

Concepts and Controversies in the Management of Cerebral Developmental Venous Anomalies

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KEY WORDS: developmental venous anomaly, cavernous hemangioma, ischemic stroke, cerebral venous sinus thrombosis, cerebral hemorrhage

IMAJ 2010; 12: 703–706

Developmental venous anomaly is a widely used synonym for venous angioma or cerebral venous malformation [1]. DVAs are the most frequently encountered cerebral vascular malformation and are frequently reported as incidental findings in computed tomography and magnetic resonance imaging studies. Radiological and autopsy series have demonstrated that DVAs occur in 2.5 to 3% of the general population and constitute approximately 60% of all vascular malformations of the central nervous system [2-4]. These purely venous malformations are considered extreme anatomic variations of the normal transmedullary cerebral vasculature that is necessary for the drainage of white and gray matter. DVAs are classified as a type of cerebral vascular malformation, along with arteriovenous malformations, cavernous malformations, and capillary telangiectasias [5]. However, some intracranial vascular lesions fall outside of this classification and have been dubbed “mixed” vascular malformations since they possess features of more than one type of classic vascular malformation [6].

DVAs are encountered in both the pediatric and adult populations, with a slight predominance in males [7,8]. DVAs are usually asymptomatic and follow a benign clinical course in the great majority of cases [9-12]. Classical DVAs have no proliferative potential and no direct arteriovenous shunts [2,13]. Although brain parenchyma drained by a DVA has historically been considered to be normal, recent reports have found abnormalities in a significant proportion of patients [8].

Developmental venous angiomas are the most common vascular malformations of the brain

Most DVAs are asymptomatic and follow a benign clinical course

NORMAL CEREBRAL VENOUS SYSTEMS AND DVA AS A VARIATION OF NORMAL VASCULATURE

The veins of the cerebral hemispheres can be divided into two systems: a superficial system draining the cerebral cortex and the subcortical white matter through visible pial veins, and a deep system consisting of the medullary veins that drain the deep white matter and the striate body. Connections between the cortical and deep venous systems through veins that cross the entire thickness of the brain parenchyma have been described as transcerebral veins [14]. The same principle of superficial and deep venous systems is also applicable to cerebellar venous architecture.

DVAs serve as venous drainage routes of the brain tissue because the typical pial or subependymal venous drainage of their territory is absent. Thus DVAs may be understood as a variation of the normal cerebral venous systems, where a deep venous territory drains centrifugally toward either the pial veins of the cerebral surface or directly into a dural venous sinus, or where a cortical and subcortical venous territory drains centripetally toward the network of deep subependymal veins [2,15].

PATHOGENESIS AND MORPHOLOGY

It is generally accepted that DVAs are formed during intra-uterine life [8,16], but no consensus exists regarding the mechanism leading to their formation. Based on imaging findings and clinical symptoms, Pereira et al. [2] identified two major pathomechanisms for symptomatic DVAs. Mechanical mechanisms, which account for 20% of cases, cause symptoms when some component of the DVA produces a compressive effect over the parenchyma, cranial nerves, ventricles, or bone, leading either to hydrocephalus or to vessel-nerve conflicts. Flow-related mechanisms, which are characterized as an imbalance of in- and outflow of blood in the DVA system, occurred in 71% of the cases reviewed and can be divided into subgroups. Increased flow into the DVA may be due to microshunting, for example, or to an AVM using

DVA = developmental venous anomaly

AVM = arteriovenous malformation

the DVA as a drainage route. Decreased outflow may be due to anatomic causes such as thrombosis of the DVA channels, or to stenosis or occlusion of the venous collector or distant draining sinus; or to functional causes such as remote arterial overload from a distant high flow shunt or AVM. Hemorrhagic or ischemic infarction around a DVA may result from acute thrombosis of the collecting vein [17,18].

DVAs are characterized by a cluster of venous radicles that converge into a collecting vein, resulting in the typical caput medusae appearance. They can affect a variable volume of brain parenchyma, ranging from a few sulci to even a whole hemisphere. They occur more frequently at the supratentorial compartment, with frontal lobe predominance [19]. Though the collecting vein is most often unique, several collectors may be observed in about 6% of DVAs, and two or more DVAs coexisting in separate regions of the brain have been observed in 1.2–16% of cases [8,19]. The collecting vein crosses a variable length of brain parenchyma to join either the superficial (70% of the cases) or deep venous system (20% of cases). In some 10% of cases, DVAs may drain into both the superficial and deep venous systems [1,20].

Many authors support the idea that venous hypertension is the underlying mechanism leading to the spectrum of brain lesions associated with DVAs. Impaired brain perfusion attributed to venous congestion in areas drained by DVAs has been documented by several authors [21]. Intraoperative evidence of increased venous pressure within a DVA has also been reported [22]. Venous outflow obstruction due to stenosis of the collecting vein may account for venous hypertension in a substantial number of cases.

