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ORIGINAL ARTICLE

Whether the Spetzler-Martin Grading Scale is Adequate to Children with Intracranial Arteriovenous Malformations?

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Background: Intracranial arteriovenous malformation (ICAVM) is a rare and life-threatening disease. Clinical presentations of pediatric ICAVMs are variable and unpredictable. The Spetzler-Martin grading scale (SMGS) is a commonly used system for predicting prognoses and guiding therapeutic protocols. However, the application of this system to children is controversial. **Objective:** The purposes of this study were to retrospectively analyze clinical presentations of children with ICAVM and to investigate the relationship between the SMGS and the prognoses of children with ICAVM. **Materials and Methods:** Based on the International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) code 747.81, we retrospectively reviewed eight children with ICAVMs admitted to a medical center from 1991 to 2012. The primary selection criterion was the diagnosis of the ICAVM, which was not irrelevant to traumatic injury or known coagulopathy. Patients' outcomes were determined based on evaluation records of admission, discharge, and clinic visit 6-month after the ICAVM episode. For purposes of data analysis, outcomes were divided into "1 = death," "2 = persistent vegetative state," "3 = severe disability," "4 = moderate disability," and "5 = low disability." The relationship between the Glasgow outcome scale (GOS) and SMGS was analyzed using a scatter plot and Spearman's correlation coefficient. **Results:** A total of eight patients with at least follow-up 6-month consisted of four males (50.0%) and four females (50.0%). Their ages ranged from 7 to 15 years, and the mean age was 12.63 years. Common sites of ICAVM nidus included basal ganglia (n = 3, 37.5%), and frontal-temporal region (25.0%). 62.5% of patients experienced bleeding on the right side of the brain. About 62.5% of patients complained of headache. 62.5% of patients showed loss of consciousness. About 37.5% of patients showed generalized seizures. The SMGS were Grade I in one patient (12.5%), Grade II in two patients (25.0%), Grade III in two patients (25.0%), and Grade IV in three patients (37.5%). The clinical outcomes for the overall series were 87.5% excellent or good (GOS score equal or above 4) and only one case dead. The correlation between SMGS and GOS, analyzed by Spearman's correlation coefficient, was insignificant. Treatment, either by stereotactic radiosurgery (SRS) or surgery, was irrelevant to the prognosis of patient with ICAVM. **Conclusion:** Intracranial arteriovenous malformation is a life-threatening disease in children. Headache is a warning. Clinical presentations, including altered level of consciousness and generalized seizures in patient with ICAVM may suggest bleeding. The use of this system in children with ICAVM should be considered patients' age for their better potential neuroplasticity and good healing capacities in higher grade of patients. Treatment, either by surgery or SRS, may be irrelevant to patients' prognoses in this study.

Key words: Intracranial arteriovenous malformations, Spetzler-Martin grading scale, Glasgow outcome scale

INTRODUCTION

The incidence of arteriovenous malformations (AVM) is approximately 1/100,000/year.[1] Although uncommon, AVM, especially inside the brain, may threaten the life of patients because these congenitally abnormal vessels may trigger massive bleeding.[2] In general, clinical manifestations are variable in adult patients, including seizures, headache, nausea,

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vomiting, alteration of consciousness, coma, and sudden death.[3,4] Children's symptoms are generally nonspecific, such as headache, loss of consciousness, nausea, vomiting, seizures, and hemorrhage, which is the most commonly occurred in children than in adults.[5-9] Statistical reports show that 75-80% of pediatric intracranial arteriovenous malformation (ICAVM) patients with bleeding presentation experience a mortality rate high to 25%, whereas the rate is only 6-10% in adult patients.[6] The location of ICAVMs in children is frequently found in the infratentorial areas, but in adults is in the supratentorial regions.[10,11] These variances suggest that the nature, disease course, and prognosis of this disease may be different between these two groups.[12]

The Spetzler-Martin grading scale (SMGS) system, containing three parameters including the lesion size, pattern of venous drainage, and neurological eloquence of the adjacent brain,[13] is widely used for accessing the risk of surgery and a consensus therapeutic guideline in adult patients with ICAVMs. Literature suggests that accessible, low-grade (Spetzler-Martin grade 1-3) AVMs are often best managed with surgery;[7,10,14-16] low-grade, but inaccessible AVMs or those in eloquent locations are often treated with stereotactic radiosurgery (SRS),[17] and the management of high-grade (Spetzler-Martin grade 4-5) AVMs has no conclusion,[18,19] suggesting that different managements may link to patients' prognoses.[19] Thus, the higher grade the patient is, the more complex and risky the surgical or medical treatment of the lesion is. However, it seems that all subjects were adult patients.[20-22] The analysis and estimation of operative versus nonoperative management of ICAVMs using this system is not certain in pediatric patients with ICAVM,[23] let alone this system can be a clear and reliable therapeutic guideline for children. Concerning this issue, we conducted a pilot study to retrospectively review pediatric patients diagnosed with ICAVMs. Their clinical symptoms, imaging data, disease courses, treatments, and prognosis were all analyzed.

