Cognitive and functional status after vein of Galen aneurysmal malformation endovascular occlusion

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Abstract

AIM: To study the clinical outcomes of treating vein of Galen aneurysmal malformations (VGAM), we assessed our patient cohort using standardized cognitive and functional measures.

METHODS: A retrospective review of patients with VGAM treated by a single practitioner between 2003 and 2009 was performed for this study. In addition to routine clinical assessment, all patients were evaluated for cognitive and functional impairment using validated measures including the Neurobehavioral Rating Scale-Revised, the Bicêtre outcome score, and the Barthel index.

RESULTS: Five patients underwent combined transarterial and transvenous embolization of their VGAM during the study period. VGAMs were classified based on angioarchitecture as either choroidal (1/5) or mural (4/5) according to the classification scheme of Lasjaunias. In total, 13 embolization procedures were performed consisting of 1 to 3 treatment stages per patient. Complete or near complete occlusion was achieved in 4 patients, while subtotal occlusion was achieved in 1 patient. During follow-up (median 62.6 mo), all patients were either unchanged or cognitively and neurologically intact.

CONCLUSION: VGAM can be safely and effectively treated by staged transarterial and transvenous embolization. Using this strategy, excellent long-term cognitive and functional outcomes can be achieved.

Key words: Cognition; Embolization; Endovascular; Hemorrhage; Interventional neuroradiology; Neurological development; Outcomes; Vein of Galen aneurysmal malformation

INTRODUCTION

Vein of Galen aneurysmal malformations (VGAMs) are a group of congenital arteriovenous fistulas that comprise up to 37% of intracranial vascular lesions in the pediatric population[1]. Rather than a brain arteriovenous malformation of the true vein of Galen, VGAMs rep-
represent an arteriovenous fistula with drainage to a persistent embryonic vein, the median prosencephalic vein of Markowskii\(^\text{[3]}\). These lesions can present with high-output congestive heart failure, seizures, failure to thrive, hydrocephalus, and brain hemorrhage. High surgical mortality and mortality, exceeding 90% in some series, has led to the development of endovascular techniques that more safely and effectively treat these lesions\(^\text{[7-14]}\). The use of staged procedures utilizing both transarterial and transvenous catheter access routes to deliver a variety of solid and liquid embolic materials have enabled high rates of anatomic occlusion with good clinical outcomes. In large series, favorable outcomes after endovascular treatment are seen in approximately 60%-75% of patients\(^\text{[7-13]}\).

Despite advancements in the endovascular treatment of VGAMs, neurological development and cognitive function may be impaired in survivors. However, only a limited number of reports address this issue directly\(^\text{[8,11,18,19]}\). Although transvenous techniques are potentially curative in many cases, some investigators have expressed concern that transvenous embolization is associated with worse cognitive outcomes than transarterial embolization and should be avoided. To assess this concern, we retrospectively reviewed our experience in treating VGAMs using transvenous methodology, with particular attention to clinical cognitive assessments during ongoing follow-up.

**MATERIALS AND METHODS**

Between 2003 and 2009, five pediatric and adult patients with symptomatic vein of Galen aneurysmal malformations underwent evaluation and transvenous endovascular treatment at our institution. A retrospective review of all patient records, including office and hospital charts as well as of available diagnostic cerebral angiograms and other imaging studies, was performed in accordance with Institutional Review Board stipulations and approval. Baseline clinical characteristics, lesion classification, endovascular surgery details, periprocedural complications, and follow-up data were collected for this review (Tables 1 and 2).

In addition to routine clinical and neurological examination, the cognitive and functional status of each patient was evaluated during the most recent post-embolization follow-up office visit. The executive/cognitive items from the Neurobehavioral Rating Scale-Revised (NRS-R)\(^\text{[15,16]}\), the Bicêtre outcome score\(^\text{[8]}\), and the Barthel index\(^\text{[17]}\) were used in the evaluation of each patient. Factors loading under executive/cognitive in the NRS-R included patient difficulties with planning, mental flexibility, memory, disorientation, initiative or motivation, self-appraisal, conceptual disorganization, and oral comprehension\(^\text{[13]}\). As is standard for the NRS-R, each patient was graded on a four-tier scale including absent, mild, moderate, or severe difficulty for each item evaluated. The Bicêtre outcome score (BOS) is a global clinical measure for the assessment of cognitive outcome. As described by Lasjaunias et al\(^\text{[8]}\), patients with BOS 3-5 are neurologically normal, those with BOS 2 are moderately retarded, while patients with BOS 1 are severely retarded. For small children, parents were queried regarding specific cognitive and functional impairments.

