Nongalenic arteriovenous fistulas: history of treatment and technology

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Nongalenic cerebral arteriovenous fistulas (AVFs) are uncommon, high-flow vascular lesions first treated by Walter Dandy and his colleagues by using open surgery with ligation of the feeding artery. Due to advances in endovascular technology over the past four decades that make possible the control of high flow in AVFs, treatment has evolved from the sole option of surgery to include the alternative or adjunct option of endovascular embolization. The authors of this review discuss the history of nongalenic AVF treatment, including techniques of both surgery and interventional neuroradiology and the technological developments underlying them.

KEY WORDS • nongalenic arteriovenous fistula • embolization • endovascular therapy • history of neurosurgery

ARTERIOVENOUS fistulas consist of a direct high-flow connection between an artery and a vein without an intervening nidus. Arteriovenous fistulas termed “nongalenic” are uncommon vascular malformations that do not involve a persistent embryonic median prosencephalic vein; they are called nongalenic because they are a class of lesion separate from so-called vein of Galen aneurysms or malformations. In this article we first describe the historical classification, anatomy, and clinical features of nongalenic AVFs as background and then we focus on the history of their treatment. This history is necessarily recent, given the emphasis on innovations in endovascular technology that have improved the ability to diagnose nongalenic AVFs and expanded options for their treatment.

The treatment of nongalenic AVFs has changed dramatically during the past several decades due to technical advances. From the early days of neurosurgery to the 1960s, nongalenic AVFs were treated only with open surgery. As new technology has improved the potential for endovascular control over these lesions’ high flow, embolization performed by interventional neuroradiologists has become an accepted treatment, either alone or combined with surgery or stereotactic radiosurgery. The history of treatment for nongalenic cerebral AVFs is discussed in this paper in terms of technological progress—from the sole option of open surgery in the early era of treatment to the present-day adjunct and alternative option of endovascular therapy.

Historical Classification

Due to their rarity and to the difficulty in accurately defining their angioarchitecture in the preangiography era, nongalenic AVFs typically were not recognized as a distinct category of vascular lesion in historical classifications. Nongalenic AVFs were grouped by Walter Dandy in his 1928 series with the general class of vascular malformations that he called “arteriovenous aneurysms.” Later, in a classic 1945 review of intracranial vascular lesions, Noran distinguished the categories of “cerebral varix” and “arteriovenous angioma,” with no exact fit for nongalenic AVFs in his extensive classification system. When McCormick published his streamlined classification of vascular malformations in 1966, he proposed the separate categories of “varix” and “arteriovenous malformation (angioma)” without explicitly describing nongalenic AVFs, which are neither simply varices nor classic AVMs. In the past, given their infrequency and the absence of a specific classification category, nongalenic AVFs were often grouped with AVMs in clinical series. As will be described, the capacity of modern angiog-
raphy to define angioarchitecture precisely has allowed the distinction of nongalenic AVFs from AVMs, adding a category to the classification of cerebrovascular lesions and thereby improving the diagnosis and treatment of these lesions.

**Defining Features**

**Infrequency of Nongalenic AVFs**

Nongalenic AVFs are rare lesions. They arise sporadically both as isolated phenomena and in congenital, non-hereditary Wyburn-Mason syndrome; they also occur in inherited disorders such as the Rendu-Osler-Weber syndrome.6,27,30,35 The infrequency of nongalenic AVFs can best be assessed in the context of more common AVMs by considering two single-institution experiences recorded during 10-year periods. At one tertiary care institution, five (1.6%) of 320 AVMs treated in a 10-year period were found to be nongalenic AVFs;15 at another tertiary care center, in the same length of time, 12 (4.8%) of 251 cerebrovascular malformation cases (not including dura-based lesions) were diagnosed as nongalenic AVFs.36 Given an AVM incidence of approximately 1 per 100,000 per year in unselected populations, the rarity of nongalenic AVFs is clear.1

**Anatomy of Nongalenic AVFs**

Nongalenic AVFs can be single or multiple, with a higher probability of multiple lesions occurring in patients with inherited syndromes.6 The anatomical and physiological hallmark of the nongalenic AVF is the direct emptying of one or more feeding arteries into a large varix that has very high flow. This associated varix is a venous ectasia distal to the fistula that most likely develops due to the varix’s high flow and often has mural calcification.21,36–38,41 Nongalenic AVFs are always associated with such a varix and are sometimes associated with other vascular abnormalities such as AVMs or aneurysms. Such aneurysms typically are located at a bifurcation where a minor vessel branches off a major feeding artery immediately proximal to the fistula.36