MATERIALS AND METHODS

We used the International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) code 747.81 to review the charts of pediatric patients (<18 years of age) who were consecutively admitted to one medical center in Taipei, Taiwan for congenital ICAVMs from 1991 to 2012. The participants in this study were eight children diagnosed with ICAVMs in one medical center in Taipei, Taiwan. We selected patients diagnosed with ICAVMs that were not related to traumatic injury or known coagulopathy. The personal and medical histories were collected on all patients. The following factors were recorded and analyzed: The patient's sex, age at initial treatment, presenting symptoms (including headaches, loss of consciousness, nausea or vomiting, and associated seizures), the ICAVM SMGS (lesion size, neurological eloquence, and venous drainage), treatment modality, and the Glasgow outcome scale (GOS),[24] which was used to categorize the outcomes of ICAVM patients in pediatrics. After 6-month, we followed-up with the patient at the outpatient department and determined the patient's GOS according to their performance status. The retrospective reviews of medical charts were approved by the Ethics Committee of the Tri-Service General Hospital, Taiwan. The Institutional Review Board (IRB) number is TSGHIRB: 2-101-05-110.

To investigate the clinical characteristics of ICAVM and outcomes in children, we plotted the parameters of SMGS and GOS in x-and y-axis, respectively. The relationships between these factors were analyzed by the Spearman's correlation coefficient. The statistical test was based on two-sided probabilities and was conducted using SPSS software (version 20.0; SPSS Inc., Chicago, IL, USA).

RESULTS

A total of eight patients with a mean follow-up of at least 6-month consisted of four males (50.0%) and four females (50.0%). The age group ranged from 7 to 15 years, and the mean age was 12.63 years. Five (62.5%) children complained of a headache on arrival or earlier in the same day. Five children (62.5%) lost consciousness on arrival and two children (25%) complained of nausea and vomiting. Intracranial hemorrhages were present in seven patients (87.5%). Seizures were present in three patients (37.5%).

The most common site for the presence of an ICAVM was the basal ganglia (n = 3, 37.5%), followed by the frontal-temporal region (25.0%). The majority of patients (62.5%) experienced hemorrhaging at the right side of the brain. The right basal ganglion may also show a predilection for the occurrence of bleeding. The Glasgow coma scores of the eight children ranged between 8 and 15. The ICAVM was localized to the eloquent area in five patients (62.5%). The SMGS were Grade I in one patient (12.5%), Grade II in two patients (25.0%), Grade III in two patients (5.0%), and Grade IV in three patients (37.5%) [Figure 1]. Five children (62.5%) were treated by surgery and three children (37.5%) were treated by performing SRS (dosage range of 16-18 Gy). A favorable outcome occurred in 87.5% of the patients according to the GOS after the 6-month follow-up [Table 1]. The condition of case 4 was severely serious before the operation, and she expired after the operation. Apart from case 4, most cases in this study were cured after surgery and SRS. Although patients with SRS showed a trend of better improvement, the Mann-

Table 1. Clinical characteristics of pediatric patients with ICAVM

Patients	Age/sex	Symptoms			Location	Hemorrhage	Grade	Treatment	GCS (I/D)	Seizure	GOS (I/D/F)
		H	LOC	NV							
1	11/male	Yes	Yes	No	Temporal-parietal	Yes	4	o.p.	12/15	Yes	2/4/5
2	15/female	Yes	No	No	Right frontal parafalcian region	No	2	SRS	14/15	No	3/5/5
3	7/male	Yes	Yes	No	Right basal ganglion region	Yes	2	SRS	9/14	Yes	2/4/4
4	12/female	No	No	No	Right basal ganglion region	Yes	3	o.p.	3/E	No	1/1/1
5	13/female	No	Yes	Yes	Frontal-temporal	Yes	4	o.p.	15/15	No	2/4/4
6	15/female	No	Yes	No	Left frontal-temporal	Yes	4	o.p.	8/15	Yes	2/5/5
7	13/male	Yes	No	No	Right posterior parieto-occipital lobe	No	1	SRS	15/15	No	4/5/5
8	15/male	Yes	Yes	Yes	Right basal ganglion region	Yes	3	o.p.	13/15	No	2/4/5

