Cerebral AVM: Under diagnosed Reality and Rarity.

Anatomical, Pathological, Clinical and Radiological Perspective.

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Introduction:

A simple headache can represent an ordinary cause or a severe life threatening cause. Many symptoms tend to undergo unnoticed in life and even Great Physicians can miss potential dangerous and silent diseases or causes of such diseases.

A Cerebral AVM may be described as a "ticking biological time bomb", carrying an accumulated risk of spontaneous haemorrhage of more than 2-3% per year with a mortality of 6-10% at the first hemorrhage and 13% at the second hemorrhage. AVM's can be located anywhere in the brain and can produce headaches, seizures, focal neurologic deficits, or intracranial hemorrhage. Intracranial hemorrhage from vascular malformations accounts for 1% of all strokes and 10% of all SAH's. The prevalence of AVM's among the general population is uncertain, but autopsy studies of unselected patients indicate that 4 to 5% harbor some form of vascular malformation, of which only 10 to 15% produce symptoms. Familial cases of AVM's are rare, indicating that the problem reflects sporadic abnormalities in embryologic development.

Cerebral AVMs may form during prenatal stages of a child’s development, either during embryonic or fetal growth. AVMs are congenital lesions composed of a complex tangle of arteries and veins connected by one or more fistulae. The vascular conglomerate is called the nidus. The nidus has no capillary bed, and the feeding arteries drain directly to the draining
veins. The arteries have a deficient muscularis layer. The draining veins often are dilated owing to the high velocity of blood flow through the fistulae. Studies have found a certain number of cases form shortly after birth; however, the condition frequently presents in adults in their 20s or 30s.

Discussion:

AVM’s are composed of tangles of arteries connected directly to veins without intervening capillaries. The resulting vessels are thin walled owing to poorly developed elastic and muscle tissue within the media. The large arteries, which feed the AVM, usually show hypertrophy of the media and thickening of the endothelium. Brain tissue is usually absent from the AVM but when present is nonfunctional.

Cerebral AVMs are commonly misdiagnosed, with most cases found only incidentally through the performance of CT (computed tomography) scans on the brain. Patients complain of regular headaches and seizures before diagnosis. Arteriovenous malformation (AVM) of the brain is one of the important pathologic conditions which cause

- Intracerebral
- Subarachnoid hemorrhage
- Epilepsy
- Chronic cerebral ischemia.

Cerebral AVMs commonly affect distal arterial branches and are often found in the border-zone region shared by the distal anterior, middle, and/or posterior cerebral arteries.
Other neurological complications can develop including **speech and visual difficulty, dizziness, memory deficits, confusion, hallucinations, dementia and difficulty with event planning**. Physical side effects range from loss of coordination, numbness, tingling and spontaneous pain to permanent paralysis. The hemodynamic situation in and around a cerebral AVM is complex and varies from patient to patient as well as in the same patient when cardiovascular parameters change. The clinical presentation of different AVMs is therefore bound to vary.

The AVM has a lower vascular resistance than that of the surrounding normal blood vessels, which explains the sometimes observed "steal" phenomenon.

**Determinants of Blood Flow:**

The number and size of the arterial feeders, their origin, the presence of any collateral flow and the number of draining veins are major determinants of its flow pattern.

**Causes and Associations:**

**No genetic, demographic, or environmental risk factors** for cerebral AVM have been identified clearly.

Families with cerebral AVMs are rare, and such pedigrees have been too small to enable linkage studies. From the few family cases reported, the inheritance appears to be autosomal dominant.

In a small minority of cases, cerebral AVMs are associated with other inherited disorders, such as the **Osler-Weber-Rendu syndrome**, **Sturge-Weber disease**, **neurofibromatosis**, and **von Hippel-Lindau syndrome**. These may also coexist with other vascular disorders, such as **Moyamoya disease**.

Cerebral arteriovenous malformations (AVMs) are considered to be congenital disorders. However, their familial occurrence has so far been described in only 19 families in the literature.
On the basis of clinical observation and a developmental theory of cerebral laterality, Geschwind and Galaburda suggested that cerebral arteriovenous malformations (AVMs) are more common in the left hemispheres of male patients.  

The combination of intracranial aneurysms and these vascular lesions is not rare. Most patients presented with symptoms referable to their AVMs. Treating both lesions in a single operation is the best option. The prognoses for most patients was good.

Hypoxia is considered as a major factor for development of arteriovenous malformations. Hypoxia-inducible factor and vascular endothelial growth factor are expressed more frequently in embolized than in nonembolized cerebral arteriovenous malformations.

**Role of Vascular Endothelial Growth Factor (VEGF):**

Vascular endothelial growth factor (VEGF) has previously been demonstrated to be highly expressed in AVMs by immunohistochemical methods. The study included 17 patients with cerebral AVMs and 40 healthy controls. VEGF plasma concentrations were measured by a specific enzyme immuno-assay. VEGF plasma concentrations were significantly higher in patients with cerebral AVMs compared to a healthy control group.

Vascular endothelial growth factor (VEGF) is a possible candidate for this role, based on its specificity for vascular endothelium and its ability to serve as an endothelial cell mitogen both in vivo and in vitro.

