:** Infants with ruptured intracranial aneurysms treated at our institution from January 2012 to January 2018 were retrospectively analyzed. Seventeen similar cases of infant patients with seizures reported in published studies were reviewed.

■ **RESULTS:** The mean age of the 7 infant patients treated at our institution was 4.1 ± 3.3 months (range, 28 days to 11 months), with 2 male and 5 female subjects. One patient (14.3%) had an internal carotid artery aneurysm with subarachnoid hemorrhage, and the remaining 6 patients (85.7%) had middle cerebral artery (MCA) aneurysms in the distal arterial region with lobe hemorrhage. Five of the 7 infants (71.4%) had seizures, 4 of whom (4/5, 80.0%) had MCA distal arterial aneurysms with lobe hemorrhage. Management was successful for all patients with aneurysm clipping or resection surgery, and one patient experienced postoperative seizures. Of the 17 reviewed cases of infant patients with seizures, 10 patients (58.8%) exhibited the typical distal arterial aneurysm with lobe hemorrhaging, and 6 (60%) of them had aneurysms in MCA.

■ **CONCLUSIONS:** Infant patients with ruptured intracranial aneurysms have a high risk of preoperative seizures. The typical radiologic finding of distal arterial aneurysm with lobe hemorrhage was frequently observed in the MCA, and it might be related to the high risk of preoperative seizures in this population. Microsurgical techniques

effectively control postoperative seizures in infants with ruptured intracranial aneurysms.

INTRODUCTION

Seizures are common complications following the rupture of intracranial aneurysms, with an incidence of 3%–18% in adult patients.^{1,2} Several studies have reported a higher risk of seizures in pediatric patients than in adult patients,^{3,4} but few studies have focused on patients in the very young age group. The results of our previous studies indicated that an incidence of seizure in infants (≤ 1 year old) with ruptured intracranial aneurysms was the highest among all pediatric age groups.^{5,6} However, the underlying mechanism was not analyzed. The aim of this study was to identify the parameters related to the high risk of seizures in infants with ruptured intracranial aneurysms.

MATERIALS AND METHODS

Study Design and Participants

This study was a retrospective observational study that was approved by the institutional review board of West China Hospital. The hospital information system was used to collect the in-hospital data. The inclusion criteria were as follows: 1) patients identified by the discharge ICD-10 diagnosis codes I60.0–I60.9 for ruptured intracranial aneurysms and 2) age less than or equal to 1 year. One experienced neurosurgeon and one neuroradiologist confirmed the diagnoses of the selected cases. Patients with incorrect diagnoses or incomplete profiles hindering the confirmation of the original diagnoses were excluded.

Key words

- Distal arterial aneurysms
- Infants
- Intracranial aneurysms
- Lobe hemorrhage
- Middle cerebral artery
- Seizures

Abbreviations and Acronyms

DSA: Digital subtraction angiography

HH: Hunt and Hess

MCA: Middle cerebral artery

SAH: Subarachnoid hemorrhage

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Table 1. Patient Characteristics

Patient Number	Age	Sex	History	Presentation	HH Scale Grade	Imaging Findings	Modified Fisher Grade	Size (cm)	Location
1	3 months	Female	No	Vomiting; right-sided hemiparesis	III	SAH, lobe hemorrhage, SDH	III	1.1	M3 of MCA
2	4 months	Male	URI	Seizure; vomiting	IV	SAH, lobe hemorrhage, SDH	III	0.5	M3 of MCA
3	2 months	Female	No	Eye deviation; lethargy	II	Lobe hemorrhage	0	0.8	M2 of MCA
4	3 months	Female	No	Seizure; vomiting	III	Lobe hemorrhage	0	0.8	M2 of MCA
5	11 months	Female	No	Seizure; vomiting; lethargy	II	SAH, lobe hemorrhage	III	1.2	M2 of MCA
6	28 days	Male	Head trauma	Coma; seizure; vomiting	III	Lobe hemorrhage	0	0.8	M4 of MCA
7	5 months	Female	No	Seizure; lethargy	II	SAH	II	1.2	ICA

HH, Hunt and Hess; SAH, subarachnoid hemorrhage; SDH, subdural hemorrhage; MCA, middle cerebral artery; URI, upper respiratory tract infection.

