Experimental model of arteriovenous malformation in vitro using biological grafts

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Abstract: Introduction: Brain arteriovenous malformations (AVMs) represent a serious health problem all around the world. Experimental models help to better understand the pathophysiology of these lesions. Experiment: We performed an experimental model of AVM using biological grafts, arteries and veins harvested from chicken wings at the elbow joint. We used 14 vessels and we performed 20 end-to-end anastomoses to create a nidus with a single feeding artery and a single draining vein. The system was irrigated with colored solution. The experiment was done according with law in force regarding experimental research activity. Conclusions: Experimental models allow us to understand the hemodynamics and predict the outcome of brain AVMs in humans. This experimental model is a useful tool in understanding the hemodynamic properties of brain AVMs. It is very useful in vascular anastomosis training.

Key words: arteriovenous malformations, biologic grafts, chicken wings, experimental model

Introduction

Vascular malformations of the brain represent a serious health problem.(8;29) Brain arteriovenous malformations (AVMs) are not very frequently encountered, having an incidence of 0.89-1.34 cases/100.000 inhabitants/year (3;4;20) and a prevalence of 0.02-0.2% (1;2;20;31;34). Although they are no common pathology, brain AVMs represent a continuous and prolific field of research (8-10;27-29), because social impact of this disease is high. They become clinically manifest in young and active people, mean age at diagnosis varying from 29 to 33 years.(25;29) Brain AVMs carry high morbidity and mortality. They are the most common cause of spontaneous hemorrhagic stroke in young people.(7;11) Hemorrhagic stroke has devastating consequences, being a major cause of mortality, morbidity and long-term neurological deficits. Thus, after AVMs rupture with intraparenchymatal hemorrhage, mortality reaches 10% and morbidity accounts for 30-50%.(11;14;16) Other clinic forms

specific to brain AVMs are with seizures and neurological deficits.

Brain AVMs are composed by a network of dysplastic vessels (dilated arteries, arterialized veins, interconnected through shunts), from which arterial blood flows from arteries directly into draining veins, without any capillary bed.(11;21;32;35) AVMs have complex hemodynamic effects, impairing normal brain blood flow.

The aim of this article is to make an experimental in vitro model of brain AVM, using biological grafts.

Experiment

We used vessels (arteries and veins) harvested from chicken wings, at the elbow joint. Short chicken wing anatomy is summarized below. Surprisingly, chicken wing anatomy resembles human upper limb anatomy. Bones are represented by humerus, radius, ulna, carpal bones, metacarpals, alula and phalanges. Muscles of the arm are biceps and triceps and of the forearm are radialis longus and ulnaris muscles. At the elbow joint humeral artery bifurcates into radial and ulnar arteries. Radial and ulnar veins join into brachial vein.

We harvested 14 vessels (arteries and veins) from the elbow joint, at the point where they bifurcate. So all vessels were "Y" shaped. After harvesting, vessels were kept in a normal saline solution. We performed 20 end-to-end anastomoses, under operating microscope, using microsurgical instruments, according to the scheme shown in figure 1. Anastomoses were done according to the classical principals of vascular surgery. Two sutures were placed on the lateral sides, joining the two vascular ends together. The posterior wall of the anastomosis was sewed first, using a prolene 11-0 continuous suture, followed by suturing of the anterior wall in the same fashion.

This model mimics an AVM nidus with a single feeding artery and single draining vein. The afferent artery was catheterized using an intravenous cannula and the system was irrigated with colored solution (normal saline and blue ink) in a pulsatile fashion.

The experiment was done according with law in force regarding experimental research activity.