Arteriovenous malformations (AVMs) produce high flow shunts for cerebral blood flow (CBF), which decrease perfusion pressure in surrounding tissue and may lead to ischemia. However, the presence of ischemia has not been confirmed by direct measurement of brain tissue PO2, PCO2, and pH in AVM patients.

Recently, increasing attention has focused on the possible importance of venous outflow disturbance and venous hypertension in the pathogenesis and pathophysiology of AVMs.

**Hemorrhagic arteriovenous malformation (AVM) presentation, increasing age, deep brain location, and exclusive deep venous drainage** appear to be independent predictors for AVM hemorrhage during natural history follow-up. The risk of spontaneous hemorrhage may be low in AVMs without these risk factors. Higher (feeding mean arterial pressure).FMAP is an
important factor in the pathophysiology of hemorrhage from AVMs and not just a consequence of lesion size. ¹¹

**Symptomatology:**

The most frequently observed problems related to an AVM are **headaches and seizures**. These symptoms vary from extremely mild neurological events (e.g. unusual sensations) to uncontrolled grand mal seizures. Moreover, AVMs in certain critical locations may stop the circulation of the cerebrospinal fluid, causing accumulation of the fluid within the skull and giving rise to hydrocephalus.

Symptoms of bleeding within the brain (intracranial hemorrhage) include **loss of consciousness, sudden and severe headache, nausea, vomiting, incontinence, and blurred vision**, amongst others. Minor bleeding can occur with no noticeable symptoms. A **stiff neck** can occur as the result of increased pressure within the skull and irritation of the meninges. Impairments caused by local brain tissue damage on the bleed site are possible, including seizure, one-sided weakness (**hemiparesis**), a **loss of touch sensation on one side of the body and deficits in language processing (aphasia)**. A variety of other symptoms can accompany this type of cerebrovascular accident.

Thirty-eight patients had bleeding caused by the AVM in a follow-up of 1205 patient-years (mean, 3.1 years per patient). In analyses adjusted for multiple AVM characteristics, large AVMs bled more frequently than small lesions. Deep-seated and large AVMs were significantly more prone to hemorrhage during prospective follow-up. ¹²

**Diagnosis:**

Brain AVMs can be diagnosed using a few methods, with the most non-invasive techniques being **CT and MRI scans**. Both scans reveal lesions while CT scans are particularly helpful in showing hemorrhaging. Three dimensional representations of cerebral AVMs can be detected by CT and MRI imaging.

A more intricate process in identifying an AVM of the brain involves **angiography**. A contrast agent, or water-soluble dye, is injected into the brain allowing an x-ray to deliver more precise images that highlight blood vessel structure. This procedure carries the risk of causing a stroke,
but more research has led to vast improvements with angiography thereby reducing stroke potential.

**Treatment:**

Invasive treatment of AVMs may include endovascular embolization, surgical resection, and focal beam radiation, alone or in any combination. The surgical treatment risk has traditionally been estimated by the Spetzler-Martin grade. This grading system assigns 1 point to AVMs smaller than 3 cm in largest diameter, 2 points to AVMs between 3 and 6 cm in largest diameter, and 3 points for AVMs larger than 6 cm. A further point is added if the AVM is located in functionally critical brain (e.g., language, motor, sensory, or visual cortex), and another point if the AVM has a deep venous drainage.

**Microsurgical removal,** which eliminates the risk of bleeding immediately, is preferred for lesions in non-eloquent areas. Radiosurgery is an effective treatment modality for small lesions in eloquent areas, but has a substantial risk of hemorrhage during the latency period. Results of this study suggest that microsurgical removal should be considered for lesions in eloquent areas with high haemorrhage risk, such as prior haemorrhage, medium to large size lesion, and single deep venous drainage. ¹³

**Endovascular embolization** involves guiding a catheter through the arterial pathway into the site of the AVM. A substance is injected into the site reducing the blood flow through the lesion. Blood flow reduction is a proven method in making surgery a safer process for patients.

**Radiosurgery** is another option for patients with localized lesions. Radiosurgery involves targeting the center of the lesion with a radiation beam damaging the blood vessel walls. Over several months following radiation treatment, the vessels begin to degenerate and ultimately close. Clinical trials assessing the safety and efficacy of coil embolization for cerebral aneurysms were based on the use of bare platinum, helical coils. Since then, endovascular operators have been testing and using new materials such as bioactive coils, expandable coils, and complex-shaped coils. Based on the data so far obtained, third and fourth generation coil designs are rapidly emerging. New open- and closed-cell designs allow the navigation and deployment of stents in extremely tortuous vessels. With regards to the Embolisation of vascular malformations, it is possible to safely navigate microcatheters and microwires through very small arteries previously considered not accessible. In addition,
Emboli\onsation materials such as n-butyl cyanoacrylate and ethylene-vinyl alcohol copolymer are now routinely injected to safely reduce or obliterate large and complex arteriovenous malformations and fistulae.\(^\text{14}\)

**Conclusion:**

Taking into account the dangers associated with large Cerebral AVMS, Physicians can sometimes miss the rare causes of simple presentations. Cerebral AVMS have a high accumulated risk of spontaneous haemorrhage and can be located anywhere in the brain and can produce headaches, seizures, focal neurologic deficits, or intracranial hemorrhage. Hence a look out for such a rare cause is warranted.
“Radiographs Demonstrating Cerebral AVM”

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