The varix of a nongalenic AVF is typically extraparenchymal, with the fistula itself in a superficial cortical location and often obscured by the varix.21,36 The location of the varix correlates with the arterial supply of the AVF, with frontal and medial parietal varices fed by the anterior cerebral artery, temporal and parietal convexity varices associated with the MCA, and occipital varices supplied by the posterior cerebral artery (Fig. 1).21 More posteriorly located lesions are sometimes supplied by branches of the basilar artery.21,36 The route of venous drainage depends on the location of the nongalenic AVF, with most interhemispheric and convexity varices draining into the superior sagittal sinus and many temporal and occipital AVFs reported as draining into both the superior sagittal and transverse sinuses.21

**Clinical Aspects**

**Clinical Presentation**

The size, angioarchitecture, and high-flow state of nongalenic AVFs, as well as the age of the patient, dictate their clinical presentation, which takes different forms depending...
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Fig. 2. Pretreatment T1-weighted MR images, axial views, obtained in a patient recently treated with endovascular embolization at UCLA, showing large flow voids, consistent with the diagnosis of right temporal nongalenic AVF (A) and right medial parietal nongalenic AVF (B).

Fig. 3. Magnetic resonance angiography image obtained in the same patient as in Fig. 2, demonstrating dilated feeding arteries without a nidus, consistent with the diagnosis of two discrete nongalenic AVFs, each associated with a giant varix. TOF = time of flight.

on the presence of mass effect, arterial steal, or venous hypertension.\textsuperscript{36,38} Although commonly congenital, nongalenic AVFs typically present after the neonatal period.\textsuperscript{21} Those that are diagnosed in the neonatal period are usually found secondary to congestive heart failure, similar to vein of Galen malformations. After the neonatal period, infants with nongalenic AVFs present with increasing head circumference or focal neurological deficit. Adolescents and adults who have nongalenic AVFs present with headache, seizures, and focal neurological deficit.\textsuperscript{21,35,36,38} Acute presentation due to subarachnoid or intracerebral hemorrhage is much less common but does occur.\textsuperscript{21,36,38}

Asymptomatic adults with nongalenic AVFs have rarely been described. In a 1987 case series at the UWO, all of the adults with high-flow nongalenic AVFs associated with giant intracranial varices were symptomatic due to neurological and/or cardiac disease.\textsuperscript{38} All patients in a 1989 series at the University of California San Francisco and all adults with these cerebral lesions in a 1993 Mayo Clinic series were symptomatic.\textsuperscript{15,36} Described in a case report published in 2004, an adult patient with Rendu-Osler-Weber syndrome came to medical attention as a result of neurological symptoms due to a spinal AVF, underwent an examination that revealed a field cut, and was found also to have a cerebral AVF.\textsuperscript{27} One adult with nongalenic AVFs described in a UWO–UCLA 1992 series as both asymptomatic and without neurological deficits came to medical attention because of a vascular abnormality: this 25-year-old woman presented with a massive cirrroid aneurysm (AVF) of the scalp and was found to have two ipsilateral nongalenic cerebral AVFs.\textsuperscript{21} A truly asymptomatic patient who recently underwent successful endovascular treatment at UCLA was found to harbor two large, discrete nongalenic cerebral AVFs, one right temporal and the other right medial parietal (Figs. 2–6). These lesions were incidentally discovered when the patient underwent cerebral imaging for staging after melanoma diagnosis.

Diagnosis of Nongalenic AVFs

In Dandy’s era, the diagnosis of a nongalenic cerebral AVF was based on clinical symptoms and signs (for exam-
ple, auscultation of bruits), substantiated by pneumoencephalography, and then confirmed by direct visualization at craniotomy. Currently, initial computerized tomography and MR imaging studies are routinely obtained, followed by digital subtraction angiography, the diagnostic gold standard. In a 1993 Mayo Clinic series, the following three angiographic criteria were suggested for the diagnosis of cerebral AVFs: 1) rapid circulation time due to high-velocity flow; 2) enlarged feeding arteries; and 3) direct filling of a large varix (described as “jet phenomenon” on MR angiography). Currently, precise delineation of lesion angiographic architecture using biplanar and three-dimensional rotational selective and superselective angiography permits accurate diagnosis of nongalenic AVFs and also serves as a guide for planning treatment. Overlapping arterial and venous collateral vessels may make visualization of an AVF difficult during routine angiographic injections. It is crucial to use superselective angiography to distinguish nongalenic cerebral AVFs from AVMs, given that the treatment strategies for these lesions differ.