Data Collection

The baseline information included age, sex, family history of seizures, low gestational age, low birth weight, pregnancy or delivery complications, psychomotor retardation, febrile seizures, a history of head trauma, hypertension, diabetes mellitus, prior hemorrhagic stroke, renal insufficiency (acute or chronic), fever or other infectious disease, cerebral palsy, coronary artery disease, asthma, sickle cell disease, connective tissue diseases, endocarditis, arteritis, collagen vascular disorders, a family history of aneurysm or other hereditary diseases, Hunt and Hess (HH) grade on admission, and preoperative seizures. Radiologic findings included the results of cranial computed tomography, computed tomographic angiography, and digital subtraction angiography (DSA) and the modified Fisher grade on admission. The aneurysm features included the number, location, type, and size (aneurysms with diameters larger than 25 mm were considered giant, and those with diameters 15–25 mm were considered large).

Seizures

A seizure was defined as repetitive, rhythmic jerking with or without preceding tonic spasm that was focal or generalized in nature and occurred with or without loss of consciousness. When seizures occurred outside the hospital, only seizures observed by medical staff members, relatives, caregivers, or paramedics were included.

Statistical Analysis

SPSS software (version 22.0; SPSS Inc., Chicago, Illinois, USA) was used to perform all statistical analyses. For quantitative data, means \pm standard deviation (SD) are presented. Categorical data are presented as frequencies and percentages.

RESULTS

Baseline Information

Forty-three pediatric patients (<18 years old) with ruptured intracranial aneurysms were treated in the Department of Neurosurgery of West China Hospital, Sichuan University, from January 2012 to January 2018. Data for 7 infant patients (16.3%) were evaluated. Patient information is shown in Table 1. Age range was

28 days to 11 months (mean 4.1 ± 3.3 months), with 2 male and 5 female subjects. One patient had a medical history of infectious disease (fever and upper respiratory tract infections), and 1 patient had suffered head trauma before seizure onset. No patient had a family history of seizures, complications during pregnancy or delivery, low gestational age, low birth weight, a history of seizures or other diseases. Six patients (85.7%) had good clinical presentation (HH grade I–III) on admission. One patient (10.6%) had an internal carotid artery aneurysm with subarachnoid hemorrhage (SAH), and the remaining 6 patients (85.7%) had middle cerebral artery (MCA) aneurysms, which were all located distal to the main branch, with 3, 2, and 1 lesions in M2, M3, and M4, respectively. Notably, all 6 patients (85.7%) with distal MCA aneurysms exhibited a lobe hemorrhage, and 2 patients (33.3%) also had subdural hemorrhage. The modified Fisher grade was 0 for 3 patients, II for 1 patient, and III for the remaining 3 patients. No patients had large or giant aneurysms.

Preoperative Seizures and Typical Image Features

Preoperative seizures were observed in 5 of 7 patients (71.4%), 4 of whom experienced generalized tonic-clonic seizures, while the other experienced focal motor seizures. The remaining 2 patients (28.6%) did not experience seizures. Notably among the patients with seizures, except for 1 patient with an internal carotid artery aneurysm with SAH, 4 patients (4/5, 80.0%) had distal MCA aneurysms with lobe hemorrhage, accounting for 4 of 6 (66.7%) of the patients with this radiologic presentation. The data from the 6 patients with distal MCA aneurysms with lobe hemorrhage are shown in Figure 1.

Treatment and Postoperative Seizures

All 7 infant patients received microsurgical treatments involving aneurysm clipping (resection) or hematoma evacuation. Complete obliteration of aneurysms was achieved in all 7 infant patients, together with an improvement of neurologic deficits. The follow-up time ranged from 0.33 to 5.5 years (mean, 2.88 years). Postoperative seizures recurred in 1 patient before the age of 2 years (patient 4).