**RESULTS**

Five patients underwent catheter cerebral arteriography and transvenous embolization of their VGAM during the six-year study period (Table 1). The cohort underwent 13 embolization procedures including 1 to 3 treatment stages per patient. VGAMs were initially diagnosed in the neonatal period (2/5), in early childhood (2/5), and during adulthood (1/5). One patient (Patient 5) originally presented at the age of 21 mo with macrocephalus and cranial bruising, but underwent definitive endovascular embolization as an adult at the age of 32 years for complaints of progressive dementia, severe headaches and intractable seizures. The two neonates presented acutely with congestive heart failure (CHF) while the other patients presented in a delayed fashion with headache, macrocephalus, cranial bruising, prominent scalp veins, or progressive presenile dementia. A variety of preliminary diagnostic imaging modalities were employed including head ultrasound, skull radiography, head computed tomography, and brain magnetic resonance imaging (Figure 1).

Diagnostic catheter cerebral angiography was performed in all patients for treatment planning and as a guide to endovascular therapy. VGAMs were classified based on angioarchitecture as either choroidal (1/5) or mural (4/5) according to the classification scheme of Lasjaunias\(^\text{[8,11,18,19]}\). Choroidal lesions are characterized by an extensive arterial network interposed between larger arterial feeders prior to high flow drainage into the venous malformation (Figure 2A-D). Mural lesions do not have an interposed arterial network and consist of one or more direct fistulas to the median prosencephalic vein (Figure 2E and F).

All patients were placed under general anesthesia prior to endovascular treatment. Staged embolizations \textit{via} combined transarterial and transvenous routes were then performed with systemic heparinization (Table 2). In one patient (Patient 3) who underwent a single-staged embolization, catheter access to the median prosencephalic vein was achieved by passing the microcatheter tip from the arterial side into the recipient draining vein. Thrombogenic platinum coils and a liquid embolic agent (Trufill\(^\text{®}\) NBCA, Codman Cordis; Raynham, MA, United States) were primarily used to occlude the fistulas comprising the malformation.

There were a total of three periprocedural complications in two patients during the study period (Table 2). Patient 1 developed a small, subclinical left parietal infarct and subsequently a small, asymptomatic intraventricular hemorrhage (IVH) after the third stage of embolization. Patient 3 developed a small, subclinical germinal matrix hemorrhage. The left parietal infarct (Patient 1) was thought to be due to stagnation and retrograde thrombo-
sis of an embolized arterial feeder. The IVH (Patient 1) occurred in the setting of a consumptive coagulopathy and was treated by aggressive resuscitation with platelets and fresh frozen plasma. The germinal matrix hemorrhage (Patient 3) was identified during a routine outpatient follow-up transfontanelle ultrasound three weeks

Table 1  Patient characteristics

| Patient | Age¹ | Gender | Presenting symptoms | Initial diagnostic imaging |
|---------|------|--------|---------------------|--------------------------|
| 1       | Birth/5 d  | Male    | Congestive heart failure, cranial bruit | Non-contrast head computed tomography |
| 2       | 5 mo/8 mo | Male    | Macrocephalus, cranial bruit | Magnetic resonance imaging brain +/- contrast |
| 3       | Prenatal/5 d  | Female | Congestive heart failure | Prenatal ultrasound |
| 4       | 24 yr/27 yr | Male    | Face pain, dementia | Magnetic resonance imaging brain +/- contrast |
| 5       | 21 mo/32 yr | Female | Macrocephalus, cranial bruit | Skull X-ray |

¹At presentation/ at stage 1 embolization

Table 2  Galen aneurysmal malformations endovascular occlusion

| Patient | Angio-architecture | Endovascular access | Extent of occlusion | Clinical endpoint | Embolic agents | Periprocedural complications |
|---------|-------------------|---------------------|---------------------|------------------|----------------|-----------------------------|
| 1       | Choroidal         | 3 Transarterial and transvenous | Complete | Normalization of cardiac function | Fibered and non-fibered platinum coils, N-butyl cyanoacrylate | Left parietal infarct post stage 2 embolization, consumptive coagulopathy and IVH post stage 3 embolization |
| 2       | Mural             | 3 Transarterial and transvenous | Complete | Normalization of head circumference | Fibered and non-fibered platinum coils, NBCA, Berenstein liquid coils | None |
| 3       | Mural             | 1 Transarterial and transvenous | Subtotal | Normalization of cardiac function | Fibered and non-fibered platinum coils | Small germinal matrix hemorrhage 21 d post embolization |
| 4       | Mural             | 3 Transarterial and transvenous | Complete | Resolution of vascular dementia and hemifacial pain | Fibered and non-fibered platinum coils, NBCA | None |
| 5       | Mural             | 3 Transarterial and transvenous | Near complete | Resolution of vascular dementia, seizures, and headaches | Fibered and non-fibered platinum coils, NBCA, hydrogel coils, polyvinyl alcohol, ethanol | None |

¹At presentation/ at stage 1 embolization. IVH: Intraventricular hemorrhage.

