MORPHOLOGY AND PATHOMORPHOLOGY

Tissue Reaction to a Titanium-Nickelide Mesh Implant after Plasty of Postresection Defects of Anatomic Structures of the Chest

E. B. Topolnitskiy, G. Ts. Dambaev, V. N. Hodorenko*, T. I. Fomina, N. A. Shefer, and V. E. Gunther***

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 153, No. 3, pp. 366-370, March, 2012
Original article submitted January 11, 2011

We studied morphological features of the regenerate formed after postresection defect plasty of the pericardium, diaphragm, and thorax with a mesh implant made of nanostructural titanium-nickelide threads. The newly formed tissue grew through the implant with the formation of an integrated tissue regenerate ensuring anatomic and physiological restoration of this area.

Key Words: *repair of postresection defects; nanotructural thread; titanium-nickelide*

Teflon, polycaproamide, polypropylene, mersilene, lavsan, and polytetrafluoroethylene meshes and tissues are now widely used for repair of postresection defects of various anatomic structures of the thorax (pericardium, diaphragm, chest wall) [1,3,4,6,7,9,10]. However, low biocompatibility of these materials reduces their efficiency and limits their application. After ingrowth and maturation of the connective tissue, they become rigid; their plasticization and changes in size disturb function of the heart, excursions of the diaphragm and chest wall, and respiration biomechanics. Moreover, synthetic materials are liable to infection and in some cases promote persistence of lingering exudative pericarditis and pleurisy, while in case of purulent postoperative complications they maintain inflammation and complicate sanation of the suppurative inflammation focus [5,8].

Department of Hospital Surgery, Siberian State Medical University; *Research Institute of Medical Shape-Memory Materials and Implants, Tomsk State University; **Institute of Pharmacology, Siberian Division of Russian Academy of Medical Sciences, Tomsk, Rossia. ***Address for correspondence:*** e_topolnitskiy@mail.ru. E. B. Topol'nitskiy

Creation of a new class of titanium-nickelide mesh explants possessing well-known biochemical and biomechanical compatibility and their active introduction into clinical practice [2] opened the prospects of development of new reconstruction techniques for extensive defects of anatomical structures of the chest. This dictates the need of studying the peculiarities of integration of mesh implants made of superelastic titanium-nickelide thread with the adjacent tissues after postresection plasty of pericardium, diaphragm, and chest defects.

MATERIALS AND METHODS

Experiments were carried out on mongrel male and female dogs (n=30) weighing 10-16 kg. The experiments were performed with strict adherence to the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (Strasburg, 1986). All manipulations and sacrifice was performed under general anesthesia. The study was approved by Ethic Committee of Siberian State Medical University. The animals were obtained from and the

0007-4888/12/1533-0385 © 2012 Springer Science+Business Media, Inc.

surgeries were performed at Central Research Laboratory of Siberian State Medical University. We used mesh titanium-nickelide implants created and manufactured at the Research Institute of Medical Shape-Memory Materials and Implants.

Preoperative and postoperative periods and anesthesia were similar in all animals. Postresection defects of the pericardium, diaphragm, or chest wall were modeled under general anesthesia with jet ventilation and when repaired with titanium-nickelide mesh implants. The animals were divided into 3 groups according to the localization of the defect. Group 1 animals (n=10) underwent combined pneumonectomy with extensive resection and plasty of the pericardium; in group 2 (n=10), diaphragm resection and plasty were performed; in group 3 dogs (n=10), fenestrated resection and plasty of the chest wall were made. The implant for postresection defect plasty represents a fine-profile tissue (120-240 μ mesh cells) manufactured from 60-μ superelastic titanium-nickelide thread by the textile technology. The thread is manufactured from a composite material consisting of a nanostructural monolithic titanium-nickelide core and a porous surface titanium oxide layer (5-7 μ). Monolith titanium-nickelide core is responsible for elastic properties, while porous surface ensures high adaptation properties of the thread in body tissues. Fine-meshed structure and porous surface of the composite thread determine capillary properties of the implant: it can be soaked in antibiotic solutions and then applied to infected wound surface [2].

