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Morphological Assessment of Different Ways of Bronchial Stump Closure after Pneumonectomy

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A method is developed to close the stump of the primary bronchus by outer compression with a shape-memory device. The process of bronchial stump healing under compression suture was morphologically examined. The novel method was compared with the routine Sweet-type hand-operated and the mechanical sutures. The compression suture heals the stump by primary intention with restoration of the typical airway epithelium on the stump bottom and prevention of the development of the bronchial fistulas.

Key Words: *pneumonectomy; bronchial stump closure; titanium nikelide*

Postoperative bronchial fistulas are severe complications in pulmonary surgery observed in 2-16% patients subjected to pneumonectomy [2-4,7-8]. The development of fistulas after various methods of bronchial stump (BS) closure prompted us to examine the processes of stump healing. According to universal inflammation principles, the basic stages in wound healing do not significantly differ in wounds of various genesis and localization, while the most favorable factor in wound healing by primary intention.

At present, two types of sutures are widely used in pulmonary surgery: mechanical suture (MS) and hand-operated suture (HOS). Both of them are characterized by the same disadvantages originated from penetrating character and formation of ligature-produced bronchopleural pathways [2,4]. Experiments on animals showed that BS healing by primary intention after its closure with routine sutures took place in only 18% cases [1]. Similar data were obtained during the bronchoscopic examination of postoperative patients [5]. More often, BS healing developed with secondary intention due to problems in coupling of the edges of the mucous tunic and impossibility of their reliable fixation because of elastic resistance of the chondroskeleton. The sutures in BS play a temporary role in providing impermeability of the stump until maturation of the connective tissue. Later, the sutures are usually cutting themselves out and can be observed either under the bronchial epithelium or outside in the scars. In clinical practice, the patients frequently expectorate the ligatures or surgical metal staples with the sputum. Most often, BS healing develops to the detriment of peribronchial tissues, because the internal contacting bronchial walls are lined with the epithelium, and fibrotization processes can develop here only after atrophy of the mucosa [2,10].

Disadvantages of available suture techniques stimulated the development of novel methods of BS closure without putting the sutures [6]. Among them, the most promising is the method of external compression of the bronchus, which preserves biological impermeability of BS and prevents contamination of the bronchial wall and the pleural cavity. However, it

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did not become popular due to technological problems in mass production of the clamps, their insufficient biomechanical compatibility, and unreliable BS impermeability. Introduction of novel materials based on titanium nikelide (TiNi), which were successfully used in various fields of surgery, created prerequisites to realize the technique of BS closure by external bronchial compression.

Our aim was to examine the peculiarities of BS healing after the treatment with a shape-memory device in comparison with the routine technique employing HOS and MS.

MATERIALS AND METHODS

Experiments were carried out on random-bred male and female dogs (*n*=36) weighing 10-16 kg with strict adherence to European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes. All manipulations were performed under general anesthesia. The design of the experiments was approved by Ethic Committee of Siberian State Medical University. The animals were obtained from and the experiments were carried out in Central Research Laboratory of Siberian State Medical University. The TiNi-based implants were produced in Research Institute of Medical Materials and Shape-Memory Implants (Tomsk).

Preparation for surgery, anesthesia, and postoperative care were the same in all animals. The surgery was carried out under general anesthesia and artificial ventilation. The left pneumonectomy was performed with individual treatment of the elements of radix pulmonis.

The dogs were randomized into three groups depending on the mode of BS treatment. In group 1 dogs (*n*=9), BS was closed with MS; in group 2 (*n*=9), closure was performed with polypropylene HOS according to the method of Sweet; and in group 3 (*n*=18), the treatment was carried out by external compression of the bronchus with a TiNi shape-memory device. This device is made of a pair of the arc-like parallel branches with bending radius similar to that of the chondral semiring (RF Patent No. 2229854). BS closure is effected by displacement of the membranous element towards the chondral part with the branches of the device. In all groups, DS were not subjected to pleurization.

The animals were sacrificed on days 3, 7, 14, 21, 30, and after 3, 6, and 12 months. BS were subjected to histological and histotopographic examination. The sections (5-7 μ) were stained with hematoxylin and eosin or according to van Gieson method. In longitudinal section of BS, the wide proximal part (situated proximally to the compression site or the sutures) and narrow distal aspect were examined individually. The blindly terminated subdivision of the wide part was termed here as BS bottom.

RESULTS

On postoperation day 7, the proximal region of BS subjected to either MS or HOS demonstrated edema, hyperemia, diapedetic hemorrhages into the mucosa and peribronchial tissue, which were more severe after MS. Mucosa epithelium was swollen, and some cells were desquamated into the lumen. In the distal BS segment, edema, hyperemia, the necrotic sites expanding to all the layers of bronchial wall were seen; this processes were accompanied by organization, dystrophic and necrobiotic alterations of the chondral laminae, and proliferation of the cambial elements into perichondrium. The narrow lumen was preserved in the contacting sites of bronchial wall, although deprived of epithelial lining. BS bottom was lined with flattened epithelium. The granulation tissue with a great number of cellular elements was revealed near the staples and ligatures.

