Endovascular treatment of aneurysms with a tissue engineered fibrin biopolymer in a rabbit elastase aneurysm model

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Existing treatments for intracranial aneurysms include surgical clipping and endovascular coil embolization. However, coiling is associated with a relatively high rate of recanalization, thought to be due to lack of endothelialization across the aneurysm ostium. We attempt a tissue engineering approach. Endothelial progenitor cells (EPCs) are seeded within bioabsorbable fibrin matrix and delivered endovascularly into the aneurysm. The goal is to occlude blood flow into the aneurysm and promote endothelialization across the ostium.
Model aneurysms were created in New Zealand White Rabbits using the elastase aneurysm model. Pancreatic elastase was infused into a trapped segment of the right common carotid artery at its bifurcation from the brachiocephalic artery. The arterial segment was then ligated distally and flow restored proximally. At aneurysm creation, EPCs were isolated from the mononuclear fraction of peripheral blood and cultured in vitro for 10 days. Rabbits were untreated, or treated endovascularly via right femoral artery catheterization with either fibrin matrix alone or fibrin plus autologous EPCs. Degree of aneurysm occlusion was determined by conventional and computed tomography angiography. Rabbits were sacrificed up to 18 weeks post-treatment. Aneurysms were resected and evaluated by histology for recanalization. Extent of endothelial growth at the aneurysm neck was evaluated by expression of Platelet/Endothelial Cell Adhesion Molecule-1 (PECAM-1), an endothelial cell marker.

Aneurysms left untreated remained patent throughout the study period. Aneurysms treated with fibrin alone recanalized within 4 weeks post-treatment. Histology reveals few PECAM-1 positive cells at the aneurysm neck. Aneurysms treated with fibrin and EPCs remained occluded throughout the 14-week follow-up period. Histology demonstrated formation of a PECAM-1 positive cell layer across the aneurysm ostium.

Fibrin biopolymer can be delivered endovascularly to an experimentally created aneurysm and the EPC-seeded fibrin construct can induce formation of a neointima across the ostium. A tissue engineering approach utilizing autologous endothelial progenitor cells addresses the lack of endothelialization that limits the long-term success of coil embolization. Future experiments will evaluate other biopolymers for ease of endovascular delivery and suitability as a matrix for endothelial growth.