**History of Surgical Treatment: Dandy and Drake**

The goal of nongalenic AVF treatment is obliteration of the fistula via occlusion of its arterial supply without premature occlusion of its venous drainage. This objective can be achieved using surgical or endovascular therapy, separately or in combination. Historically, nongalenic AVFs were treated at craniotomy by occluding feeding arteries as close as possible to the site of the fistula, initially by ligation and later by clipping. A review of cases of nongalenic cerebral AVF reported between 1928 and the
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Open surgery with ligation was at first the only treatment option for nongalenic AVFs. In his 1928 series of “arteriovenous aneurysms of the brain,” Dandy reported the surgical treatment of a lesion that he described as a “pure arteriovenous fistula,” that is, a nongalenic AVF supplied by a single feeding artery off the right MCA, which connected directly to an enlarged venous trunk (Fig. 7). At the initial operation, Dandy performed a craniotomy, observed the massive venous drainage of the lesion on the surface of the right temporal and frontal lobes, and then closed. He wrote, “Since any attempt to treat the aneurysm surgically appeared to involve a risk greater than my co-workers and I were justified in assuming, the dura was closed and the bone flap was replaced.” At reoperation, the feeding artery was ligated and the varix was then observed to collapse immediately (Fig. 8). Although the 52-year-old patient’s seizure disorder was cured by the surgical treatment of his AVF, postoperatively he had a new permanent deficit of mild left hemiparesis. Dandy reached a cautionary conclusion in summarizing his clinical experience with this lesion and other types of cerebral arteriovenous aneurysms. He wrote, “Radical ligations or extirpations alone are curative, but are exceedingly dangerous to life and function and are indicated in the minority of cases. . . .” Dandy’s surgical treatment of these cerebrovascular lesions was limited by the technology available in his time (Fig. 9 left).
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teristic of nongalenic AVFs—the associated dilated varix—has made the fistulas especially amenable to
modern endovascular techniques, given that this venous outlet can be used in the endovascular approach.

Despite the anatomical differences between nongalenic AVFs and other cerebrovascular lesions, technical advances
originally made in the endovascular treatment of intracranial AVMs and aneurysms have been directly applicable to
the embolization of nongalenic AVFs. These innovations have included the optimization of embolic agents, the de-
velopment of new types of catheters, and the use of preembolization superselective angiography.

Surgical Treatment by Drake

In the 1960s and 1970s, technological innovations led to intraoperative and transfemoral embolization as a new strat-
egy for treating cerebrovascular lesions. Yet open surgery with clip occlusion of feeding arteries remained the treat-
ment option of choice for most cerebral AVMs and inevitably also for nongalenic AVFs in the 1970s. In his 1979
series of 166 patients with cerebral AVMs, Charles Drake (Fig. 9 right) included two cases of nongalenic AVFs asso-
ciated with huge varices. Although five AVMs in this series were treated with flow-directed or direct selective plastic bead embolization, this type of procedure was not an option for nongalenic AVFs, given the dangers posed by the AVFs’ high flow and associated massive varix. The two patients with nongalenic AVFs in Drake’s series underwent surgical clip occlusion of feeding arteries. This was a success in one patient, but the other patient died 24 hours after the operation due to intracerebral hemorrhage attributed to hemodynamic alteration. In this case of death resulting from hem-
orrhage, the venous outlet of the AVF was not surgically occluded during the operation, and later autopsy confirmed
the patency of the varix. As in the case of Dandy’s patient, the varix collapsed on itself after Drake occluded the soli-
tary large feeding artery of the AVF (in this case with a single clip). Drake hypothesized that the cause of hemorrhage was rupture of a deep normal artery.

Surgical treatment of nongalenic AVFs poses some disadvantages particular to the lesions’ anatomy. For example, at craniotomy, visualization and access to the fistula itself are often hindered by the presence of a massive associated varix. Endovascular therapy avoids this problem and is now a frequently selected treatment option for nongalenic AVFs. The modern history of the innovations underlying the optimization of endovascular treatment for nongalenic AVFs is discussed in the following section.

History of Innovations Leading to Endovascular Treatment

Challenges of Endovascular Treatment

Due to the high flow in these lesions, treatment of nongalenic AVFs always carries the danger of rapid hemody-
namic alteration, also known as normal perfusion pressure breakthrough, which may result in cerebral injury and death. In addition, given their high flow and dilated venous drainage, the risk of inadvertently occluding the venous outflow of nongalenic AVFs has posed a particular challenge to treating these lesions with endovascular em-
bolization. Currently, however, this particular anatomical charac-
teristic of nongalenic AVFs—the associated dilated varix—has made the fistulas especially amenable to
modern endovascular techniques, given that this venous outlet can be used in the endovascular approach.

