BIOMOLECULAR INSIGHT OF REVASCULARIZATION SURGERY IN CEREBROVASCULAR DISEASE

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Abstract

Moyamoya disease is a progressive occlusive cerebrovascular disease of the intracranial internal carotid arteries or their proximal branches with compensatory development of a fine collateral network at the base of the brain (moyamoya vessels). Revascularization surgery is recognized as useful treatment for moyamoya disease. This treatment is believed to form vascular anastomoses between the extracranial tissue and the brain to supply blood flow to the ischemic tissue. Numerous surgical procedures exist for the treatment of moyamoya disease, including direct anastomosis such as superficial temporal artery (STA)–middle cerebral artery (MCA) anastomosis,[4] indirect anastomosis such as encephaloduroarterio-synangiosis[6] and encephalomyosynangiosis (EMS)[5], and combined direct and indirect anastomosis.[2]

At several months after surgical treatment, the blood supply from the external carotid artery to intracranial vessels (MCA area) was generally confirmed by angiography in any kind of anastomosis. There are various patterns of revascularization depending on the dominancy of the donor arteries, such as STA, middle meningeal artery (MMA), or deep temporal artery. In the case of direct anastomosis, the STA grows larger and more robust than before surgery. In the case of indirect or combined anastomosis, the dominancy of the donor arteries varies in each case. Some cases showed dominant STA compared with the deep temporal artery or MMA. Others showed the same dominancy of the STA and MMA. A question emerges: What is the key factor that determines the dominancy or patency of the donor artery?

To interpret the results of revascularization surgery with profound insight, the histopathologic concept of two types of vessel growth, angiogenesis and arteriogenesis, needs to be understood because these types of vessel growth play a pivotal role activating the growth of compensatory blood vessels that may help to cure the ischemic lesion. Angiogenesis and arteriogenesis are initiated by distinct initial triggers.[1] Angiogenesis is induced by hypoxia under pathologic conditions such as ischemic or damaged tissue and results in new capillaries. Arteriogenesis describes the remodeling of preexisting arterioarteriolar anastomoses induced by physical forces, mostly fluid shear stress.

Recently, we have unveiled the mechanism of revascularization after indirect anastomosis with EMS in an experimental miniature pig model of moyamoya disease.[7] The study disclosed functional revascularization because EMS required two distinct processes of angiogenesis and arteriogenesis. Angiogenesis was the initial step to generate the new vessels in the newly formed connective tissues within 1 week after surgery, which resembles the process of wound healing associated with repair processes. The next step, arteriogenesis, required specific and critical conditions, such as hypoperfusion of the cortex, which involves net forward flow from the donor artery to the recipient artery of the pial artery owing to the pressure gradient between the interconnecting arterial networks.

Based on our basic research providing the profound insight with the concept of angiogenesis and arteriogenesis, we have analyzed our own results of patients with moyamoya disease who were treated by revascularization surgery.[3] Our strategy was to construct wide-range revascularization for the frontal lobe. Combined direct (STA-MCA) and indirect (EMS) anastomosis was applied in patients older than 10 years. Indirect surgery

(encephaloduroarteriosynangiosis plus EMS) was applied in patients younger than 10 years. Twenty-three patients (29 hemispheres) with moyamoya disease who had angiography performed after surgical treatment were enrolled for the investigation.

The eventual patterns of revascularization were categorized into four classes based on the dominancy of donor arteries. In cases of combined anastomosis, there were four hemispheres with dominant STA compared with EMS (STA - EMS), seven hemispheres with dominant EMS compared with STA (EMS - STA), five hemispheres with nearly the same dominancy of STA and EMS (STA - EMS), and 1 hemisphere without any anastomosis. In cases of indirect anastomosis, there were no hemispheres with dominant STA compared with EMS (STA-EMS), five hemispheres with dominant EMS compared with STA (EMS-STA), and seven hemispheres with the same dominancy (STA-EMS).

