Critical Review of Clinical Aspects and Treatment Strategies of Cranial Dural Arteriovenous Malformations: Experience of a Single Institution

Revisão crítica de aspectos clínicos e estratégias terapêuticas em malformações artério-venosas cranianas durais . Experiencia de uma Instituição.

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ABSTRACT

The authors discuss the treatment strategies for dural arteriovenous fistulas, considering anatomical features such as the presence of cortical venous reflux (CVR) and patterns of cerebral venous drainage. Illustrative cases are presented with the different clinical and angiographic features, focusing on patterns of arterial and venous anatomy, normal cerebral venous drainage and the presence of cortical venous reflux. A review of the pathophysiology and current classifications are presented. The treatment strategies are discussed, focusing on the endovascular procedures available.

Dural arteriovenous fistulas should be treated considering the significant risks of hemorrhage related to the presence of CVR. Treatment strategies should aim angiographic and clinical cure, achieved with low risk of complications when using a multidisciplinar approach, after carefull understanding of the venous drainage, respecting the anatomy of the lesion and the normal cerebral venous drainage.

Keywords: angiography, cerebrovascular disorders, intracerebral hemorrhage, vascular malformations, dural arteriovenous fistula

SUMÁRIO

Os autores discutem as estratégias de tratamento para fístulas arteriovenosas durais, considerando as diversas configurações anatômicas, como a presença de refluxo venoso cortical (RVC) e os padrões de drenagem venosa. Casos ilustrativos são apresentados com as diferentes características angiográficas, enfocando nos padrões de anatomia arterial e venosa, drenagem venosa normal e a presença de refluxo venoso cortical. Uma revisão da fisiopatologia e atuais classificações é apresentada. As estratégias de tratamento são discutidas, com foco nas terapias endovasculares disponíveis. As fístulas arteriovenosas durais deveriam ser tratadas levando-se em consideração os elevados riscos de hemorragia presentes quando existe RVC. As estratégias de tratamento devem objetivar a cura angiográfica e clínica, conseguida com baixo risco de complicações quando se utiliza um manejo multidisciplinar, após cuidadosa análise e entendimento da drenagem venosa cerebral, respeitando-se a anatomia da lesão e a drenagem venosa cerebral normal.

Palavras-chave: Angiografia, desordens cerebrovasculares, hemorragia intracerebral, malformações vasculares, fistula arteriovenosa dural
INTRODUCTION

Dural arteriovenous fistula (dAVF) are rare complex vascular lesions, with heterogeneous morphology and clinical picture. These abnormalities are potentially dangerous, especially if they reflux to the cerebral venous system and increase cerebral venous pressure leading to venous congestion and hemorrhages. We currently present a series of 15 cases, with a review of the most common clinical and angiographic characteristics of patients presenting with dAVF reported on the literature and with a discussion of the treatment employed in our center. This current strategy takes in consideration specially the anatomical configuration of the dAVF, the presence of CVR and the pattern of the cerebral venous drainage. The results presented in this study were established by previous clinical experience and ensures satisfactory levels of cure with low incidence of adverse outcomes.

PATIENT AND METHODS

A review of all intracranial dAVF managed at the Department of Interventional Neuroradiology of the Hospital de Clínicas de Porto Alegre using a prospective protocol adopted since 2005 was performed. A total of 15 cases of dural arteriovenous fistulas was seen at a single institution since 2006, which were managed using a prospective algorithm of surgical and endovascular approaches. This consisted in embolization of arterial afferents with glue, venous occlusion with coils and surgical clipping of arterialized veins with retrograde drainage to the brain.

The fistulas were located at the cavernous sinus in 2 cases, in the lateral sinus in 7, in the paraclinoid region in 2, in the frontobasal region in 2 and, in the petrous apex in one and in the tentorium in 2. The predominant age of presentation was the fifth decade and there was a female predominance (9/15). History of previous minor cranial trauma, with a scalp scar, was present in 9 patients.

Initial presentation was hemorrhage in 2, with other visual and neurologic manifestations such as trigeminal neuralgia, headache and blurred vision in 4. It was an incidental finding in 3 and 4 patients referred unilateral acuphens. The two cavernous sinus lesion presented with conjunctival hyperemia.

