Constructive Remodeling of CorMatrix Extracellular Matrix After Aortic Root Repair in a 90-Year-Old Woman
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An acellular, noncrosslinked, extracellular-matrix bioscaffold patch was used for aortic root reconstruction after aortic valve replacement in a 90-year-old woman. After her death 3 years later, histologic examination showed constructive remodeling and host-tissue regeneration at the site of the extracellular matrix bioscaffold patch.


The clinical use of extracellular matrix (ECM), which is derived from porcine small-intestinal submucosa, for the repair of cardiac tissues is based on preclinical evidence of biological integration and constructive tissue remodeling after implantation [1]. However, specific clinical evidence of remodeling potential remains scarce. Moreover, concern exists regarding the ability of ECM to undergo constructive remodeling when it is implanted in elderly patients. This case describes histologic analysis of ECM 3 years after its use as a patch for aortic root repair during aortic valve replacement.

A 90-year-old woman with a previously healthy and active lifestyle presented with a 4-month history of progressive dyspnea. Echocardiography and cardiac catheterization confirmed critical aortic valve stenosis (peak gradient = 116 mm Hg; mean gradient = 76 mm Hg; calculated valve area = 0.6 cm²). After a discussion of risks, the patient consented to bioprosthetic valve replacement.

In January 2010, the patient underwent a median sternotomy, cardiopulmonary bypass, and cardioplegic arrest for an aortic valve replacement. An aortotomy was performed above the sinotubular junction and extended proximally into the noncoronary sinus. Extensive decalcification of the aortic wall was required at the sinotubular junction. Although a 19-mm tissue valve was appropriate for the patient’s small size and advanced age, her small aortic root and extensive mitral valve calcification precluded a Manouguian procedure to enlarge the aortic annulus. A decision was made to ameliorate the technical difficulty of the procedure by enlarging the proximal ascending aorta with an ECM bioscaffold patch beginning at the level of the annulus. The aortic valve was removed, the annulus was debrided, and a 19-mm Perimount Magna Ease aortic valve (Edwards Lifesciences Corp, Irvine, CA) was seated over Teflon felt with sutures pledgeted on the ventricular side. The ascending aorta, which had been incised down to the annulus, was patched with a teardrop-shaped piece of CorMatrix ECM (CorMatrix Cardiovascular Inc, Roswell, GA). Single-layer, 5-0 polypropylene sutures were placed around the annulus, with the incorporation of some soft tissue below the annulus to help bolster the repair. Double-layered, running 5-0 polypropylene sutures were used to close the remainder of the aortotomy. Postbypass transesophageal echocardiography demonstrated excellent prosthetic valve function with no periprosthetic leak and preserved left ventricular function.

The patient recovered without complications and resumed normal activities. She died 34 months later at age 93, of cardiac arrest secondary to myelodysplastic syndrome. According to her wishes and with family consent, the ascending aorta and aortic valve were explanted en bloc and submitted to an independent pathologist for evaluation.

Paraffin-embedded sections were stained with hematoxylin and eosin, Movat's pentachrome (fine architectural analysis), and von Kossa (calcification). Immunohistochemistry was performed to detect smooth muscle actin (SMA) for connective vascular-wall differentiation, c-kit,
von Willebrand factor (endothelial cells and neovascularization), telomerase (cell proliferation), and CD34 (dendritic cells, endothelial cells, and hematopoietic progenitors).

Gross examination of the proximal ascending aorta showed little difference between the patched area and native aortic tissue (Fig 1). Histology of the native aorta extending to the healed aortotomy and polypropylene sutures was unremarkable (Fig 2). The ECM bioscaffold patch appeared to be viable and vascularized, with advanced biointegration and excellent biocompatibility (Fig 3). Both the patch and the distal segment of native aorta were covered by a mature, stable, SMA-positive fibromuscular neointima (Fig 3). Neovascularization was present along the adventitial aspect of the patch and polyester ring (Fig 3). Von Willebrand factor staining did not show conclusive evidence of neovascularization within the ECM bioscaffold patch. Erosion of the luminal surface of the patch during handling precluded definitive confirmation of endothelial coverage, but the surface tissue features were consistent with healed and fully endothelialized neointima.

Evidence of inflammatory response was limited to minor infiltration of macrophages and lymphocytes along the adventitial interface between the ECM bioscaffold...
patch and native aortic tissue (Fig 3E). Calcification was restricted to the margins of the patch-aorta anastomosis, where there was hyalinization and limited viability caused by suture entrapment. There were no c-kit-positive cells within the ECM bioscaffold patch, and c-kit and telomerase immunostaining were observed only occasionally along the edge (not shown). CD34 staining was ubiquitous in the perivascular connective tissue and absent from both the patch and the native aorta (not shown).

Comment

This case provided a rare opportunity not only to examine an ECM bioscaffold patch 3 years after clinical implantation but to do so in an elderly patient. Gross and microscopic evidence of tissue integration and recellularization was suggestive of constructive vascular remodeling consistent with preclinical observations [2, 3].

Common materials used for aortoplasty and other vascular reconstruction include polyethylene terephthalate (Dacron), expanded polytetrafluoroethylene (Gore-Tex), polytetrafluoroethylene (Teflon), polyurethane, and crosslinked bovine pericardium. These synthetic and biosynthetic materials induce an inflammatory foreign-body reaction and do not biodegrade or support extensive endothelialization in humans, although limited endothelialization has occasionally been noted at the anastomotic junction [4–6].

In contrast, the observations made in this patient support the hypothesis that the ECM material is sufficient to support tissue regeneration by supplying a dynamic bioscaffold and biochemical microenvironment that direct cellular recruitment, differentiation, and matrix remodeling [1]. This raises several interesting questions. Of central relevance to the field of regenerative medicine is the nature and origin of the cells that repopulated the ECM bioscaffold. Any attempt to determine the populating cell type 3 years after implantation would be speculative at best, but possible sources include cardiac stem cells (SC), circulating hematopoietic SC, mesenchymal SC, or some other pluripotent cell type [7]. In any case, it is intriguing that the apparent tissue remodeling of the ECM bioscaffold occurred in a patient of such advanced age, because the resident stem cell population in elderly persons would be expected to be diminished or senescent [7].

In conclusion, the ECM bioscaffold patch provided durable structural support for aortic root reconstruction after aortic valve implantation for approximately 3 years. It is a suitable material for surgical repair of cardiac structures and may support constructive tissue remodeling, even in patients of advanced age.

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