The animals were sacrificed on days 7, 14, and 30 and after 3 and 6 months of the experiment. The implant with adjacent tissue regenerate was examined under a QUANTA 200-3D scanning electron microscope in medium mode; the samples were cut immediately before examination and were not dried. The preparations were fixed in neutral formalin. After fixation, the implant was precisely removed and tissue regenerate and adjacent tissues were examined by histological methods. The sections (5-7 μ) were stained with hematoxylin and eosin and after van Gieson.

RESULTS

During repair of postresection defects of different chest structures the thread pores and implant cells were rapidly filled with tissue fluid due to wettability and capillary properties of the implant material. Tissue fluid wetted the implant structure and due to surface tension formed a film, thus creating a barrier separating the pericardial and pleural cavities, to a certain extent separating the peritoneal cavity from the pleural one, and preventing air leakage from the pleural cavity at the site of resection. Elastic properties of involved chest structures and titanium-nickelide mesh are similar, therefore stretch deformation of the tissue–implant complex is concordant. Peculiarities of implant fixation allowed uniform load distribution along the contacting surface and secure implant fixation to the defect edge. In none cases implant migration and postoperative complications were noted.

Morphological examination on day 7 after surgery revealed accumulation of granulocytes and agranulocytes, minor edema, and hemorrhagic foci with signs of organization at the site of implant contact with the pericardium, diaphragm, or chest muscles. These changes were considered as signs of aseptic inflammation induced by surgery. At the outer and inner sides of the implant, granulation tissue enriched with cells (primarily macrophages, lymphocytes, neutrophils, and fibroblasts), blood capillaries, and collagen fibers was formed. In group 1, the epicardium had usual structure without inflammatory infiltration. In groups 2 and 3, histological examination of organs involved in adhesion process revealed no structural disorders. In group 2, changes were observed only in the omental adipose tissue fixed to the implant, where plethoric blood vessels, fibroblasts, and fine collagen fibers were seen. In distant sites of the greater omentum, no considerable changes were seen at this and later terms. In group 3, initial signs of regeneration were noted at the level of residual ribs in the form of granulation tissue formation in the rib bed and initial osteoblastic proliferation of the periost.

On day 14, the forming tissue regenerate was presented by loose connective tissue with moderate content of fibroblasts and fibroblast-like cells and collagen fibers with a tendency to perpendicular structure. In groups 2 and 3, organization foci with moderate infiltration replaced hemorrhagic foci in the diaphragm and chest wall muscle fibers. Muscle bundles located at a distance from the area of interest had usual structure. In group 2, plethoric vessels and numerous fibroblasts and fibrous fibers were found in the adipose tissue. Small foci of adipose tissue degeneration and edema surrounding the fibrous tissue were also noted. In some fields of view, signs of fibrosis were seen in the adipose tissue of the greater omentum fixed to the implant. In group 3, fibrous tissue of different degree of maturity was found at the ends of resected ribs, solitary newly formed young osseous trabeculae were seen in the bone tissue.

On day 30, the structure of tissue regenerate around the defect along the implant surface differed from that at the previous term only by the degree of granulation tissue maturity; collagen fibers were arranged along titanium-nickelide threads and formed bundles. In turn, connective-tissue bundles were primarily arranged perpendicular to each other, thus forming a peculiar reticular structure. In adjacent muscles and internal organs, no inflammatory changes were detected. In group 1, active growth of the connective tissue enriched with fibroblasts, capillaries, and newly formed vessels was observed at the site of contact between the implant surface and pericardium. In the pericardium, the inflammatory reaction to the implant was moderate and local and did not induce adhesive pericarditis. The epicardium had usual structure without inflammatory infiltration. In group 3, fibrous tissue was found at the ends of resected ribs, newly formed osseous trabeculae were seen in the bone tissue. At later terms, organ-specific tissue differentiation in the newly formed regenerate occurred. At later terms (6 months), the morphological picture of the regenerate on the implant surface only little changed (Fig. 1, *a, c*). In group 1 animals, the inner layer of the regenerate was completely lined with single-layer epithelium (Fig. 1, *b*). In group 3, osseofibrous callus with cartilaginous tissue fragments was formed at the ends of distal and proximal rib residues.

