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Cerebral Arteriogenesis and Angiogenesis: Distinct Angioarchitecture of Innate and EDAS Collaterals in Intracranial Arterial Steno-Occlusive Disease

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Introduction

Patients with intracranial arterial steno-occlusive disease (ICASD) associated with atherosclerosis and moyamoya form various degrees of spontaneous collateralization. However, those innate collaterals tend to fail over time contributing to symptom progression. Indirect revascularization via encephaloduroarteriosynangiosis (EDAS) establishes collateral flow through new vessels formed from external carotid branches in both moyamoya disease (MMD) and non-moyamoya (NM) ICASD. We hypothesize that the EDAS neovascularization differs in terms of angioarchitecture when compared to spontaneously formed collaterals in ICASD.

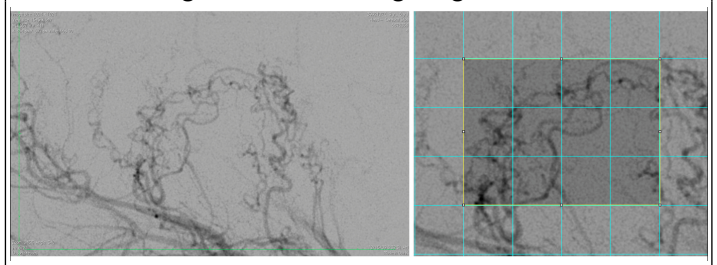
Methods

We conducted a prospective cohort observational study to analyze with advanced imaging techniques the pre and post-operative digital subtraction angiograms (DSA) of patients enrolled in a prospective trial of EDAS surgery.
Images were post-processed for homogeneity. We performed quantitative evaluations using ImageJ software (http://imagej.nih.gov/ij).
The angioarchitectural differences between innate and post-EDAS collaterals were established by comparing their branching angioscore (BA) and artery tortuosity index (ATI). A senior neuroradiologist identified in each patient's DSA images the areas most representative of the collateral vascular morphology. Four independent observers evaluated the number of quantitative endpoints in each square of the grid. The BA is defined as the summation of the total number of branching points in each square divided by the total number of squares as shown in figure 1. The ATI is calculated by comparing the actual distance of a vessel trajectory over the straight line distance between the entry and exit point of each vessel in a square of the grid as shown in figure 2.

Results

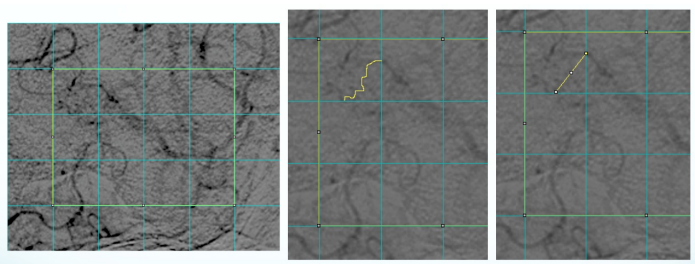
Images from 26 patients, ages 4 to 84 (mean: 37 SD+/-19.5) were evaluated. Patients included 13 MMD and 13 NM-ICASD.

Figure 1. Branching Angioscore



Branching Angioscore is calculated as the summation of total number of branching points in each square /total number of squares

Figure 2. Artery Tortuosity Index



Artery Tortuosity Index = [actual distance/straight line distance-1] x 100.

The images used for evaluation of the EDAS collaterals were obtained in average after 14 months from the surgery. The analysis of the BA and ATI demonstrated that the post-EDAS collaterals had significantly higher BA than innate collaterals. (Post-EDAS BA= 9.8, Innate collaterals = 5.5 [p<0.001]). Post-EDAS collaterals also demonstrated a lower ATI than innate collaterals (Post-EDAS ATI = 110. Innate collaterals = 167 [p<0.001]). Analyses of the differences between BA and ATI for patients with MMD and NM-MMD demonstrated the same response after surgery for each group with higher BA for post-EDAS collaterals and lower ATI for innate collaterals (MMD: BA: 9.6 vs. 5.2, and ATI 107.7 vs.176.5, NM-ICASD: BA: 9.9 vs. 5.8, and ATI: 153.7 vs.115.4 p=0.01). Type of ICASD, age, and time after angiography did not affect the indexes.

Discussion

The structural features of vascular collaterals can be of importance to determine the durability of the flow provided by those vessels and the risk of hemorrhage associated with vessel fragility. The differences between collaterals formed spontaneously in ICASD and those formed as response to revascularizations with EDAS have not been systematically evaluated before this study. The consequences of these differences have a significant impact in patient care and prognosis. For example, aneurysmal dilatations have been described in the lenticulostriate collaterals that form spontaneously in patients with MMD, which have been associated with the risk of hemorrhage in adult patients. The study presented here demonstrates that the collaterals formed after EDAS differ in angioarchitecture to innate collaterals in MMD and NM-ICASD. The patterns or branching and tortuosity that EDAS collaterals develop resemble the normal vascular tree and differ from the abnormal structure of innate collaterals. The morphological differences observed are consistent with two distinct mechanisms of vessel formation: innate collaterals formed by arteriogenesis display high tortuosity and low branching as expected by a shear stress process acting on pre-existing conduits. Conversely, post-EDAS collaterals have higher branching and lower tortuosity as expected in a process of angiogenesis in which collaterals form through sprouting and splitting from the donor vessels.

Conclusions

Collaterals formed after EDAS differ in angioarchitecture to innate collaterals in MMD and NM-ICASD. The morphology of post EDAS collaterals resemble mature normal vascular patterns, consistent with a mechanism of angiogenesis characterized by higher branching and lower tortuosity indexes.