Figure 1  Preliminary diagnostic imaging in Galen aneurysmal malformations patients. A: Portable chest radiograph in a newborn (Patient 1) with clinical signs of congestive heart failure and a cranial bruit demonstrates cardiomegaly and pulmonary vascular congestion; B: A non-contrast head computed tomography shows an enlarged midline vascular structure in the posterior fossa consistent with a Galen aneurysmal malformations (VGAM); C, D: In another patient (Patient 2) who presented similarly, color Doppler ultrasound (C) indicates the presence of a posterior midline vascular pouch subsequently shown by magnetic resonance (MR) venography to be a VGAM (D); E, F: Alternatively, contrast-enhanced brain MR imaging was the initial diagnostic imaging used to diagnose a VGAM in Patient 2 who presented with macrocephalus and cranial bruit.
after completion of embolization. No long-term clinical sequelae were seen in either patient. Patient 5 initially presented with residual neurological deficits secondary to a remote stroke and ICH which occurred after an embolization in the 1970s using non-selective arterial injection of silastic beads (Figure 3).

Follow-up ranged from 2 to 97.2 (median 62.6) mo. At the time of last follow-up, all patients were neurologi-
Follow-up
74.8
None
Bicêtre outcome
None

100
5
100
Neurologically intact, facial pain relief
CHF resolved, neurologically intact
5
- 
- 

100
62.6
97.2

- 
- 
- 
Neurologically intact
Mild disorientation, memory, self-appraisal, planning, and decreased initiative/motivation

Small ischemic stroke occurred in the study group. These however, two minor intracranial hemorrhages and one small ischemic stroke occurred in the study group. These complications were not associated with residual cognitive or functional deficits. Prior observations that hemorrhage is not incompatible with a good outcome in VGAM patients are supported by this study. Importantly, within the cohort of patients treated during this study, no deaths or serious morbidity were seen.

No strict protocols were employed in the management of the VGAM patients presented. For each patient, a multi-disciplinary approach was taken with the help of neonatologists, neurointensivists, adult and pediatric cardiologists, neurologists, pediatricians, neurointerventionists, and neurosurgeons. Treatment decisions were based on age, presenting symptoms, and clinical status. While not ideal, embolization during the early postnatal period may be warranted to reduce arteriovenous shunting and improve cardiac status. Early intervention may also reduce the risk of brain parenchymal loss which is associated with permanent neurological deficits. Conversely, it has been argued that severe CHF and low neonatal scores may warrant withholding treatment. When a decision was made to proceed with treatment, the goals of therapy were individualized, tailored to the unique clinical scenario. For example, whereas in general multi-stage embolizations, a goal of complete or near complete VGAM occlusion is often desired, subtotal obliteration may be a sufficient temporizing measure as was the case in Patient 3.

A technical strategy employing combined transarterial and transvenous embolization routes was used for all patients in this series. This is in contrast to alternative strategies which include: (1) purely transvenous embolization; (2) maximal transarterial embolization followed by transvenous occlusion in select cases; or (3) purely transarterial embolization with strict avoidance of transvenous occlusion. Reasons often cited for avoidance of transvenous embolization include venous infarction, distal migration of embolic material, and normal perfusion pressure breakthrough syndrome resulting in malignant cerebral edema or hemorrhage. In our experience, the simultaneous use of both transarterial and transvenous embolization facilitated VGAM occlusion without the introduction of technical difficulty or additional serious complications. Indeed, the use of a transvenous route is sometimes necessary as the VGAM may have arterial

Table 3  Treatment outcomes

| Patient | Follow-up | Clinical status | Bicêtre outcome score | Barthel index score | NRS-R executive/cognitive item difficulties |
|---------|-----------|----------------|----------------------|--------------------|---------------------------------------------|
| 1       | 97.2      | CHF resolved, neurologically intact | 5 | 100 | None |
| 2       | 62.6      | Neurologically intact | 5 | 100 | None |
| 3       | 30.9      | CHF resolved, neurologically intact, meeting all developmental milestones | 5 | NA | NA |
| 4       | 2         | Neurologically intact, facial pain relief | 5 | 100 | None |
| 5       | 74.8      | Neurological deficits including: abducens nerve palsy, left sided hemiparesis (ambulates independently with leg brace), and decreased visual acuity | 2 | 95 | Mild disorientation, memory, self-appraisal, planning, and decreased initiative/motivation |

*Months post Galen aneurysmal malformations embolization. NRS-R: Neurobehavioral Rating Scale-Revised; CHF: Congestive heart failure; NA: Not available.