H = headaches, LOC = loss of consciousness; NV = nausea and vomiting; E = expired, o.p. = operation; SRS = stereotactic radiosurgery; I/D GCS = initial GCS and discharge GCS; I/D/F GOS = initial GOS; discharge GOS and 6-month follow-up GOS; ICAVM = Intracranial arteriovenous malformation, GCS = glasgow coma scale, GOS = glasgow outcome scale

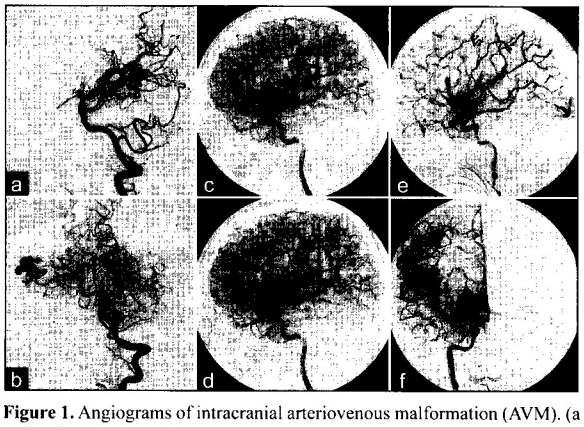

Figure 1. Angiograms of intracranial arteriovenous malformation (AVM). (a and b) lateral view and anteroposterior view of a patient with Grade I AVM, which size is <3 cm in diameter (1 point); location is at the right posterior parieto-occipital lobe (0 point), and superficial drainage (0 point). (c and d) lateral view and anteroposterior view of a patient with Grade II AVM, which size is <3 cm in diameter (1 point); location is at the right basal ganglion region (1 point), and deeper drainage (1 point). (e and f) lateral view and anteroposterior view of a patient with Grade III AVM, which size is <3 cm in diameter (1 point); location is at the intra-venticular, right frontal parafalcian region, splenium of corpus callosum (0 point), and deeper drainage (1 point)

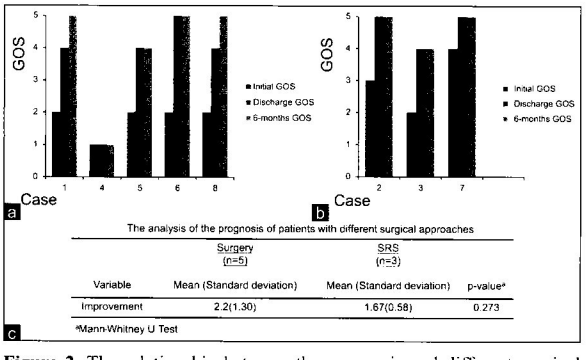

Figure 2. The relationship between the prognosis and different surgical approaches, including surgery (a) and stereotactic radiosurgery (SRS) (b). The y-axis represents the parameter of Glasgow outcome scale; the x-axis represents patients with arteriovenous malformations in this study. (c) The analysis of the prognosis of patients with different surgical approaches, including surgery and SRS). A Mann-Whitney U-test. $P \leq 0$ 0.05 represents significance

Whitney test shows no significance between patients with traditional removal of hematoma and SRS [Figure 2].

DISCUSSION

Although symptoms of children with ICAVM are variable, in this study, 62.5% (5/8) of patients initially presented with headaches.[25] Therefore, headaches may be a warning sign for this disease, especially in children. It is not clear how headache is induced. The expansion may cause raised intracranial pressure or other signs and symptoms such as nausea/vomiting, bradycardia, hypertension, and impaired respiratory patterns.[20] Although vessels are more elastic in children than in adults, the abnormal embryogenesis of vessels makes their structure more fragile and inelastic. The microcirculation and micrometabolism within the ICAVMs and surrounding environments are subtle and complex. When the expansion and outgrowth of vessels outweigh the demands, consequences, such as an unprecedented ictus, nausea, vomiting, loss of consciousness, and/or sudden death, may occur.[26]

Altered level of consciousness is an emergent condition and possibly caused by a more violent and massive bleeding leading to hemorrhagic stroke.[27] Bleeding, especially in the subarachnoid area, may cause communicating hydrocephalus and exacerbate increased intracranial pressure.[20] In this study, 75% (6/8) of the children experienced loss of consciousness

at the initial presentation and subarachnoid hemorrhage was found in them. Among them, 37.5% (3/8) showed generalized seizure pattern. Therefore, seizure may be a vicious sign of hemorrhage in ICAVM.