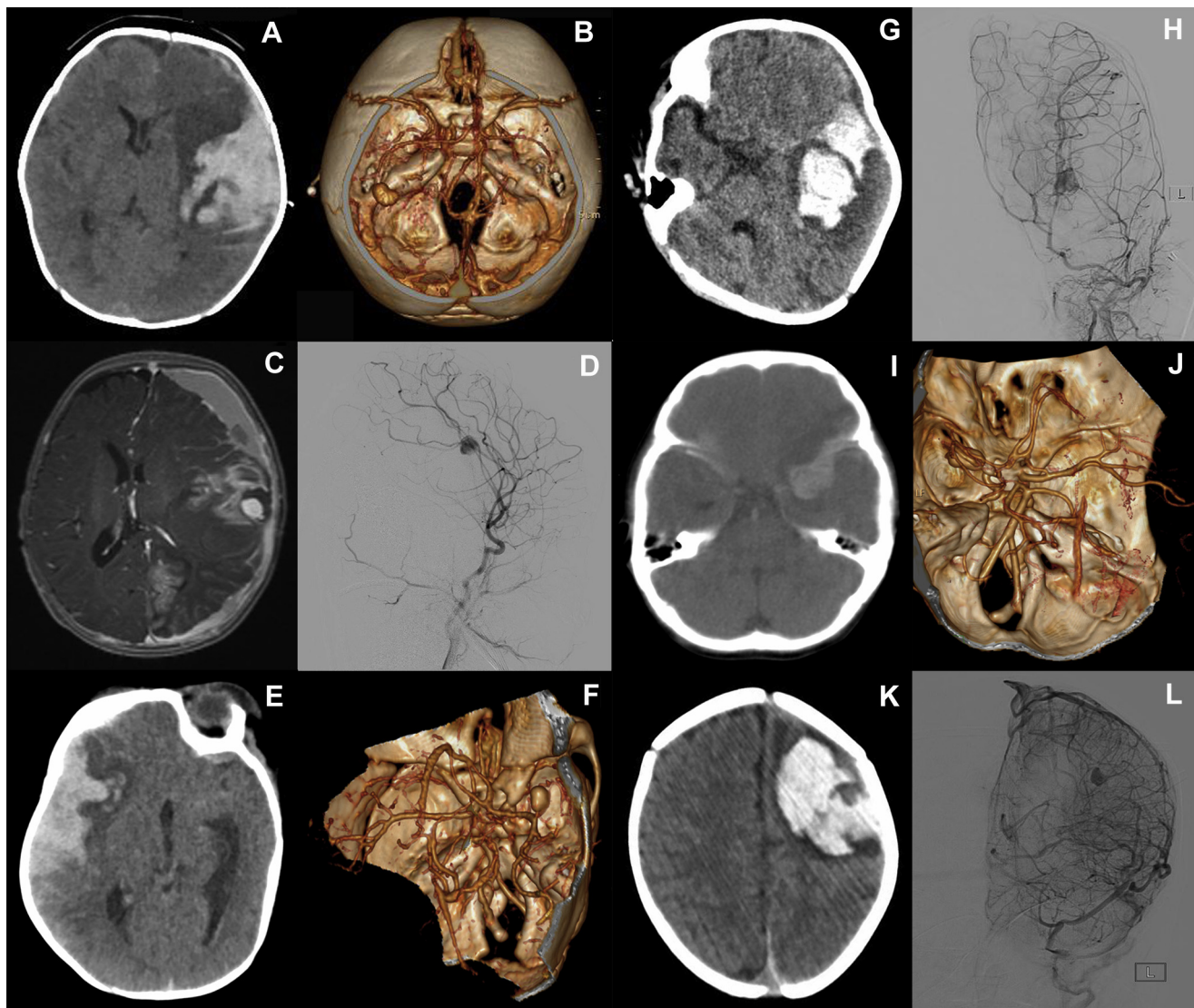


Figure 1. Images of infant patients with distal middle cerebral artery (MCA) aneurysms with lobe hemorrhage. Infant patients with distal middle cerebral artery aneurysms with lobe hemorrhage. (A, C, E, G, I, K) Computed tomography (CT) showed that patients 1–6 had hemorrhage in

the lobe close to the cerebral cortex, with patients 1 (A) and patients 2 (C) also exhibiting subdural hemorrhage. (B, D, F, H, J, L) CT angiography or digital subtraction angiography showed aneurysms in the MCA located distal to the main branch of the artery.