On day 14, edema and hyperemia of the mucosa decreased in both groups, but after MS the inflammatory signs were less pronounced. The proximal epithelium was spotted with dystrophic sites, and the goblet cells were widened. In group 1, the granulation tissue developed around the dystrophically altered cartilage and metal staples in distal region of BS. By this time, the walls of the distal segment of BS accreted together by newly formed connective tissue characterized by numerous collagen fibers of different diameter and irregular direction. This union was not sufficiently strong, because removal of the staples before morphological examination resulted in separation of the BS borders. The bottom of BS had no epithelial lining. The bronchial wall thickened due to the development of peribronchial granulation tissue with numerous blood vessels and collagen fibers. Sites with hemosiderin deposits were usually revealed. The development of peribronchial tissue was also observed after HOS. In this case, the epithelium in BS bottom was well formed. The foci of suppurative inflammation were revealed under the epithelium, around the sutures, and in the distal region of BS, which melted the suture area and the bronchial wall itself (Fig. 1).

On day 21 after MS, the wall of the proximal segment of BS had normal structure. Pronounced peribronchial sclerosis was seen around BS. A connective tissue scar formed in the distal segment. A clearly developed fibrous capsules were observed near the staples. BS bottom was lined with multilayer epithelium having 5-6 and somewhere more layers. After HOS, pronounced peribronchial fibrosis was observed in the proximal and distal parts of BS. In the proximal part,

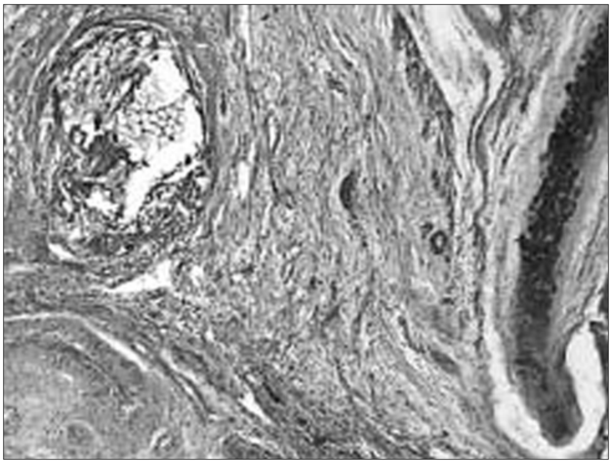

Fig. 1. Histological picture of hand-operated suture (HOS) in bronchial stump on postoperation day 14 with a focus of suppurative inflammation near the ligature channel. Hematoxylin and eosin staining, ×200.

the epithelium near the contacting walls was flattened; similar epithelium lined the BS bottom. The granulation tissue with a large number of cellular elements and newly formed vessels was revealed in the joining region of the walls, near the sutures, and in the distal segment of BS. In both groups, the bronchial wall in the distal part of BS demonstrated sites of dystrophically altered cartilage, which resolved gradually. On day 30, the proximal part of BS wall was normal in both groups, but after HOS, it was thickened due to peribronchial fibrosis (Fig. 2). In the proximal segment and in the bottom of BS, the multilayer differentiated epithelium restored completely. The distal region of BS was replaced with the connective tissue, which after MS was composed of thick collagen fibers, but after HOS it preserved a great number of cells, while the collagen fibers were thinner and chaotically directed. After MS, there were cysts in the scar region, which were lined with epithelium that had the signs of proliferation. The connective tissue capsules were formed near the staples and ligatures.

The data on MS and HOS agree with published data [1,5,9]. For this reason, we limited the length of our study to 30 days.

In group 3, moderate edema and somewhat enhanced accumulation of granulo- and agranulocytes were observed in the surface epithelium of the proximal part of BS on day 3 after pneumonectomy, although epithelium integrity was not disturbed. In the compression region, the greatest changes were observed in the mucosa. The epithelial layers of the membranous and chondral parts of the bronchus were tightly joined, but the epithelium was absent in some regions.