Scanning electron microscopy showed that connective tissue formation started from the thread surface at the site of its knots, while filling of the implant with tissue regenerate progressed from the peripheral to the central zones of mesh cells (Fig. 2, *a*). The newly formed tissue around the defect and on the implant surface had fibrillary structure (Fig. 2, *b*). Collagen fibers densely wrapped the titanium-nickelide threads and formed peculiar plexuses resembling "country fence" or "vine", thus strengthening and sealing the contacts. The tissue regenerate replacing the pericardial defect had a wavy inner surface reproducing the implant relief (Fig. 2, *c*). We hypothesized that epithelium migrates from the pericardium defect after filling of the mesh structure of the implant with the connective tissue. By the 6th month after surgery, the strength of implant contact with chest wall tissue in group 3 considerably increased. At the level of rib residues, a fixing plate is formed from fibroosseous and osteochondral tissues originating from periosteum or perichondrium remnants. It was found that the osteochondral tissue of the connective tissue regenerate is closely adjacent and partially covers the implant surface, while peculiar coalescence in these sites via interweaving and ingrowth of connective tissue bundles through the mesh structure of the implant ensures junction stability and strength.

Morphological examination of the operated area in all animals attested to the formation of structurally similar tissue regenerate replacing the defect; no appreciable changes in adjacent organs disturbing the function of the organ were noted. The implant was fixed to the muscular part of the diaphragm and chest wall muscles via a dense, but fine connective tissue regenerate with low cell content and typical orientation of the connective tissue bundles along titanium-nickelide threads; along the free edge of the implant, the regenerate formed a cuff (Fig. 3). These findings attests to similar pattern of integration of the superelastic titanium-nickelide implant are integrated in postresection defects of various anatomic struc-