In comparison to normal veins, DVAs are characteristically a network of thin walled vessels draining into a large caliber vein with a thicker fibrous wall that lacks a smooth muscle layer and elastic lamina [15,23]. Stenosis is frequently seen in superficial DVAs at the point where the collecting vein penetrates into the draining dural venous sinus [8,24].

Brain parenchyma drained by a DVA was long thought to be normal, but imaging and histological studies have recently challenged this assumption [8]. Parenchymal abnormalities such as locoregional cerebral atrophy were the most frequent abnormalities identified, followed by white matter lesions and dystrophic calcification.

ASSOCIATION WITH CAVERNOUS HEMANGIOMA AND OTHER VENOUS LESIONS

The most common and clinically significant entity associated with DVAs is cavernous malformation (also known as cavernoma). In 13–40% of cases, DVAs are associated with one or more CMs, which are typically located in the region

of the DVA's caput medusae [25,26].

The pathogenesis of acquired CMs is still unknown, but evidence of subclinical microhemorrhages may be found in the parenchyma surrounding a DVA, possibly resulting from blood diapedesis through the walls of the venous radicles of the caput medusae, or its rupture [15,27]. Repeated microhemorrhages around DVAs are thought to induce the formation of CM-like lesions by activating angiogenic growth factors leading to reactive angiogenesis with vessel formation and coalescence, a process that has been referred to as hemorrhagic angiogenic proliferation [27].

Recently, Hong and associates [18] concluded that anatomic angioarchitectural factors might be the key factors causing CMs within the territory of DVA, by causing blood flow disturbance. It has been hypothesized that solitary CMs (those not associated with visible DVAs) are related to microscopic venous malformations [22].

Rare forms of arterialized DVAs may follow a more aggressive clinical course and likely carry a hemorrhagic risk similar to AVMs. Digital subtraction angiography is required to establish this diagnosis and should be proposed for all cases of DVAs presenting with a cerebral hemorrhage where CT or MRI fail to demonstrate a collecting vein thrombosis or a cavernoma.

DVA drainage into a sinus pericranii may also be seen in unusual cases. Precise analysis of the cerebral venous anatomy is required when planning the treatment of a sinus pericranii [28].

DVAs are also associated with superficial head and neck venous malformations, lymphatic malformations of the orbit region, and other vascular malformations [29].

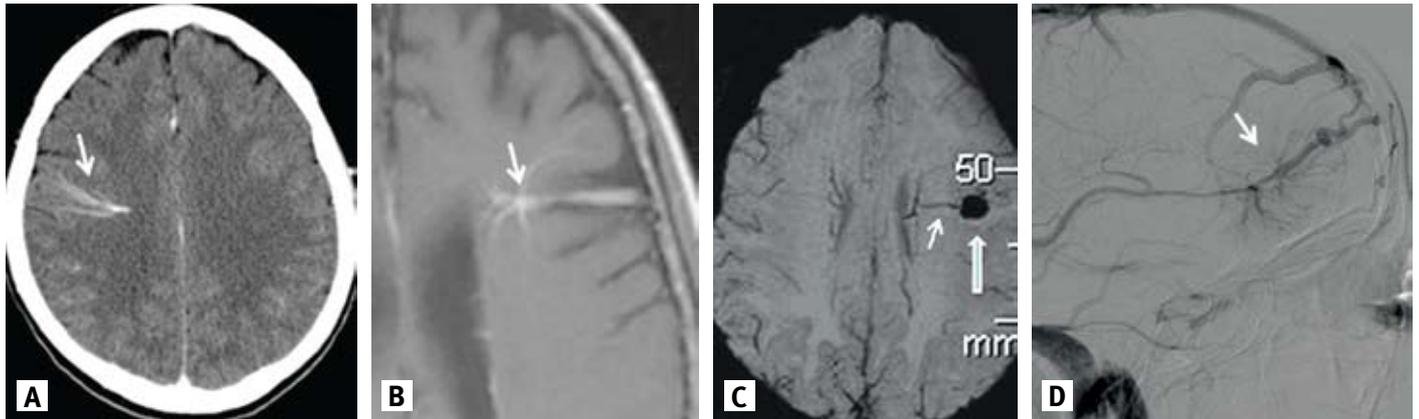
NEURORADIOLOGICAL FEATURES

Non-invasive neuroradiological examinations such as CT and MRI generally permit diagnosis of DVAs and detection of associated cavernoma [30,31]. Digital subtraction angiography is reserved for cases presenting with ischemic or hemorrhagic infarction, or whenever an associated vascular malformation is suspected. In every imaging modality the diagnosis of a DVA relies on demonstrating a typical caput medusae draining into a collecting vein.

On contrast-enhanced CT, the venous collector of the DVA is readily detectable as a linear or curvilinear focus of enhancement, typically coursing from the deep white matter to a cortical vein or a deep vein or to a dural sinus. Both the collecting vein and the caput medusae are enhanced following administration of contrast material, and are best demonstrated by thin section CT venography [Figure 1A] [3,4,6,8].

