

Clinical Course of Cranial Dural Arteriovenous Fistulas With Long-Term Persistent Cortical Venous Reflux

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Background and Purpose—The natural history of aggressive (Borden 2 and 3) cranial dural arteriovenous fistulas (DAVFs) is not well described. Reported annual mortality and hemorrhage rates vary widely and range up to 20% per year. A consecutive single-center cohort of 236 cases that presented with a cranial DAVF between June 1984 and May 2001 was reviewed for the consequences of long-term persistent cortical venous reflux (CVR).

Methods—A group of 118 cranial DAVFs was selected for the presence of CVR. All patients were offered treatment aimed at the disconnection of the CVR. Patients who declined or had partial treatment with persistence of the CVR had long-term clinical and angiographic follow-up to study the disease course of this select group.

Results—Treatment was instituted in 101 of the 118 patients (85.6%). Three patients were lost to follow-up. The remaining 14 nontreated patients (11.9%) and the partially treated patients (n=6) were assessed clinically and angiographically over time. The mean follow-up in this select group was 4.3 years (86.9 patient-years). During follow-up, 7 patients suffered an intracranial hemorrhage (35%). The incidence of nonhemorrhagic neurological deficit was 30%. Nine patients (45%) died: 6 patients expired after a hemorrhage, and 3 patients died of progressive neurological deterioration. Two patients demonstrated a spontaneous closure of the DAVF (10%).

Conclusion—Persistence of the CVR in cranial DAVFs yields an annual mortality rate of 10.4%. Excluding events at presentation, in this series the annual risk for hemorrhage or nonhemorrhagic neurological deficit during follow-up was 8.1% and 6.9%, respectively, resulting in an annual event rate of 15.0%. (*Stroke*. 2002;33:1233-1236.)

Key Words: central nervous system vascular malformations ■ natural history ■ reflux, cortical venous ■ treatment outcome

To justify treating a cranial dural arteriovenous fistula (DAVF), the expected risk of sequelae in its natural course should be compared with the risk and the expected success rate of the proposed treatment. It is generally accepted that the risks of cranial DAVFs are dictated by their pattern of venous drainage, with features such as cortical venous reflux (CVR), galenic drainage, and venous congestion believed to contribute to an aggressive presentation with hemorrhage, nonhemorrhagic neurological deficit (NHND), or death.¹⁻⁴ However, the reported annual morbidity and mortality rates of DAVFs with an aggressive presentation differ widely, ranging from 1.8% to 20% per year.^{5,6} Moreover, nearly all studies are restricted to the events at presentation, and the minority of studies focus on the follow-up behavior of DAVFs.

Davies et al⁷ validated the popular classification scales of Borden et al⁸ and Cognard et al.⁹ Both scales only looked at presentation events; however, they can be used to categorize DAVFs into benign or aggressive based on the presence of CVR. The disease course of lesions without CVR has been

predicted as benign.^{10,11} However, despite attempts from several authors,^{5,6,12} evidence is limited about the disease course of the aggressive lesions after presentation. In this article, we aim to clarify the behavior of aggressive cranial DAVFs with long-term persistence of the CVR.

Methods

The University of Toronto Brain Vascular Malformation Study Group has consecutively assessed 236 patients with cranial DAVFs. All cases were evaluated at The Toronto Western Hospital between June 1984 and May 2001, prospectively since 1989. The patients were clinically and radiologically assessed in a multidisciplinary clinic, attended by both neurosurgeons and interventional neuroradiologists. The assessment included a detailed medical history, a full neurological examination, and at least 1 angiogram.

The Borden classification and the Cognard classification were used to categorize the cranial DAVFs (Table 1). A cohort of 118 patients with an aggressive cranial DAVF was selected for the presence of CVR (Borden grade 2 or 3; Cognard type IIb, IIa+b, III or IV) on the initial angiogram, which was reviewed by an experienced neuroradiologist.