Intracranial arteriovenous malformation in different regions of brain may affect the prognosis of patients.[11,25,27-29] ICAVMs are frequently found in the supratentorium in adult patients.[11] We and others[6,10,18,30] found that lesions in children are common in the basal ganglia. Interestingly, our cases with high grades were found in the temporal lobes (3/8; 37.5%). Whether our observation that ICAVM in the temporal lobe links to a higher grade of children is worthy of further investigation.

Although hemorrhage is the most common phenomenon in the pediatric group, their outcomes are always better than those of adults.[2,3,31] Case 4 is an exception. She experienced diffused intra-ventricular hemorrhage in the lateral, third, and fourth ventricles at a late stage. This female patient's large hemorrhage in the infratentorial region, recurrence of bleeding, and the formation of acute hydrocephalus might have caused her death. Therefore, patients with infratentorial AVMs, especially located in the ventricles and posterior fossa, may have a poor prognosis because the on-going and less sensitive hemorrhage in this region may directly compress brainstem leading to catastrophe.[2,3,6]

Most our cases showed a good prognoses. If higher grade of a patient with ICAVM suggests a poorer prognosis, how and why did most of our patients with high grades survive? Our data analyzed with Spearman's correlation coefficient, showed that there were no significance between these parameters, suggesting that the system may be inadequate to our patients [Figure 3]. However, our intention is not to criticize the weakness of SMGS. Instead, we would like to highlight the differences between adult and pediatric patients. The differences between children and adults are not only size and weight. And the better improvement in pediatric patients with AVM than adults is well known.[32] This consensus has not been addressed in the use of SMGS. Improper use of this system in pediatric patients may mislead clinicians to a wrong conclusion, prognosis, and therapeutic plans.

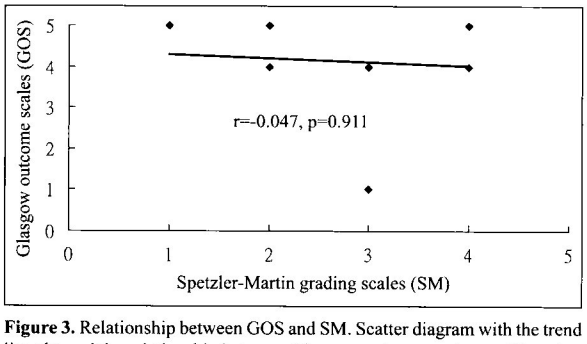

Figure 3. Relationship between GOS and SM. Scatter diagram with the trend line showed the relationship between Glasgow outcome scales and Spetzler-Martin grading scales. Spearman's Correlation statistics revealed correlation coefficient (r)=-0.047, p=0.911, it showed that Glasgow outcome scales and Spetzler-Martin grading scale doesn't had linear relationships

Different managements in patients with ICAVM may have variable prognosis.[19,30] Some articles argued discrepancies between the SMGS and patient outcomes, especially with regard to high-grade AVM with SRS.[33,34] Therefore, it seems that SMGS may be inadequate and inappropriate for patients managed by SRS.[35] Furthermore, patients with SRS in our data showed a trend of better improvement, but the statistical analysis by the Mann-Whitney test showed no significance between patients with surgery and SRS. We think that SMGS, in agreement with references,[33,34] may be not indicative to patients managed by SRS. A prospective cohort study with a large case numbers may answer this question.

This study has a number of limitations. First, the sample size was small and the duration of follow-up is only 6-month. It is quite possible that statistical significance would have been found if our study would have enrolled more patients and longer duration. Second, this study is a retrospective, not a prospective one. These limitations may have led to some bias in analyzing the patient's data and different treatments in children with ICAVMs.

CONCLUSION

Intracranial arteriovenous malformation is a threatening disease in children. Headache is one of common signs. Altered level of consciousness and generalized seizures may suggest hemorrhage. SMGS is a widely used system for guiding the treatment and predicting the prognoses. However, application of this system should be careful in pediatric patients for their potential neuroplasticity and good healing capacities. Users should consider patients' conditions, especially age.

DISCLOSURE

The authors declare that they have no conflict of interest.

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