Most patients were treated with embolization (10/15) and surgery was performed in 2. One fistula cured spontaneously and 2 patients refused treatment.

Embolization consisted in occlusion of the compromised cavernous sinus by venous approach in 2 cases and afferent embolization with glue in 9. Surgery was performed to resect the fistula directly in one case and to disconnect an arterialized vein with retrograde drainage to the brain in another one.

All treated patients had a good outcome and were cured of the lesion, except for the one submitted to surgical disconnection of the draining vein, in whom the surgical aim was only to stop the cortical venous reflux and to eliminate the risk of hemorrhage. In one case located at the left lateral sinus, the fistula appeared de novo in the opposite side and in the straight sinus and was treated successfully again with embolization.

DISCUSSION

Demographics and Initial Clinical Picture

The average age and clinical pictures found in this report did not differ from the majority of the previous reports in the literature. Although there are some reported cases of dural fistulas in children, it seems that this disease is more prevalent among aged individuals. The gender distribution over previous studies seems to be almost equal, with slight and non significant variations. There is a reported a tendency of hemorrhagic presentation in male individuals, but this was also strongly related to a higher presence of CVR.

The predominant initial clinical picture on the majority of the series was composed of non-significant symptoms, as the presence of acuphens or pulsatile tinnitus, diplopia and other ophtalmological manifestations. It is noticeable that in one case initial symptoms were episodes of facial pain, mimicking a trigeminal neuralgia. This rare manifestation was also noted on a previous study in one patient with a cavernous sinus fistula.

Pathophysiology

The association between dAVF and different etiologic factors, such as cranial trauma, venous thrombosis, intracranial aneurysms and intracranial surgery have been mentioned since the early reports of the disease. Many authors have reported the association of sinus thrombosis and dural fistula and its role in the genesis of the dural
fistulas has been suggested by other studies\textsuperscript{13,17}. Accordingly, the thrombosed sinus may recanalize and progress to the formation of dural fistulas. In the other hand, it has been also suggested that the sinus thrombosis is actually a consequence of the increased haemodynamic stress caused by the arteriovenous fistula\textsuperscript{25}.

Chronic venous hypertension associated with sinus thrombosis has been used as a model to generate dural arteriovenous malformation in rats. These experimental studies employed an animal model of induced venous hypertension with the appearance of histopathological and angiographic characteristics of dural arteriovenous fistulas\textsuperscript{23,33}.

Histopathological findings described on dural fistulas included thickening of the venous intima, collagen proliferation and areas of elastic lamina disruption\textsuperscript{15,25}. (Fig. 1) The dural sinus may also have these features or be partially occluded. In some cases, signs of recanalization after thrombosis are present, with an abnormal network of vascular channels replacing the dural lumen. It is noticeable the dramatic changes on the sinuses when compared it with normal controls\textsuperscript{20}. These experimental studies support clinical and angiographic observations of dynamic changes during the clinical course of dAVF\textsuperscript{24,30}.

Similar to the arterial side of dAVf, venous drainage varies at different intracranial locations. From the anatomical point of view, however, the drainage follows its course throughout three distinct trajectories: dural sinus, arachnoid veins or pial veins\textsuperscript{28}.

If the fistula is located directly to the sinus, the drainage may follow anterograde or retrograde directions, as classically described. In these cases, veins connected directly to the compromised sinus may be submitted to high pressure and eventually inversion of blood flow. In some cases, the sinus may be partially thrombosed or even “trapped” due to the endothelial degeneration generated by the hemodynamic stress, with cortical drainage being the only passage out to allow the venous drainage of the fistula. All these situations with cortical venous reflux are reportedly related with increased risks of hemorrhagic events\textsuperscript{1,3}. (Fig. 2)

In some instances, however, a fistula may result from a connection between a dural vessel directly to an arachnoid or pial vein. In this situation, this cortical vein is submitted to increased intraluminal pressure, runs throughout the cortical surface or cerebral parenchyma and eventually finds a way out to drain on a major sinus. This pattern of drainage also seems to carry an increased risk of hemorrhage. (Fig. 3)
classify and group the dural fistula have been proposed, with a progressive severity related to a greater degree of cerebral venous reflux from the fistula.