CM = cavernous malformations

Figure 1. [A-C] Typical DVA presentation on contrast-enhanced CT, magnified axial T1-weighted, contrast-enhanced MR image, and susceptibility-weighted MR imaging (SW-MRI) showing a small cavernoma (thick arrow) associated with a DVA (thin arrow). **[D]** Digital subtraction angiography showing opacification of the caput medusae of a DVA during the venous phase.



Non-contrast T2 and T1-weighted MRI may demonstrate flow voids and phase-shift artifact produced by the collecting vein of a DVA and by the larger venous radicles of the caput medusae [3,4,30,31]. As with CT, the caput medusae and the collecting vein are readily enhanced after gadolinium administration on T1-weighted sequences [Figure 1B]. MRI multiplanar reconstructions provide excellent morphological assessment of the DVA. On MRI, DVAs typically have a transhemispheric flow void on both T1 and T2-weighted images. After the administration of gadolinium, because of the slow flow, significant enhancement of the caput medusae of the medullary veins and venous collector is observed.

MRI is superior to CT in demonstrating associated parenchymal abnormalities such as white matter lesions and CMs [8]. Because CMs are frequently associated with DVAs, they should be specifically sought out, using hemosiderin or deoxyhemoglobin-sensitive sequences such as gradient-echo T2-weighted images or susceptibility-weighted images [Figure 1C] [32]. CMs may be difficult to identify in the setting of a DVA presenting with acute hemorrhage and may only become apparent after the hemorrhage is fully reabsorbed, 3–6 months after the initial event.

Because of its higher temporal resolution, DSA remains the best imaging technique to study the hemodynamic behavior of DVAs. Typically, DVAs are opacified during the venous phase of the angiogram [Figure 1D]. Delayed outflow of a DVA, suggesting drainage impairment, may sometimes be observed, even in the absence of a demonstrable collecting vein stenosis. Exceptionally, early angiographic

opacification may be seen. This pattern corresponds to either a mixed vascular lesion that combines features of DVAs and AVMs (arterialized DVA), or the rarer form of an AVM draining into a venous angioma [6,32-34]. DSA remains necessary to adequately characterize this atypical form of DVA. Functional brain MRI may also play a significant diagnostic role [33].

CLINICAL PRESENTATION AND MANAGEMENT

The most common presenting symptoms are headache and seizures. As mentioned earlier, bleeding is generally related to associated cavernomas or other lesions, rather than to the DVAs themselves [10,26]. Similarly, seizures have been localized to areas not associated with the DVA in several studies [9,35], or to associated cortical dysplasias [36].

In the vast majority of cases, DVAs follow a benign clinical course. They are only rarely symptomatic, with a very low rate of symptomatic hemorrhage (0.22–0.68% per year) [9-12]. However, 18–40% of DVAs are associated with one or more CMs [25,26], which are at higher risk of bleeding. In these cases, management decisions are usually focused on the cavernoma rather than on the DVA.

Rare forms of arterialized DVAs may follow a more aggressive clinical course and many of these lesions may carry a hemorrhagic risk similar to AVMs [15,37]. DSA is required to establish this diagnosis and should be proposed for all cases of DVAs presenting with a cerebral hemorrhage where

In cases where a cavernoma or AVM is associated with a development venous angioma, the focus of management transfers from the DVA to the associated vascular lesion

CT or MRI fails to demonstrate a collecting vein thrombosis or a cavernoma.

While surgery will not be required in the majority of patients with DVA alone, individuals diagnosed with a DVA

DSA = digital subtraction angiography

should be referred for neurosurgical assessment and more thorough radiological evaluation to exclude the possibility of a coexisting lesion.

When a surgical procedure is indicated due to the presence of a related lesion, it must be undertaken with the objective of preserving the DVA and collecting veins. Catastrophic venous ischemic and hemorrhagic complications may result from the surgical removal of a DVA or damage to a collecting vein, due to the important contribution of DVAs in the normal cerebral venous drainage [12,23]. A more thorough discussion of DVAs may be obtained from two recent reviews of the entity by Ruiz et al. [15] and Rammos et al. [16].

SUMMARY AND REMARKS

Cerebral DVAs are frequently encountered on routine neuroradiological studies and are currently considered extreme variations of the cerebral venous anatomy. In most cases, DVAs follow a benign clinical course and do not require specific treatment. Their association with cavernomas is frequent, and usually accounts for cases presenting with cerebral hemorrhage or seizure activity. These cases require neurosurgical assessment and may require surgery. Rare forms of arterialized DVAs may follow a more aggressive clinical course and likely carry a hemorrhagic risk similar to AVMs. Clinicians should be aware that, though generally benign, DVAs and their associated lesions may represent a complex entity with potential for clinical complication requiring, in certain cases, additional imaging investigations and specific medical management.

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