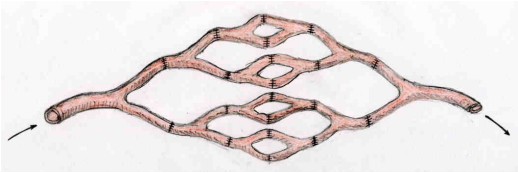


Figure 1 - Schematic view of the experimental model of AVM

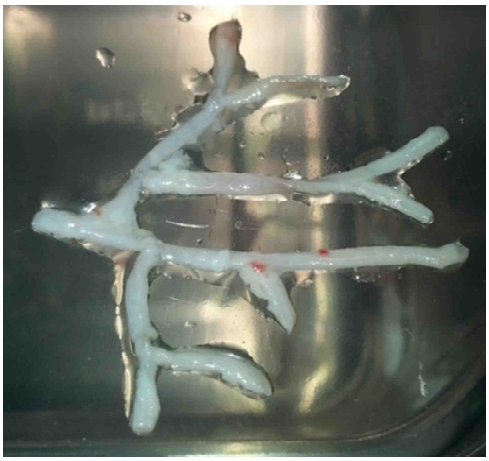


Figure 2 - Part of experimental model of AVM

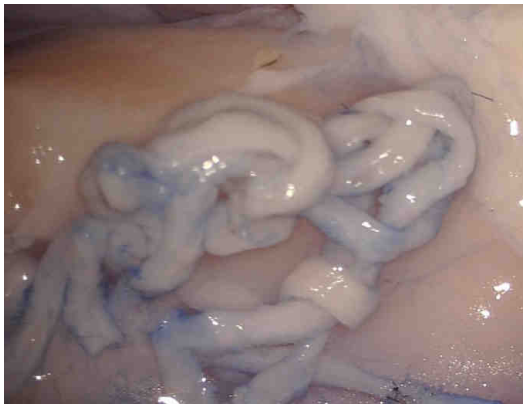
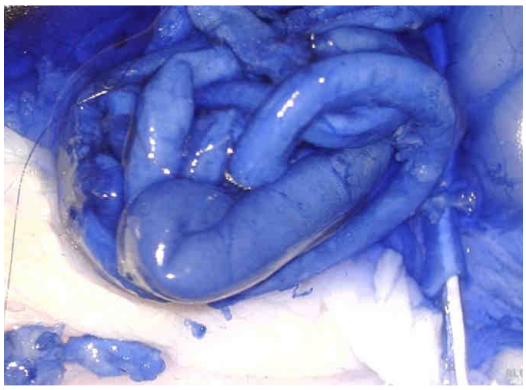


Figure 3 - Final view of the experimental model of AVM



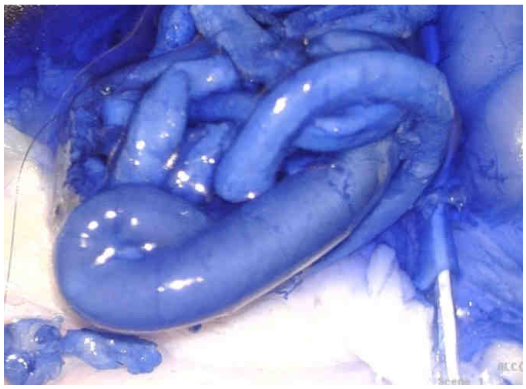


Figure 3 - Experimental model of AVM irrigated with colored solution, by catheterizing the afferent vessel with an intravenous cannule

Disscusions

Over the time, researchers from the field of medicine, tried to build experimental models of brain AVMs.(5;6) Experimental models can be true or virtual. True experimental models can be built in vitro or in vivo. Grafts used to recreate the network of a brain AVM can be synthetic (Dacron or Goretex) or biological.

True in vivo models were done in experimental animals. Massoud et al performed an experimental AVM in swine, using a side-to-side carotid-jugular anastomosis and ipsilateral endovascular occlusion of occipital artery, external carotid artery and muscular branch of the ascending pharyngeal in the pig's neck, with subsequent forming of a rete mirabilis, mimicking a nidus, with feeding artery and draining veins.(22-24)

Qian et al. performed an in vivo experimental AVM model in sheep, making a side-to-side carotid-jugular anastomosis, jugular vein ligation above the arteriovenous fistula and ligation of common carotid artery proximal to the anastomosis.(26)

Schumacher et al. designed an experimental model in dogs, performing a bilateral high-flow carotid to external jugular vein fistula, which was later occluded with a coated stent on one side, whereas the contralateral side remained patent.(30)

Other experimental models in animals were performed in rats. Herman et al. performed an anastomosis between common carotid artery and external jugular vein, accompanied by occlusion of the sagittal sinus and of the vein draining the transverse sinus.(15)

Experimental models were used not only to design an anatomical network of vessels with specific hemodynamic properties, but also to explain consequences secondary to associated AVMs, such as normal perfusion pressure breakthrough.(12)

Animals models proved to be faithful copy of brain AVMs.(33) Animal models of AVMs can be used to apply several therapies, such as radiosurgery ot endovascular embolization.(6)

Also virtual models of brain AVMs were designed for research purposes. Computer and biomathematical models were used to imitate a brain AVM and its consequences.(13;36) Computer and biomathematical experimental models are a theoretical method of investigating AVM. Hademenos et al. constructed an electrical networks based on the biomathematical AVM model, in order to provide an accurate rendering of transnidal and intranidal hemodynamics.(13) Computer models are useful for pathophysiological studies. The advantage of these models is the flexibility, which cannot be found in an intact system.(36) The disadvantage is that they are dependent on the assumptions made by their constructors.(36)

Kerber et al. performed an experimental model of brain AVM using an open pore cellulose sponge and a wax wire, 4.5-6.5 in diameter, simulating single draining vein and one to three wax wires, 2.6 mm in diameter, simulating feeding arteries, attached to the sponge with adhesive elastomer.(18)

Inagawa et al. created an artificial nidus model, using one milliliter syringe, in which they put small beads, 2.5x4.5 mm in size, which was connected through tubes to a active, pulsatile flow circuit.(17)

Human placenta was used as an ex vivo vascular model in research because its vessels resemble brain AVM.(19)

Conclusions

Experimental models allow us to understand the hemodynamics and predict the outcome of brain AVMs in humans. This experimental model is a useful tool in understanding the hemodynamic properties of brain AVMs. It is very useful in vascular anastomosis training.

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