The Effect of Age, Sex, and Lesion Location on Initial Presentation in Patients with Brain Arteriovenous Malformations

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OBJECTIVE: **To identify whether age, sex, and lesion location are associated with initial presentation in patients with brain arteriovenous malformations (AVMs).**

METHODS: **Collected data of 3299 consecutive patients with AVM treated at Beijing Tiantan Hosptial from January 1980 to January 2015 were analyzed. The variables assessed were age at diagnosis, sex, AVM location, and mode of initial presentation.**

RESULTS: **Initial presentation was AVM hemorrhage in 57.9%, seizure in 20.9%, chronic headache in 14.9%, focal neurologic deficit in 5.2%, and incidental in 1.2%. Younger age and female sex were associated with initial hemorrhage (all $P < 0.05$). Hemorrhage was more likely to occur in patients with AVMs in the basal ganglia, the corpus callosum, the ventricles, the cerebellum, and the brainstem (all $P < 0.05$). Male sex was associated with initial seizure ($P < 0.05$). Initial seizure was more likely to occur in patients with AVMs in the frontal, temporal, parietal, frontotemporal, and frontoparietal lobe (all $P < 0.05$). Compared with frontal AVMs, temporal AVMs were more likely to present with hemorrhage ($P < 0.05$) and less likely to present with seizure ($P < 0.05$). AVMs involving the occipital lobe were more likely to present with chronic headaches ($P < 0.05$).**

CONCLUSIONS: **Initial AVM presentation varied with patient age, sex, and AVM locations. Younger age, female sex, and deep and infratentorial locations may be associated with initial hemorrhage. Male sex and frontal, temporal, and parietal AVM locations may be predictors of initial seizure. Chronic headache was more likely to occur in patients with AVMs involving the occipital lobe.**

INTRODUCTION

Patients with brain arteriovenous malformations (AVMs) may present with hemorrhage, seizure, chronic headache, focal neurologic deficit, or asymptomatic AVMs. The natural history of brain AVMs is still largely unknown.[1] The mode of initial presentation may be associated with many factors. The initial presentation may vary across different age classes.[2] Multiple factors may be associated with increased risk of hemorrhage: previous hemorrhage, AVM location, size, male gender, venous outlet restriction, deep venous drainage, associated aneurysms, mean pressure, type of feeding arteries, and age.[1-5] However, divergent information exists regarding the risk factors of hemorrhage at presentation, especially when age, sex, and AVM location are included to assess hemorrhage risk. Previous studies have linked various factors to AVM-related seizures: age, male gender, AVM size, AVM location, absence of intranidal aneurysms, and presence of venous varix.[6-10] However, divergent information also exists. Neurologic deficits and headache as initial clinical symptoms of AVMs have not been described in detail in the literature. These 2 symptoms, together with seizures, are often overlooked because of the devastating effect of AVM hemorrhage, which is the most frequent and feared component of the natural history of an AVM.[6] Most previous studies were performed in relatively small or medium-sized cohorts and only a few studies included a sample size of over 1000. Patient age, sex, and AVM location may be correlated with

Key words
- Age
- AVM location
- Brain arteriovenous malformation
- Initial presentation
- Sex

Abbreviations and Acronyms
AVM: Arteriovenous malformation
CI: Confidence interval
CPA: Cerebellopontine angle
OR: Odds ratio
SD: Standard deviation

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different types of initial presentation at diagnosis. In this study, we retrospectively reviewed our AVM database to find out whether patient age, sex, and AVM location are associated with the mode of initial presentation.

METHODS

Patient Population

This study was approved by the institutional review board of Beijing Tiantan Hospital Affiliated to Capital Medical University. Our prospectively maintained brain vascular malformation database was searched to identify patients with brain AVMs who were admitted to Beijing Tiantan Hospital between January 1980 and January 2015. Inclusion criteria were brain AVMs diagnosed by brain imaging and cerebral angiography. Exclusion criteria were patients with other congenital vascular lesions such as vein of Galen malformations, dural arteriovenous fistula, cavernous malformations, and venous malformations. A total of 3299 patients (2123 men, 1176 women) met the inclusion criteria. The baseline patient characteristics (sex, age, and initial presentation) and the AVM features (size, side, location, angioarchitecture, associated aneurysms, and Spetzler-Martin grade) were collected.

Definition of Initial Presentation

The definition of initial presentation was consistent with previous reports.[2] The initial AVM presentation was defined as the clinical index event that led to the diagnosis of the AVM.[2] AVM hemorrhage was defined as any clinically symptomatic event (any focal neurologic deficit, sudden-onset headache, or seizure) that is associated with imaging findings of bleeding at the time of the index event. The hemorrhage was detected by computed tomography or magnetic resonance brain imaging or the cerebrospinal fluid laboratory test. Nonhemorrhagic modes of AVM presentation were stratified into seizure, focal neurologic deficit, headache, or other/asymptomatic.[2] The diagnosis of seizures was made by clinical epileptologists on the basis of the clinical history and electrophysiologic examination.