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TABLE 1. Classification of Cranial Dural Arteriovenous Fistulas

Borden classification	
1	Venous drainage directly into dural venous sinus or meningeal vein
2	Venous drainage into dural venous sinus with CVR
3	Venous drainage directly into subarachnoid veins (CVR only)
Cognard classification	
I	Venous drainage into dural venous sinus with antegrade flow
Ila	Venous drainage into dural venous sinus with retrograde flow
Ilb	Venous drainage into dural venous sinus with antegrade flow and CVR
Ila+b	Venous drainage into dural venous sinus with retrograde flow and CVR
III	Venous drainage directly into subarachnoid veins (CVR only)
IV	Type III with venous ectasias of the draining subarachnoid veins

CVR indicates cortical venous reflux.

Among the 101 patients who were treated, 95 patients were cured within 1 week (median, 2 days; range, 1 to 7 days) after the initial angiogram. They were excluded from this review.

A subgroup of 20 patients who had persistent CVR, either after refusing a procedure to disconnect the CVR or after partial treatment, were studied in detail. These patients were closely followed both clinically and by medical imaging. Clinical review was performed on a 3-month basis in the multidisciplinary clinic and in between upon deterioration or any other change in symptoms. Medical imaging consisted of a yearly MRI and an angiographic reevaluation if considered necessary.

During the follow-up period, events such as intracranial hemorrhage (both clinical and radiological), NHND, and death were considered aggressive. Headache, bruit, orbital phenomena, and cranial nerve deficit due to cavernous sinus lesions (ophthalmoplegia) were regarded as benign and not accounting for morbidity or mortality, even if considered intolerable by the patient or causing ophthalmologic sequelae. At the end of the follow-up period, the clinical status of the patients was evaluated using the following

outcome scale: death; severe disability; moderate disability; good recovery; and (spontaneous) cure. Statistical significance was calculated using the Fisher exact test.

Results

All 118 patients with an aggressive DAVF were offered treatment. This advice was followed by 101 patients (85.6%). Three patients were lost to follow-up before having treatment (2.5%) and were excluded from this review. The remaining 14 patients who declined treatment were selected to assess their disease course, together with 6 patients who had persistence of CVR despite treatment (Table 2).

The initial clinical presentation was symptomatic in all but 1 patient. Five patients (25%) presented with an intracranial hemorrhage. Eleven patients (55%) had NHND, of which 2 patients presented with generalized seizures. Four patients (20%)

TABLE 2. Summary of Patients With Persistent Cortical Venous Reflux

No.	Age/Sex	Location	Borden/Cognard	Treatment	Follow-Up (yr)	Outcome
1	28 M	Transverse sinus R	2/Ilb	No	3.1	Good recovery
2	72 M	Sup sag sinus R	3/IV	No	4.1	Moderate disability
3	71 M	Tentorial incisural	3/III	No	2.3	Died
4	66 M	Tentorial incisural	2/Ila+b	No	3.9	Good recovery
5	59 M	Tentorial incisural	2/Ila+b	No	3.3	Died
6	59 F	Sigmoid sinus L	2/Ila+b	Partial	6.4	Died
7	42 F	Tentorial incisural	2/Ilb	Partial	5.6	Moderate disability
8	65 F	Transverse sinus L	2/Ila+b	No	6.7	Good recovery
9	38 F	Sup sag sinus L	2/Ila+b	No	10.6	Moderate disability
10	86 F	Transverse sinus R	2/Ila+b	Partial	1.6	Severe disability
11	44 M	Straight sinus	3/III	No	1.1	Spontaneous cure
12	79 M	Transverse sinus R	2/Ila+b	No	3.8	Died
13	3 M	Transverse sinus L	2/Ila+b	Partial	3.3	Died
14	52 F	Torcular	2/Ila+b	Partial	4.0	Died
15	73 M	Tentorial incisural	3/III	No	1.8	Died
16	66 F	Cavernous sinus L+R	2/Ila+b	Partial	1.4	Died
17	68 F	Cavernous sinus L	2/Ila+b	No	9.1	Moderate disability
18	40 M	Cavernous sinus L	3/III	No	14.5	Spontaneous cure
19	68 F	Transverse sinus R	2/Ila+b	No	1.2	Died
20	54 M	Sup sag sinus L+R	2/Ilb	No	1.8	Moderate disability

M indicates male; F, female; R, right; L, left; sup sag, superior sagittal.