Embolization materials have gradually improved since 1930, when Brooks inserted a piece of muscle into a patient’s carotid artery to embolize a carotid–cavernous fistula. The first materials used were muscle, Gelfoam, and solid plas-
tic particles; later advancements included detachable balloons, rapidly polymerizing liquid agents, and detachable coils. In 1960, Luessenhop and Spence described the successful flow-directed embolization of a large left frontotemporal AVM by using solid particles (four spherical methyl methacrylate emboli) introduced into the surgically exposed left carotid artery. In 1974, Serbinenko reported his innovative use of detachable balloons to occlude cere-
bral vessels by percutaneously introducing balloon catheters into the vascular system and maneuvering them into the intracranial arteries. In the early 1980s, rapidly poly-
merizing cyanocrylates were established as efficacious in both the intraoperative and transfemoral embolization of cerebral AVMs. In 1990s, Guglielmi and coworkers described their successful use of electrolytically detachable platinum coils and soft microcatheters to perform endovascular electrothrombosis of intracranial aneurysms. On the basis of these innovations, vascular neu-
rosurgeons and interventional neuroradiologists began to work together to combine open surgery with intraoperative and/or transfemoral embolization of nongalenic AVFs as well as AVMs.

Successes and Failures in Embolization of Nongalenic AVFs

This technological progress improved the efficacy of en-
dovascular embolization as treatment for cerebrovascular lesions in general and made possible its application to non-
galenic AVFs. However, as in the history of any new tech-
ology, attempts to treat nongalenic AVFs with interven-
tional neuroradiology were initially often unsuccessful. The specific causes of failure in individual cases were diverse: inability to control the fistula’s high flow; incompleteness of balloon placement too proximal to the fistula site; development of new collateral feeding arteries after embolization; imprecise placement of platinum coils; and failure to occlude all feeding arteries, probably due to incomplete an-
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for the treatment of nongalenic AVFs. From 1928 to the present, more than 47 adults and children with nongalenic AVFs have been described, either in individual case reports or in case series, with open surgery the only possible treatment in early cases.²⁻⁶,⁸,¹¹,¹⁵,¹７,²¹,²⁵,²⁷,³⁵⁻⁴⁰,⁴² In the modern era, there remain certain nongalenic AVFs that are best approached in open surgery for anatomical reasons. Also, practitioners today still hesitate to treat nongalenic cerebral AVFs with endovascular embolization due to the danger of embolic material migrating into the lungs, cortical veins, or dural venous sinuses because of the lesions’ high flow.²⁷,³⁸ However, the technological progress in interventional neuroradiology made over the past four decades currently supports many different strategies to reduce flow during endovascular treatment and to avoid this risk. Due to such technical innovations, the success rate of interventional neuroradiological treatment has improved dramatically, and it is now the optimal treatment approach for many nongalenic AVFs. On this basis, endovascular embolization is currently established as an important alternative to open surgery for the treatment of nongalenic AVFs.

Conclusions

The impact of the technical advances described in this paper is revealed by the improved diagnosis and successful endovascular treatment of nongalenic cerebral AVFs. From 1928 to the present, more than 47 adults and children with nongalenic AVFs have been described, either in individual case reports or in case series, with open surgery the only possible treatment in early cases.²⁻⁶,⁸,¹¹,¹⁵,¹⁷,²¹,²⁵,²⁷,³⁵⁻⁴⁰,⁴² In the modern era, there remain certain nongalenic AVFs that are best approached in open surgery for anatomical reasons. Also, practitioners today still hesitate to treat nongalenic cerebral AVFs with endovascular embolization due to the danger of embolic material migrating into the lungs, cortical veins, or dural venous sinuses because of the lesions’ high flow.²⁷,³⁸ However, the technological progress in interventional neuroradiology made over the past four decades currently supports many different strategies to reduce flow during endovascular treatment and to avoid this risk. Due to such technical innovations, the success rate of interventional neuroradiological treatment has improved dramatically, and it is now the optimal treatment approach for many nongalenic AVFs. On this basis, endovascular embolization is currently established as an important alternative to open surgery for the treatment of nongalenic AVFs.

Disclosure

Dr. Vinuela is a consultant for Boston Scientific, Inc./Target, which manufactures Guglielmi detachable coils.

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