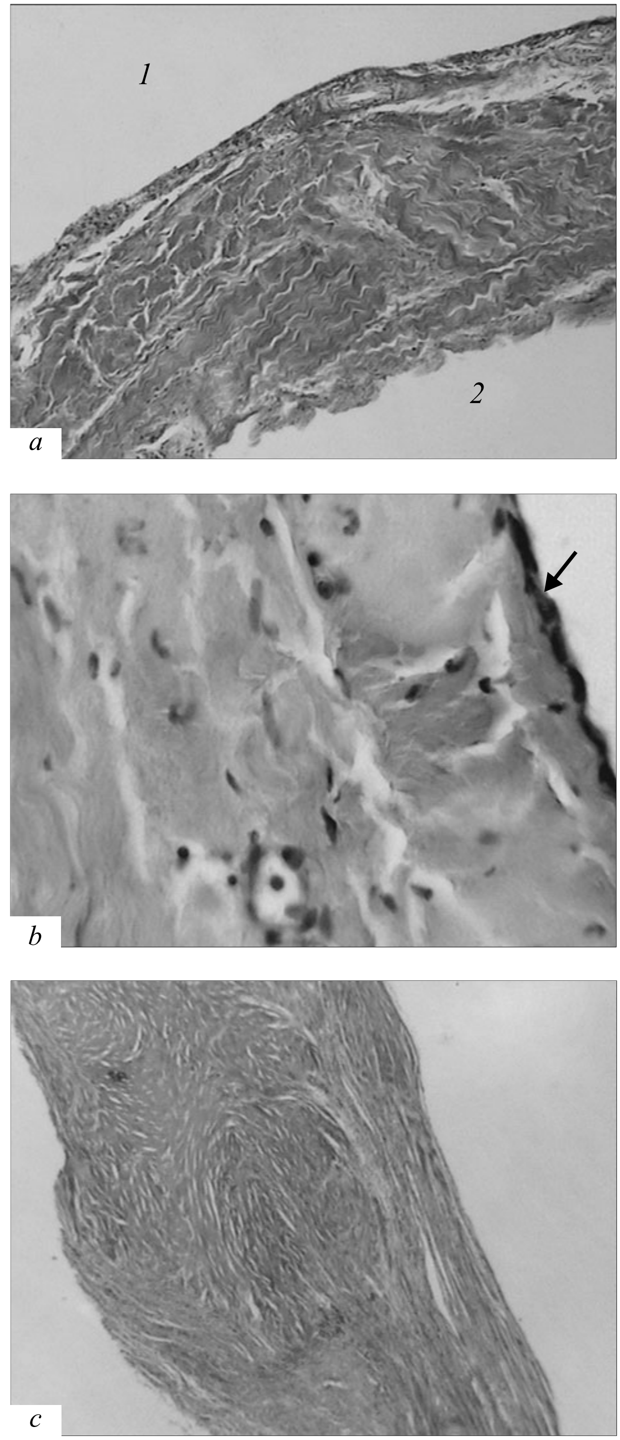

Fig. 1. Tissue regenerate on the implant surface 3 months after surgery. *a*: after pericardium plasty. Collagen fiber layer. *1*) pericardial cavity; *2*) implant. van Gieson staining, ×80. *b*: single-layer epithelium on the surface of the connective tissue regenerate (arrow). Hematoxylin and eosin staining, ×600. *c*: after diaphragm plasty. van Gieson staining, ×80.

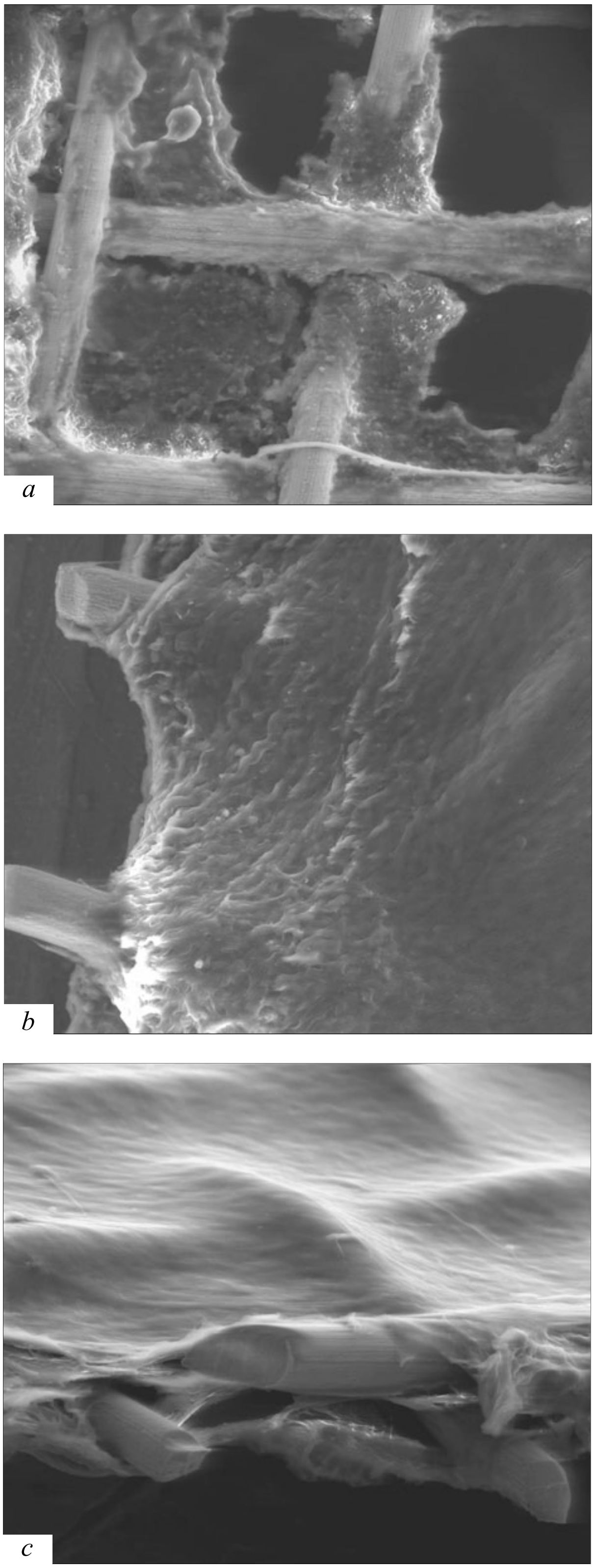

Fig. 2. Microstructure of tissue regenerate after pericardium plasty. Scanning electron microscopy. *a*: day 7 after surgery: formed tissue on the thread surface and in twisting knots, ×400. *b*: day 30 after surgery: collagen fibers and bundles closely wrap titanium-nickelide thread, ×500. *c*: 3 day after surgery: inner surface of the tissue regenerate acquired the implant relief, ×500.