The classification proposed by Djindjian and Merland\textsuperscript{11}, revised and validated by Cognard et al\textsuperscript{4}, was composed of five grades, with three subtypes. Supported by a large series of patients, they could demonstrate an association of aggressive neurological symptoms at initial presentation and the presence of cortical venous reflux. The concept of risk, however, should be carefully interpreted on transversal studies, as initial characteristics may not be confirmed as factors associated with aggressive behavior on follow up, as previously reported with brain arteriovenous malformations\textsuperscript{31,32}. This was also already discussed regarding the previous studies of dAVf in a previous report\textsuperscript{35}.

Other classification, with a more simplified scheme, have been published by Borden et al\textsuperscript{2}, based on small series of patients, also suggesting that cortical venous reflux is an unfavorable feature. This simple classification was validated by other group in a large series of cases\textsuperscript{9}.

The group of the University of Toronto have also published the analyses of an untreated cohort of patients, confirming the relationship between cortical venous reflux and risk of hemorrhage\textsuperscript{30,35}. They were able to validate two of the previously reported classifications, with no cortical venous reflux present on “benign” dAVf and its presence in different degrees (indirect venous reflux from a sinus or directly reflux to the brain) on “aggressive” lesions. In a series of 20 untreated patients with CVR, they could observe annual mortality rate of 10.4%, intracranial hemorrhage of 8.1% and NHND of 6.9%.

The same group also reported an interesting study of a cohort of 117 patients harboring dAVf without CVR. They have obtained long-term angiographic follow-up in 50 of 117 conservatively managed patients (done because of a sudden or unexpected change in symptoms) and found a changed venous drainage pattern with the appearance of CVR in two cases. One of these patients had a seizure a result of an intracerebral hematoma. Overall, the rate of benign course was 98% within a period of 27.9 months (348.1 patient-years).

These prospective cohort of patients have made major contributions to the recognition of the association between the cortical venous reflux and risk of hemorrhage. From the therapeutic point of view, lesions with CVR should be treated. It seems clear too that anatomy of the fistula and the pattern of venous drainage are important variables to be considered when managing dAVf.
It is now generally accepted that the presence of retrograde leptomeningeal venous drainage (CVR) is the key for an aggressive behavior, with higher risk of hemorrhage and unfavorable neurological outcomes. Many investigators have proposed different schemes of classification and factors linked to increased risk for intracranial bleeding. The present study focused on this group of patients.

Conversely, the clinical course of dural fistulas without retrograde venous drainage is significantly different and many reports advocate close observations of these lesions without specific treatment. Therapeutic approaches for lesions without CVR remain matter of discussion, as they present a low risk of hemorrhage and neurological complications. Further cohort studies may provide additional information about the clinical behavior of these lesions, taking in consideration that they may have potential progression to more aggressive states with CVR and there is no harmless imaging study which could demonstrate these modifications.

Another important factor to be considered is the pattern of venous drainage, as in some cases the compromised sinuses or veins are still used by the brain for venous drainage, making the treatment more difficult and risky. The compromised sinus or vein is considered “hemodinamically excluded” when it was no longer used by the brain for normal venous drainage. If they were still used for normal venous outflow, then the fistula was defined as “competing with normal brain drainage”.

**Treatment Strategies**

The first important step to choose the therapeutic approach is the recognition of the characteristics of the dAVF. It is now clear that lesions with presence of CVR must be treated, as the reported annual risks of morbidity and mortality are 15% and 10.4%, respectively.

Different methods of treatment for dAVF have been proposed since the early reports of the disease, but the therapeutic strategies remain invasive, either by embolization or surgery. The effectiveness of the classical described manual compression of the carotid and jugular is questionable, as the rates of spontaneous resolution of benign dAVF are comparable to the resolution results of this maneuver. The use of radiotherapy, specially stereotactic radiosurgery, has been presented as an alternative treatment to dAVF, but it also has been pointed out that patients remain at high risk for hemorrhage during the period of observation after treatment (until the radiation takes its effect), markedly in lesions with cortical venous reflux. It seems that radiosurgery may have a role on selected cases not suitable to embolization or surgery.

Due to the increasing comprehension of the angiographic characteristics and clinical behavior accomplished by clinical studies, treatment modalities have progressed from proximal surgical occlusion of afferent branches of the external carotid artery to more selective endovascular and surgical approaches.