Literature Review

We reviewed 17 patients with ruptured aneurysms who exhibited preoperative seizures⁷⁻²³ (Table 2). The mean age was 4.1 ± 3.7 months (range, 7 days to 11 months) and the male-to-female ratio was 64.7%. Eleven patients (64.7%) had distal arterial aneurysms, 8 patients (47.1%) had aneurysms in the MCA, and 11 had (64.7%) had lobe hemorrhage, 3 of whom also had subdural hemorrhage. HH scale data were available for 11 patients on admission, and a good clinical presentation (grade I–III) was observed in 10 of these patients (90.9%). In addition, 13 patients had modified Fisher grades of 0–II. The size of the lesions was

reported for 14 patients, and 7 patients (50.0%) had large or giant aneurysms. Ten patients (58.8%) presented with the typical distal arterial aneurysm with lobe hemorrhage, and 6 aneurysms (60%) were located in the MCA.

DISCUSSION

The incidence of seizures in our infant group with ruptured intracranial aneurysms reached 71.4%, which is higher than the results reported by other pediatric studies^{3,4} and approximately 4 times the incidence reported in adult patients.^{1,2} Considering our

Table 2. Literature Review of Infants with Ruptured Intracranial Aneurysms who Presented Preoperative Seizures

Reference	Age	Sex	History	HH Scale Grade	Distal Location	Image Findings	Modified Fisher Grade	Size (cm)	Location
Palacios et al., 2017 ⁷	5 months	Male	No	NA	No	SAH	II	NA	BA
Hidalgo et al., 2017 ⁸	26 days	Female	Heart surgery	NA	Yes	SAH, lobe hemorrhage, SDH	III	0.2	MCA
Ravindra et al., 2016 ⁹	6 months	Female	No	NA	Yes	SAH	II	0.6	MCA
Fathi et al., 2015 ¹⁰	2 months	Male	No	I	Yes	Lobe hemorrhage, IVH	0	2.9	ACA
Goncalves et al., 2014 ¹¹	3 months	Female	No	I	No	IVH	0	2.6	ACoMA
Rao et al., 2013 ¹²	3 months	Male	No	NA	Yes	Lobe hemorrhage	0	Small*	MCA
Al-Youbi et al., 2012 ¹⁵	11 months	Female	No	III	Yes	Lobe hemorrhage	0	Giant*	MCA
Sabanci et al., 2012 ¹³	47 days	Male	No	I	Yes	SAH, lobe hemorrhage	III	2.5	PCA
Mitchell et al., 2012 ¹⁴	9 months	Male	Family history of aneurysm	I	Yes	Lobe hemorrhage	0	NA	MCA
Hill et al., 2011 ¹⁶	8 months	Female	Meningoencephalitis	I	No	Lobe hemorrhage, basal ganglia infarction	0	1.2	MCA
Tai et al., 2010 ¹⁷	9 days	Male	No	NA	Yes	SAH, lobe hemorrhage, IVH	III	0.3	PICA
Iza-Vallejo et al., 2009 ¹⁸	36 days	Male	No	I	Yes	Lobe hemorrhage, SDH	0	2.0	MCA
Kasliwal et al., 2008 ¹⁹	21 days	Male	NA	I	No	SAH	II	2.6	ICA
Adeleye et al., 2008 ²⁰	8 months	Male	No	II	Yes	Lobe hemorrhage, SDH	0	NA	MCA
Ahmad et al., 2006 ²¹	9 months	Male	Congenital IgA deficiency; long-term fever and URI	IV	No	SAH	II	Small*	BA
Song et al., 2005 ²²	11 days	Female	No	NA	No	SAH, IVH	III	Large*	ACoMA
Horowitz et al., 2005 ²³	7 days	Male	Myelomeningocele	NA	Yes	Lobe hemorrhage, IVH	0	Small*	ACA

HH, Hunt and Hess; NA, not available; SAH, subarachnoid hemorrhage; BA, basilar artery; SDH, subdural hemorrhage; MCA, middle cerebral artery; IVH, intraventricular hemorrhage; ACA, anterior cerebral artery; ACoMA, anterior communicating artery; PCA, posterior cerebral artery; PICA, posterior inferior cerebellar artery; ICA, inferior cerebellar artery; Ig, immunoglobulin; URI, upper respiratory tract infection.

*Without data, based on the description in the article.

treated patients and the reviewed cases from the literature, infants with ruptured intracranial aneurysms who have preoperative seizures tend to have lesions in the distal arterial region combined with lobe hemorrhaging; this typical radiologic finding was frequently present in the MCA. During long-term follow-up, good seizure control was noted in infants who were managed promptly with microsurgical techniques.