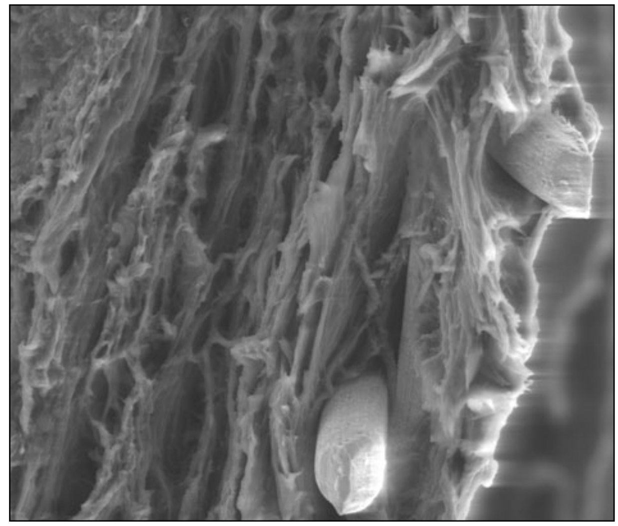

Fig. 3. Microstructure of tissue regenerate 3 months after surgery. Area of implant fixation to the diaphragm. Scanning electron microscopy, ×500.

tures of the chest (pericardium, diaphragm, and chest wall). Minor differences between the groups can be explained by topographic and anatomic peculiarities of the plasty site and initial covering of the implant with adjacent tissues.

Thus, tissue implant on the basis of superelastic titanium-nickelide thread is a good plastic material for repair of vast postresection defects of the pericardium, diaphragm, and chest wall. The newly formed tissue grew through the implant with the formation of an integrated tissue regenerate that did not impair heart contraction and excursion of the diaphragm and chest wall and ensured anatomic and physiological restoration of the damaged area.

REFERENCES

1. A. A. Vishnevskii, S. S. Rudakov, and N. O. Milanov, *Chest Surgery* [in Russian], Moscow (2005).
2. V. E. Gyunter, V. N. Khodorenko, Yu. F. Yasenchuk, *et al.*, Titanium-nickelide, A New Generation Medical Material [in Russian], Tomsk (2006).
3. *Surgery of Advanced and Complicated Lung Cancer* [in Russian], Ed. L. N. Bisenkov, St. Petersburg (2006).
4. A. R. Chapelier, M. C. Missana, B. Couturaud, *et al., Ann. Thorac. Surg*., **77**, No. 3, 1006-1007 (2004).
5. C. Deschamps, B.M. Tirnaksiz, R. Darbandi, *et al., J. Thorac. Cardiovasc. Surg*., **117**, No. 3, 588-591 (1999).
6. S. I. Menezes, P. S. Chagas, A. V. Macedo-Neto, *at al., Chest*, **117**, No. 5, 1443-1448 (2000).
7. S. Rathinam, R. Venkateswaran, P.B. Rajesh, and F. J. Collins, *Eur. J. Cardiothorac. Surg*., **26**, No. 1, 197-201 (2004).
8. J. Shimizu, Y. Ishida, Y. Hirano, *et al., Ann. Thorac. Cardiovasc. Surg*., **9**, No. 1, 68-72 (2003).
9. G. Veronesi, L. Spaggiari, P. G. Solli, and U. Pastorino, *Eur. J. Cardiothorac. Surg*., **19**, No. 1, 89-91 (2001).
10. M. J. Weyant, M. S. Bains, E. Venkatraman, *et al., Ann. Thorac. Surg*., **81**, No. 1, 279-285 (2006).