TABLE 3. Clinical Presentation

Initial Clinical Presentation	No. of Patients
Hemorrhage	5 (25%)
Generalized seizures	2 (10%)
Nonhemorrhagic neurological deficit	9 (45%)
Cranial bruit	2 (10%)
Orbital phenomena	1 (5%)
Asymptomatic	1 (5%)

had a benign presentation. Two patients were assessed because of a cranial bruit, and 1 patient presented with orbital symptoms. The asymptomatic DAVF was incidentally discovered in the work-up of a superior sagittal sinus thrombosis (Table 3).

During the follow-up time of mean 4.3 years (89.6 patient-years), 7 patients suffered an intracranial hemorrhage, of which 3 patients had presented with hemorrhage. The hemorrhages occurred at a median of 2.33 (range, 0.29 to 5.42) years after the initial presentation, without a significant difference between partially treated and untreated individuals. Hemorrhage during follow-up was the direct cause of death in 6 of these patients. The occurrence of NHND is outlined in Table 4. Six patients (30%) suffered an NHND. Four of these 6 cases developed a progressive dementia syndrome related to a diffuse venous congestive encephalopathy, which in 3 cases led to death and in 1 case to a moribund state.

Among the 20 patients with persistent CVR, 9 patients (45%) died during follow-up. One patient (5%) was severely disabled because of progressive dementia. Five patients (25%) remained stable with moderate disabilities, and 5 patients (25%) had a resolution of the preexisting symptoms, of which an angiographic cure of the DAVF was demonstrated in 2 nontreated cases. Overall, 5 of 6 patients treated partially had a bad outcome versus 6 of 14 untreated patients. This difference is not significant ($P=0.12$).

Discussion

Cranial DAVFs with CVR should be considered aggressive lesions. Their behavior includes the likelihood of intracranial hemorrhage, NHND, and death at presentation.¹ However, the disease course after their aggressive presentation is less well understood. Davies et al⁶ reported a 20% annual mortality and morbidity rate, and Duffau et al¹² published their experience of a 35% rebleeding rate in the 2 weeks after the first hemorrhage. These numbers mandate treatment of these lesions urgently, with the aim of disconnection of the CVR. This can be achieved by either surgical or endovascular procedures.^{13–18} Total resection

TABLE 4. Nonhemorrhagic Neurological Deficits

No.	Deficit
9	Venous infarction dominant hemisphere
10	Progressive dementia
12	Venous infarction nondominant hemisphere
13	Progressive dementia
14	Progressive dementia
19	Progressive dementia

of the DAVF itself with or without sacrifice of the dural sinus may not be necessary. Disconnection of the CVR alone may suffice because lesions without CVR have been shown to follow a benign course.^{10,11} Radiosurgical treatment, although reported in the literature to be effective in several case reports or small series,^{19–22} carries an unacceptable delay of 1 to 3 years in the cure of DAVFs with CVR and therefore is not recommended as primary therapy for these lesions.

Based on the aforementioned, DAVFs with CVR require treatment. However, in this series, 14 patients declined a treatment offer and 6 patients had persistence of the CVR despite attempts at cure. It is well understood that these 20 cases are subjected to a bias because they were not randomly chosen; however, they form a unique group providing more insight into the risk of a neurological event in patients harboring a DAVF with persistent CVR.

