Host Cell Infiltration to Implanted Vascular Grafts Made of Collagen Fibers in Porcine Model

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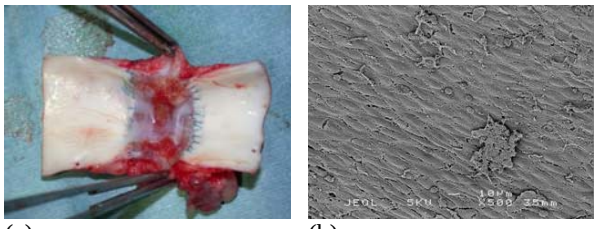
Statement of Purpose: The artificial synthetic vascular grafts have been clinically established for large diameter vessels but not for small diameter less than 4 mm because of thrombosis. The allografts or homografts which are donated from the cadavers are useful especially in the infected area, however the supply is limited. The regenerative vascular grafts which may be replaced by the host tissue after the implantation may have growth potential and be applicable to the pediatric patients. Prof. Shin'oka (Tokyo Women's Medical Univ.) has already applied PGCL vein graft (pulmonary artery) to about 50 pediatric patients and reported good clinical results. However, the biodegradable graft may not be applicable to the artery because of its rapture due to biodegradation. We are developing vascular grafts made of collagen fibers. The collagen grafts may be digested by infiltrated cells and show a different degradation profile from that of the biodegradable materials which are hydrolyzed even out of the living body. In this presentation, a regenerative profile of our collagen graft was studied in a porcine model.

Methods: Porcine skin collagen solution was extruded in ethanol to form collagen fibers. They were then collected and pressed to have non-woven fabrics sheets. The obtained collagen sheets were rolled and immersed in collagen solution followed by crosslinking in a vacuum oven. The inner diameter and length of the grafts were about 7 mm and about 2.5 cm, respectively. The collagen vascular grafts were implanted at descending aorta of the 6 Clawn miniature pigs (Japan Farm Co., Ltd.) through left thoracotomy in the surgery carried out with single clamp technique. They were then explanted at 4 or 8 weeks after the implantation and examined histologically and immunohistologically. All animals were carefully reared in compliance with the Guide for the Care and Use of Laboratory Animals published by the National Institute of Health (NIH publication No.85-23, revised in 1985).

Results / Discussion

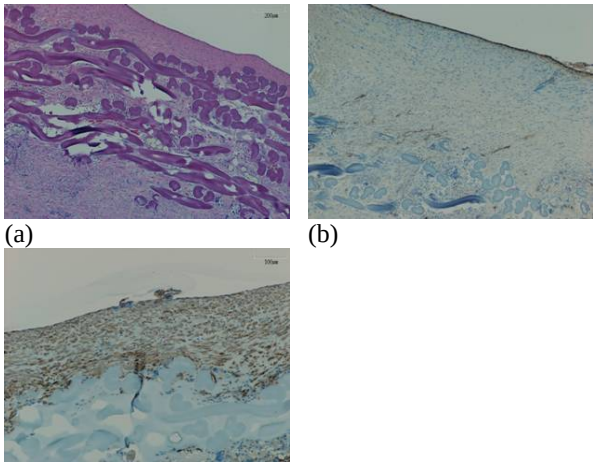
The treated animals survived after the implantation in all cases. The explanted grafts showed no macroscopical abnormality and no dilatation and aneurysmal changes including their anastomosis (Fig.1a) at 4 and 8 weeks after the implantation. The inner surfaces were smooth and had no thrombus formation (Fig. 1b). Cell infiltration of smooth muscle cellls and fibroblasts was identified at 4 weeks, and intimal thickening was observed at 8 weeks after the implantation (Fig. 2a,2c). The luminal surfaces of the aorta were partly covered with endothelial cells (Fig.2b). There was no calcification detected in the explanted tissues. However, stenosis was observed in the middle region of the graft due to the intimal thickning by the smooth muscle cells in the region at 8 weeks.

Conclusions: The novel regenerative collagen graft may be useful in the aortic system. The graft was easily infiltrated by the host cells and may be substituted by the host collagen and elastin. After the completion of the host tissue substitution, the graft may have growth potential and be applied to the pediatric patients. We are now investigating the mechanism of intimal thickning of the grafts.



(a) (b)

Fig.1 (a) The explanted vascular graft and (b) the SEM photograph of its inner surface near the anastomosis at 8 weeks after the implantation.



(a) (b)

(c)

Fig.1 (a) HE, (b) anti-vWF and (c) anti-aSMA stainings of the explanted vascular graft at 8 weeks after the implantation.

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