The risk factors for seizures in adult patients with ruptured intracranial aneurysms, including a history of hypertension, a poor HH grade upon admission, and a thick SAH clot (high modified Fisher grade), were not obvious in this infant study.^{2,24} The risk factors for large or giant aneurysms were pronounced in the reviewed cases (50%); however, none of our own treated infant patients had these lesions. This discrepancy may be due to the small sample size of our study or ethnic differences.

The results of our study indicate that infants with ruptured intracranial aneurysm who have seizures tend to exhibit the typical radiologic finding of distal arterial aneurysms with lobe hemorrhage. Given their extremely high risk of seizures, we postulate that this typical radiologic pattern might be associated with a high risk of seizures. Compared with trunk proximal aneurysms and deep hematomas, these distal lesions are close to the surface of the brain. Therefore, they directly compress and stimulate the cerebral cortex and can easily cause a sudden surge of electrical activity in the brain, promoting the onset of seizure.²⁵⁻²⁷ Our results indicate that these distal arterial aneurysms with lobe hemorrhage lesions were frequently observed in the MCA in infant patients. This predilection might be explained by the unbalanced early embryonic development of intracranial vessels in children, since cerebral blood flow in the MCA territory is reported to be more pronounced than in other areas.^{28,29}

A younger age (<40–50 years) is a risk factor associated with higher risk of seizures in adult patients with ruptured intracranial aneurysms.² This trend was also confirmed in the pediatric group. The age-related functional development of the brain might be another mechanism related to the high risk of seizures in the infant group. On one hand, the accelerated development of cortical function during early development in children results in increased changes in electrical activity in the surrounding area.^{30,31} On the other hand, the immature development of brain function makes it difficult to resist or adjust to the injury or stimulation caused by head trauma and ruptured aneurysms, which can increase the risk of seizure in this age group.³²

Infant patients with ruptured intracranial aneurysms have a high incidence of seizures. In the clinical setting, because very young patients are unable to express uncomfortable feelings such as headache, symptoms such as seizures should be important clues for the diagnosis of ruptured intracranial aneurysms in this age group. Meanwhile, our results from the infant group indicate

that the presence of aneurysmal intraparenchymal hematoma was more common other than subarachnoid hemorrhages. Patients with small aneurysms embedded in hematomas have a higher risk of misdiagnosis with spontaneous ICH, particularly during the rapid preparation for emergency surgery or an evaluation by a less experienced physician. Therefore, for infant patients with seizures who have been confirmed to have a brain hemorrhage on computed tomographic scan, a careful evaluation of computed tomographic angiography or DSA images by experienced physicians is highly recommended to screen for possible small aneurysms to avoid unexpected fatal bleeding in these small children.

Based on our study, good seizure control was noted during long-term follow-up of infants who were treated with microsurgical techniques. By clipping or resecting the aneurysms and evacuating the intracranial hematoma (if necessary), surgical interventions reduce the mass effect of the lesions and therefore control their stimulation of the cortical surface. In addition, flushing of the hemorrhage in subarachnoid space and replacing the cerebrospinal fluid decreases the stimulation of the cerebral arteries, reducing the incidence of vasospasm, cerebral infarction complications, and risk of seizure.³³ These advantages of the surgical approach could improve the control of postoperative seizures; however, none of our infant patients underwent the endovascular approach, and the sample size of our study is small. To date, studies discussing the proper treatment for pediatric patients with intracranial aneurysms in regard to control of seizure symptoms are still rare. Additional studies on this topic using larger sample sizes and treatment comparisons are needed to support our results.

Limitations of our study include the nonrandomized retrospective design and the small sample size because of the rarity of this disease; thus, we were unable to perform additional statistical analyses. In addition, all infant patients received microsurgical treatments; therefore, our study lacks a comparison between the effects of surgical and endovascular approaches on controlling postoperative seizures. Additional well-designed studies with larger sample sizes are still warranted to support our results and identify additional risk factors for seizures in pediatric patients with intracranial aneurysms.

CONCLUSION

Infants with ruptured intracranial aneurysms have a high risk of preoperative seizures. The typical radiologic presence of distal arterial aneurysms with lobe hemorrhage was frequently observed in the MCA and might be related to the high risk of preoperative seizures in this population. Microsurgical techniques effectively control postoperative seizures in infants with ruptured intracranial aneurysms.

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