Because combined anastomosis includes STA-MCA anastomosis, the surgical procedure constructs the condition of arteriogenesis. In most cases of moyamoya disease, cerebral cortex is exposed to the hypoperfusion. The pressure gradient from the donor to recipient artery must be significant. Arteriogenesis satisfactorily developed functional revascularization. In cases in which blood flow was not sufficiently supplied by the STA-MCA anastomosis in some areas of cortex, EMS covered the blood supply for these areas. This is why in cases of direct anastomosis, there are various patterns of donor artery, the development of which depends on the degree of local hypoperfusion.

Indirect anastomosis requires at least both processes of angiogenesis and arteriogenesis, which means it takes several weeks for functional revascularization. First, vascular beds (angiogenesis) emerge in the fibrous coat developing between the transplanted muscle and the arachnoid membrane, which consists mainly of a matrix of collagen fiber and fibroblasts enriched with high proliferation of macrophages. The second process is the development of arteriogenesis. Because arteriogenesis needs the pressure gradient, the extended area of revascularization depends on the degree of the hypoperfusion of the cortex.

Our clinical results showed that EMS provides a compensatory blood supply via revascularization in the case of direct bypass and in indirect bypass surgery. EMS is a reasonable surgical treatment for moyamoya disease because flexible revascularization is developed adequately in accordance with the requirement of blood supply in the ischemic lesion.

Revascularization surgery for moyamoya disease improves the cerebral blood flow. As Wu et al. mentioned, however, little is known about the dynamic changes of blood flow during the acute phase after surgical treatment for moyamoya disease. One conceivable reason is the lack of suitable method with enough sensitivity to detect the small change of the flow with less invasiveness. Wu et al. introduced the unique method of using color Doppler with high sensitivity and reproducibility to assess the dynamic change after direct anastomosis to predict the patency of anastomosis in angiography. Wu et al. also referred to some notable findings in this study. The hemodynamic changes of STA after surgery mainly occurred at an early period after operation instead of the little change at 3 months' follow-up. They also mentioned that the increase of blood flow in STA may be because of the low resistance of the intracranial vascular bed. This finding is consistent with what we mentioned previously regarding the suitable conditions for arteriogenesis. For the construction of functional arteriogenesis, the pressure gradient from the donor to recipient artery, which generates the shear stress, is essential. Wu et al. have recognized the critical situation from the hemodynamic study of STA by using color Doppler assessment. This method seems to have several advantages, such as easy, safe, economical, and reproducible examination. This method could be used widely for assessment after STAMCA anastomosis and possibly become a routine examination in the near future.

References

1. Heil M, Eitenmuller I, Schmitz-Rixen T, Schaper W: Arteriogenesis versus angiogenesis: similarities and differences. J Cell Mol Med 10:45-55, 2006.
2. Houkin K, Kamiyama H, Takahashi A, Kuroda S, Abe H: Combined revascularization surgery for childhood moyamoya disease: STA-MCA and encephaloduro-arterio-myo-synangiosis. Childs Nerv Syst 13:24-29, 1997.
3. Imai H, Nakamura M, Kubota C, Puentes S, Faried A, Yoshimoto Y, Saito N: The insight of revascularization mechanism based on angiogenesis and arteriogenesis from the experimental and clinical works in moyamoya disease. J Cereb Blood Flow Metab 29:S377-S378, 2009.
4. Karasawa J, Kikuchi H, Furuse S, Kawamura J, Sakaki T: Treatment of moyamoya disease with STA-MCA anastomosis. J Neurosurg 49:679-688, 1978.
5. Karasawa J, Kikuchi H, Furuse S, Sakaki T, Yoshida Y: A surgical treatment of "moyamoya" disease "encephalo-myo synangiosis." Neurol Med Chir (Tokyo) 17:29-37, 1977.
6. Matsushima Y, Takasato Y, Fukumoto T, Tsuruoka S, Yamaguchi T, Inaba Y: A case of internal carotid artery occlusion successfully treated by encephaloduro-arterio-synangiosis. Childs Nerv Syst 1:363-366, 1985.
7. Nakamura M, Imai H, Konno K, Kubota C, Seki K, Puentes S, Faried A, Yokoo H, Hata H, Yoshimoto Y, Saito N: Experimental investigation of encephalomyo-synangiosis using gyrencephalic brain of the miniature pig: histopathological evaluation of dynamic reconstruction of vessels for functional anastomosis. J Neurosurg Pediatr 3:488-495, 2009.