In the present management tree, it is mandatory to consider the presence of cortical venous reflux, largely emphasized by previous cohort studies. It is clear now the notion that CVR is a dangerous feature related to increased risk for hemorrhage, so patients harboring such lesions should be protected with aggressive endovascular or surgical approaches. The main treatment goal is to assure the disappearance of the CVR, either with complete cure or simply with the disconnection of the cerebral veins from the fistula.

Different methods of embolization have been proposed for dAVF, varying from transarterial to transvenous approaches. The most common agents used for afferent embolization are PVA particles, polymeric embolic agents such as N-butil cyanoacrylate (NBCA) and detachable coils. More than one of these agents may be necessary to achieve devascularization of a fistula, according with the type and diameter of the arterial pedicle.

Transarterial embolization has been reported in small series to promote cure in up to 100%, considering the whole group of dAVF. However, these results may present an important bias as they mix types of fistula with different clinical behaviors: cavernous sinus fistula, for example, usually have a tendency to thrombosis with flow reduction after afferent embolization. For this approach, it seems that it is necessary to take on consideration the particular anatomy of the lesion, as the results for cure are highly influenced by the type of afferent and by the location.

Based on a careful observation of angiographic and clinical features present on previous cases, an anatomical scheme could be constructed in order to understand and categorize the different types of dAVF. This assortment is now used to determine the strategies of treatment of dAVF in our institution. Basically, it takes in consideration the arterial afferent, location and pattern of venous drainage of the lesion. The strategy for treatment took also on consideration the presence of cortical venous reflux (CVR).

Two different types of fistula were described, following anatomical and angiographic characteristics. This work was preceded by an analysis of the morphological characteristics of the dAVF present in the literature and the lesions were separated on a group draining directly to the sinus (either patent or trapped) and other group finding the way of drainage directly through intracranial veins.

In the group of sinus fistulas, we found those located at the
lateral and cavernous sinus. For the lateral sinus group, the first choice is to perform arterial embolization with glue, mainly ONYX® (EV3). This group has a lot of external carotid afferents, which make it safe to use glue without major risk of intracranial arteries. (Fig. 4) When this approach fails, it can be considered the occlusion of the sinus at the site of the fistula if it is hemodinamically excluded, as stated earlier. In the second group, with more direct short branches from the internal carotid artery, embolization with glue has high risk of reflux, so arterial approaches are limited. In this instance, the cavernous sinus can be occluded safely by venous approach. (Fig. 5)

Surgical disconnection of the CVR are preferred in cases when preservation of the sinus’ patency is necessary or when arterial embolization fails or cannot be performed safely. In cases without evident CVR and in which hemodinamic exclusion of the sinus cannot be demonstrated, the treatment of choice is observation. Arterial embolization with ONYX can be an alternative if the symptoms cannot be tolerated.

Fistulas with drainage directly through intracranial veins need to be treated by occlusion of the fistulous site, either by endovascular or surgical methods. In these cases, occlusion of the sinus is believed to worsen the venous hypertension, as the compromised veins would not have a path for drainage. Endovascular access to the fistulas can be performed by arterial or venous approaches.

Surgical methods were chosen according with the type of the fistula and its location, with the goal of complete resection or disconnection of the CVD. Surgery also provides access for transvenous approaches through direct sinus puncture. Burr holes over the compromised sinus can be performed guided by angiography, using standard neurosurgical methods.

**Conclusion**

The treatment approach to dAVF should take into consideration three important variables: the presence of cortical venous reflux, the type of the fistula and the patency of the dural sinus.

The paramount issue is that there is a clear association between hemorrhagic presentation and the presence of cortical venous reflux reported on prospective studies of untreated patients harboring dAVF, so these lesions demand treatment.

Diversified anatomical patterns resulted from clinical and angiographic observations and these have to be considered when choosing different therapeutic approaches. Lesions draining directly into a sinus should receive therapeutic approach distinct from those draining into intracranial veins. When a venous structure is no longer used by normal venous drainage, it is hemodinamically excluded. This concept is important to the decision to occlude a compromised sinus or vein when necessary.

The currently protocol is in accordance with the widely accepted concepts management of dAVF: using an established management decision tree, we could accomplish high cure rates with acceptable levels of morbidity and mortality.
REFERENCES


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