DISCUSSION

In several large series, serious long-term morbidity or death was the outcome after endovascular therapy in a significant number of VGAM patients. The use of transvenous occlusion methodologies have been implicated in at least a subset of these poor outcomes. However, the long-term cognitive effects of transvenous VGAM endovascular obliteration are unknown. Prior reports either do not address this issue directly or include patients who were treated a decade or more ago, and thus do not reflect outcomes seen with the use of modern equipment and techniques. Our group routinely utilizes transvenous embolization as part of a broader strategy to effect maximal VGAM occlusion. Therefore, we reviewed our contemporary experience in the endovascular treatment of VGAMs and specifically delineate the cognitive and functional outcomes observed using standardized assessment measures.

Based on results from a developmental questionnaire, Fullerton et al specifically reported the neurodevelopmental outcomes of patients with VGAMs and found that 39% of surviving patients had significant developmental delay. Various groups have utilized other measures including Bicêtre outcome scores and found similar rates of developmental delay or retardation in the VGAM population. While we present a smaller cohort of patients, our results indicate that very good cognitive and functional outcomes can be obtained after endovascular treatment of VGAMs with low attendant complication rates. All patients reviewed for this study had excellent clinical, cognitive, and functional outcomes during near- and long-term follow-up. Cognitive impairment secondary to therapeutic embolization was not observed. However, two minor intracranial hemorrhages and one small ischemic stroke occurred in the study group. These

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The optimal endovascular strategy for treating VGAMs is unclear. Strategies including (1) purely transvenous embolization; (2) maximal transarterial embolization followed by transvenous occlusion in select cases; (3) purely transarterial embolization with strict avoidance of transvenous occlusion; and (4) combined transarterial and transvenous embolization have been advocated by various practitioners. Some practitioners try to avoid multiple embolization procedures, believing that the excellent cognitive outcomes seen in our patients are, in part, the result of appropriate treatment staging. The staging of embolization allows for gradual lesion occlusion and thrombosis which promotes the development of alternative physiologic, non-fistulous drainage pathways. Additionally, prolonged single-session radiation and iodinated contrast exposure are avoided by use of this strategy.

Vein of Galen aneurysmal malformations can be safely and effectively treated by current endovascular techniques with low attendant risks of morbidity or mortality. Patients treated with a strategy of staged transarterial and transvenous embolizations can have excellent long-term cognitive and functional outcomes. A multidisciplinary approach with individualized therapeutic goals, tailored to the unique clinical scenario will ensure the best possible outcome for each patient.

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**COMMENTS**

**Background**

Vein of Galen aneurysmal malformations (VGAMs) are arteriovenous fistulas that drain to a persistent embryonic vein, the median prosencephalic vein of Markowski. These lesions can present with high-output congestive heart failure, seizures, failure to thrive, hydrocephalus, and brain hemorrhage. The treatment of VGAM has historically been associated with significant morbidity and mortality. While current endovascular techniques enable better outcomes to be achieved, it has been suggested that long-term cognitive deficits may be seen after therapeutic embolization.

**Research frontiers**

The optimal endovascular strategy for treating VGAMs is unclear. Strategies including (1) purely transvenous embolization; (2) maximal transarterial embolization followed by transvenous occlusion in select cases; (3) purely transarterial embolization with strict avoidance of transvenous occlusion; and (4) combined transarterial and transvenous embolization have been advocated by various groups.

**Innovations and breakthroughs**

Despite advancements in the endovascular treatment of VGAMs, neurologic development and cognitive function may be impaired in survivors. In this experience the best outcomes are achieved when a multi-disciplinary approach is taken with the help of neonatologists, neurointensivists, adult and pediatric cardiologists, neurologists, pediatricians, neurointerventionalists, and neurosurgeons. In this report we show that patients treated with a strategy of staged transarterial and transvenous embolization can have excellent long-term cognitive and functional outcomes.

**Applications**

The findings show that VGAMs may be effectively treated using the endovascular strategy we outline. As there are currently a number of endovascular options for either palliating or curing VGAMs, this study shows that staged transarterial and transvenous embolization with a goal of complete obliteration is a viable strategy.

**Peer review**

It is an useful and innovative research which has been presented well.
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