AVM Classification According to Age and Locations

The AVMs were stratified into 7 age classes (0–9, 10–19, 20–29, 30–39, 40–49, 50–59, and older than 60 years). With regard to laterality, there were 4 AVM types: left ($n = 1563$), right ($n = 1532$), middle ($n = 193$), and bilateral ($n = 11$). The AVM locations were then classified as supratentorial and infratentorial. For the supratentorial AVMs, the locations were in the frontal lobe, temporal lobe, parietal lobe, occipital lobe, frontotemporal lobe, frontoparietal lobe, temporoparietal lobe, temporo-occipital lobe, parieto-occipital lobe, frontotemporoparietal region, temporoparieto-occipital region, basal ganglia, thalamus, corpus callosum, ventricles, and multiple lobes (≥4 lobes involved). For the infratentorial AVMs, the locations were the cerebellum, brainstem, and cerebellopontine angle (CPA).

Statistical Analysis

Statistical analyses were performed with the Statistical Package for the Social Sciences software (version 20.0 [SPSS Inc., Chicago, Illinois, USA]). A χ^2 test was used to assess the effect of the age classes, sex, and location on each mode of initial presentation. An independent sample t test was used to compare the mean age (analyzing age as a continuous variable) between groups with or without each mode of presentation. Statistical significance was established at a value of $P < 0.05$.

RESULTS

Demographic Data

Baseline characteristics are summarized in Table 1. The patient age at diagnosis ranged from 1 year to 75 years (mean, 27.9 years; 95% confidence interval [CI], 27.4–28.3 years). There were 2123 males and 1176 females. The male/female ratio was 1.81:1. Of the 3299 patients, initial presentation was AVM hemorrhage in 57.9% (95% CI, 56.3%–59.6%), seizure in 20.9% (95% CI, 19.5%–22.2%), chronic headache in 14.9% (95% CI, 13.6%–16.2%), focal neurologic deficit in 5.2% (95% CI, 4.5%–6.0%), and incidental in 1.2% (95% CI, 0.8%–1.5%). Most patients (92.7%) had AVMs of Spetzler-Martin grade I–III and 96.8% of the patients had AVMs larger than 6 cm.

Age Distribution and Initial Presentation

Figure 1 demonstrates the variation of initial presentation according to the different age classes. The 3299 patients with AVM were stratified into 7 different age classes: 245 patients <10 years of age, 782 patients 10–19 years of age; 873 patients 20–29 years of age; 743 patients 30–39 years of age; 403 patients 40–49 years of age, 144 patients 50–59 years of age, and 109 patients ≥60 years of age. Young patients (<20 years) accounted for 31.1% and elderly patients (≥60 years) accounted for 3.3%. Of the 3299 patients, 80.1% were diagnosed before the age of 40 years and 92.3% were diagnosed before 50 years. The bleeding frequencies were highest in patients <10 ($n = 178$, 72.7%), 10–19 ($n = 527$, 67.4%), and 20–29 ($n = 522$, 59.8%) years of age. The bleeding rates were relatively lower in patients 30–39 ($n = 380$, 51.1%), 40–49 ($n = 182$, 45.2%), 50–59 ($n = 63$, 43.8%), and ≥60 ($n = 58$, 53.2%) years of age. The seizure frequencies were relatively higher in patients 20–29 ($n = 197$, 22.6%), 30–39 ($n = 173$, 23.3%), 40–49 ($n = 94$, 23.3%), and 50–59 ($n = 30$, 20.8%) years of age. The seizure frequencies were relatively lower in patients <10 ($n = 36$, 14.7%), 10–19 ($n = 143$, 18.3%), and ≥60 ($n = 13$, 13.8%) years of age. With regard to headache as the initial presentation, the highest rates occurred in patients 40–49 ($n = 90$, 22.3%), 50–59 ($n = 31$, 21.5%), and ≥60 ($n = 25$, 22.9%) years of age. The rates of headaches were relatively lower in patients <10 ($n = 20$, 8.2%), 10–19 ($n = 74$, 9.5%), 20–29 ($n = 116$, 13.3%), and 30–39 ($n = 134$, 18.0%) years of age. The rates of focal neurologic deficits were highest in patients 40–49 ($n = 33$, 8.2%), 50–59 ($n = 16$, 11.1%), and ≥60 ($n = 10$, 9.2%) years of age. The rates were relatively lower in patients <10 ($n = 6$, 2.4%), 10–19 ($n = 30$, 3.8%), 20–29 ($n = 31$, 3.6%), and 30–39 ($n = 47$, 6.3%) years of age. The frequencies of asymptomatic AVMs were 0.8%–2.8% in the age groups and the highest was 2.8% in patients 50–59 years of age.

As demonstrated in Figure 2, the mean age ± standard deviation (SD) was 25.9 ± 13.8 years in patients with hemorrhage and 30.6 ± 13.8 years in those without hemorrhage. The difference showed great significance ($P < 0.001$). The mean age ± SD was 28.6 ± 13.1 years in patients with seizure and 27.7 ± 14.2 years in