Pathophysiology and Treatment of Brain AVMs*

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Abstract
Cerebral arteriovenous malformations (AVMs) are a major source of intracerebral hemorrhage in younger adults. First, some basic ideas about AVM anatomy, the influences of pressure, macrovascular flow, perfusion and the "steal effect", and some recent observations in the field of inflammatory markers and genetics are briefly discussed. Then, some clinical aspects in the presentation and the natural course of AVMs are highlighted, with special emphasis on the prediction of hemorrhage. Finally, some problems of the current treatment options are mentioned, and future directions in diagnostics and therapy considered.

Key Words: Arteriovenous malformation · Angioma · Remodeling · Embolization

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Zusammenfassung

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Introduction
Arteriovenous malformations (AVMs) are a major source of parenchymal hemorrhage in younger adults. The predisposition to these malformations is congenital. They are developing over time, may increase in size and show vascular remodeling resulting in pedicle feeder aneurysms, fistulae, and venous stenoses. The underlying pathophysiological principle is “high-flow and low-pressure” in most cases. In this review, we relate some fundamental pathophysiological concepts to current clinical practice and future directions of research.

AVM Anatomy
The basic anatomy of an AVM is the direct communication of arteries to abnormally tortuous and dilated veins which communicate directly within a nidus without interposing capillaries [1]. There are dynamic changes at the arteriovenous junctions: the arterial wall normally resists the arterial pressure, and the veins with their much thinner wall are unable to resist the same pressure resulting in incremental dilatation from arterial pulsation [2]. The vessel wall of several arterial feeders is hypotrophic with a thin muscular layer, contrary to the angiographic appearance of a seemingly hypertrophic artery (Figure 1)

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The arteries feeding the AVM are classified according to their relation to the AVM nidus as circumferential (“en passage”), terminal and penetrating feeding arteries. These arterial feeders differ in size and histological composition, especially in the absence (terminal feeders) and presence (all others) of shunting arterioles. The shunting arterioles in circumferential feeding arteries constrict and reduce flow when the blood pressure is lowered to < 60 mm Hg. The nidus is composed of anomalous venous loops, and is almost always located subcortically with rare exceptions [2]. The flow from the arteries or arterioles within this nidus runs directly into the communicating venules representing the free communication system within the nidus. Communicating venules also connect the nidus and surrounding cerebral veins and may dilate immediately if the systemic blood pressure rises inadvertently [2].

The major draining vein travels in the sulcus and is surrounded by sulcal cortex. The often spiral-formed juxtanidal veins originate from the AVM core, detour around it and also pass arterial blood from the core to the cortical venules. Oxygenated blood circulates through the major draining vein into the cortical veins, giving an appearance of so-called red veins.

The basic concept of a multicompartment AVM originated from surgical experience and segmental embolization [4]. In 1990, Yamada et al. proposed the existence of hemodynamic compartments, each of which has its own feeding arteries and draining veins based on angiography. From surgical experience, multicompartment AVMs (> 3 cm in diameter) have at least two feeding arteries and one or two draining veins in each compartment [2]. Multicompartment AVMs are also found to have blood supply from many small perforating arteries, because they extend deep into the hemisphere. Within the nidus these various connected compartments may be in hemodynamic balance [2, 5] showing no transfer from one compartment to the other in conventional digital subtraction angiography. However, even a large AVM may be filled entirely with dye or contrast agent from one feeding artery [6] which may be explained by intercompartmental venules or small veins.

**Pressure**

Arterial pressure in cortical surface arteries has been reported to be 85–90% of systemic blood pressure in patients without occlusive vascular disease [7, 8]. The direct communication of arteries to veins in AVMs without interposing pressure-lowering capillaries results in a high blood flow through the malformation and a decrease in perfusion pressure and the perfusion in dependent vascular territories [9, 10]. This hypothesis is supported by our data showing the perfusion to be lowest in the presence of the highest macrovascular flow [11]. It has been hypothesized that the observed hemispheric asymmetry in territorial perfusion is a result of arterioarterial redistribution on a macrovascular level. It has been reported that, in over half of brain AVMs, nidal arterial blood pressure is below the lower limit of cerebral autoregulation [9] and that microvascular flow in the perinidal brain increases.

**Figures 1a to 1c.** a) Analog of remodeling on the south coast of England (Seven Sisters, East Sussex, England). These trees are exposed to a steady heavy wind blowing from the English Channel toward the land. The permanent “aerodynamic” stress leads to a remodeling of the direction of the trunk. b) Analogously, in an AVM “hemodynamic” stress leads to remodeling of the vessel with widening of the lumen and the development of flow-dependent aneurysms (arrow). c) After AVM resection from the circulation and the stopping of the high-flow condition the aneurysms shrink (arrow).