In the literature, several large series describe the aggressive findings related to DAVFs with CVR; however, they are restricted to events at presentation. Malik et al³ recognized CVR as an important factor. They presented case histories of 6 patients with hemorrhages among 10 patients in their own experience, and they reported 213 earlier published cases. Only 1 of their personal cases had persistent CVR after treatment, with repeated rebleeding as a result. Awad and coworkers¹ described their experience of 17 cases and reviewed 360 cases from the literature. They discriminated between benign and aggressive DAVFs and related the latter group to venous features such as CVR and galenic drainage. However, again, they just looked at the presenting symptoms. Cognard et al⁹ followed only 120 of their 258 patients over a mean period of 52 months, treated and not treated. Although they give a good overview of the incidence of aggressive neurological events, they do not elucidate in how many cases the CVR was obliterated after treatment, nor do they discriminate between events occurring at presentation versus during follow-up. A statement about the expected disease course of DAVFs with CVR can therefore not be determined. The only studies predominantly focused on events later than the initial presentation were performed by Duffau et al,¹² Brown et al,⁵ and Davies et al.⁶ Duffau et al¹² looked at their short time frame between the diagnosis and treatment, which lasted a mean of only 20 days. Brown et al⁵ followed patients for a mean of 6.6 years; however, they did not specifically select for CVR, making the present study unique in concentrating on the disease course of DAVFs with persistent CVR during a long-term follow-up, disregarding the signs and symptoms at presentation. The present study examines an expanded patient cohort initially published in 1997 by Davies et al.⁶ They calculated an annual mortality of 19.2%, with a 19.2% annual rate of hemorrhage and a 10.9% annual rate of NHND during the disease course of DAVFs with persistent CVR. The present study recalculates these rates based on a larger population and 4 times the follow-up time.

In the present study, 16 (80%) of the 20 patients had an aggressive presentation, as outlined in Table 3. During the combined follow-up time of 86.9 patient-years, 9 of the 20 patients died (45%), resulting in an annual mortality rate of 10.4%.

Seven patients suffered a hemorrhage (35%), 6 of whom died as a direct result of the hemorrhages. As a result, the

annual hemorrhage rate was calculated as 8.1%, exactly 4.5 times the annual rate of 1.8% reported by Brown and coworkers.⁵ An explanation for this remarkable difference might be the fact that Brown et al⁵ did not discriminate for the presence of CVR in their whole group, because in their series a full angiographic study was only available in 27 patients (50%). It is therefore likely that the great majority of the DAVFs of their whole group of 54 patients were benign, ie, without CVR. Although Brown et al⁵ mentioned the occurrence of 3 intracranial hemorrhages in a subpopulation of 14 patients during their follow-up, they did not find a significant relationship with CVR. However, they reported a significant influence of venous drainage into the petrosal or straight sinus and of the occurrence of a venous ectasia of a draining vein. These anatomical factors were not of significant influence in the current study. As stated in Table 2, there was only 1 case with drainage into straight sinus and 1 case with a venous ectasia (Cognard type IV). Moreover, the former case had a spontaneous cure.

In the present series, NHND occurred in 6 patients (30%), 4 of them suffering from a progressive dementia syndrome due to generalized venous hypertension. This phenomenon was already described by Lasjaunias et al² and further elaborated by others.^{23–25} As described by Cognard et al, all patients with a dementia syndrome in this series demonstrated retrograde flow in the draining sinus (Cognard type II), causing the venous hypertensive state.²³ It resulted in death or severe disability in all 4 cases. The other 2 patients with an NHND in this series suffered venous infarction, resulting in a 6.9% annual event rate.

Although 5 cases had a favorable outcome, with angiography-proven spontaneous occlusion in 2 cases (10.0%), the combined annual hemorrhage and NHND rate of 15.0%, together with the annual mortality rate of 10.4%, mandates prompt diagnosis and subsequent surgical or endovascular treatment of these lesions.

Of course, this study also has its limitations. During the study period of 17 years, the understanding and treatment possibilities of cranial DAVFs have changed, although the 20 studied cases were equally distributed over the whole period. Moreover, the possibility exists that the favorable outcome in the 3 cases without angiographic occlusion of the DAVF reflects a too short follow-up at the time of evaluation.

Conclusion

DAVFs with CVR carry a high risk for neurological sequelae or death, both at presentation and in their disease course. During the disease course, in this series the persistence of CVR yields an annual mortality rate of 10.4%. In addition, disregarding aggressive events at presentation, the annual risk of intracranial hemorrhage or NHND is 8.1% and 6.9%, respectively, adding up to a 15.0% annual event rate. These numbers mandate prompt diagnosis and treatment of these aggressive lesions.

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