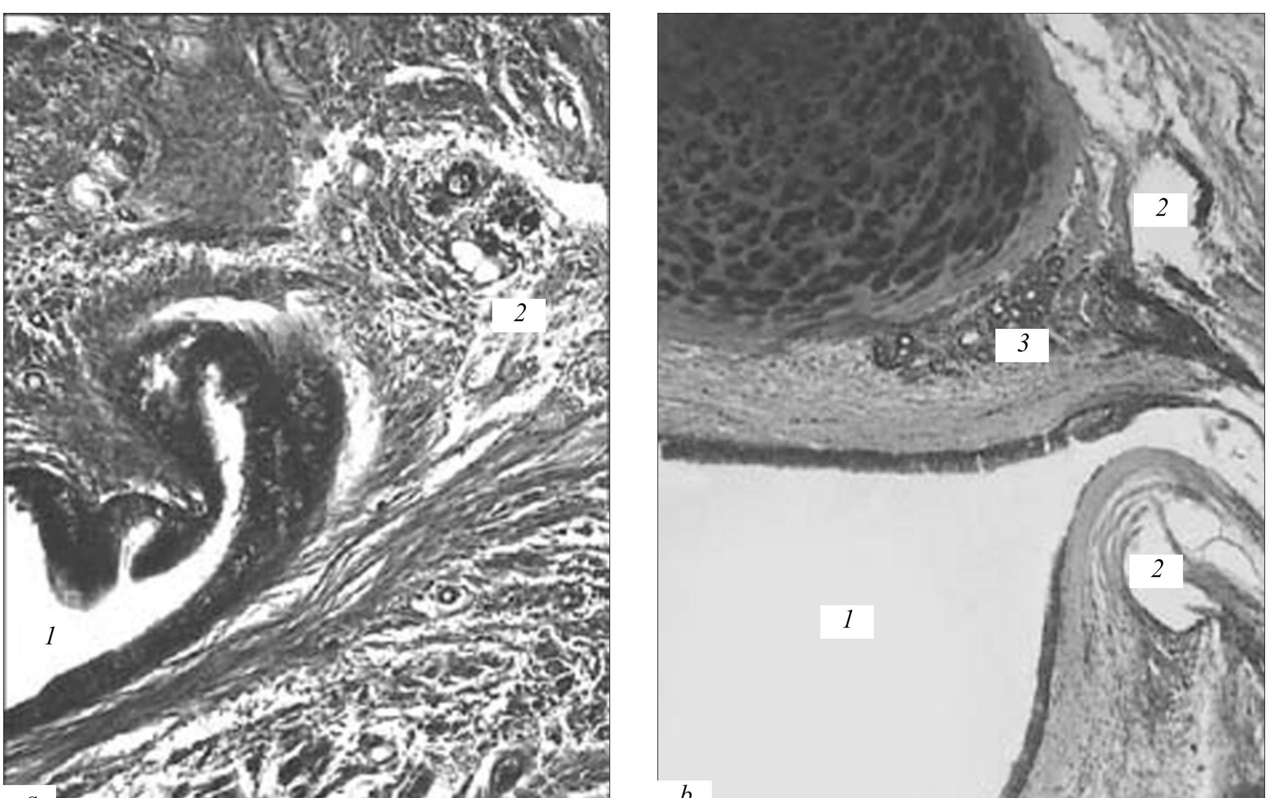

Fig. 2. Epithelization of BS bottom on postoperation day 30. *a*) HOS; *1*) lumen of BS; *2*) mature connective tissue with chaotically arranged collagen fibers; van Gieson staining, ×80; *b*) MS; *1*) lumen of BS; *2*) localization with metal staples; 3) cysts in the area of staple-made suture. Hematoxylin and eosin staining, ×80.

The mucosa and submucous layer were edematous and contained a large number of leukocytes. By their structure, the fibrochondral and muscular layers as well as adventitia were similar to the control sections taken from the analogous part of the bronchus on the opposite side of the bronchial tree. The distal part of BS was characterized by edema, infiltration, and the vascular hyperemia with hemorrhagic and necrotic foci in some locations of the bronchial wall. On day 7, the morphological outline of the proximal segment of BS was similar to that of control bronchus (Fig. 3, *a*). At the compression site of the bronchus, the most parts had no epithelium. The granulation tissue developed around the elements of the device and in the distal part of BS, which replaced all the bronchial layers. This tissue contained numerous cellular elements, mainly macrophages, lymphocytes, neutrophils, and fibroblasts. Here we also observed newly formed vessels and collagen fibers. On day 14, the proximal part of BS retained all the bronchial layers. The BS bottom was formed by well-developed granulation tissue, and almost complete restoration of epithelial lining with signs of multilayer structure was observed at the side of bronchial lumen. There was no epithelium at the contacting area of membranous and chondral parts of the bronchus. In the compression area, the bronchial wall layers were replaced with granulation tissue. The distal part of BS contained hemorrhagic and necrotic foci. On day 21, the entire length of the mucosa of the proximal part of BS was covered with multilayer prismatic epithelium, which passed from one BS wall to another and lined the bottom. In the proximal segment of BS, the structure of bronchial wall was normal. The BS bottom was covered by maturing granulation tissue located between the elements of the device forming the capsule of connective tissue around them. The distal part of BS was also lined with maturating granulation tissue. On day 30, the structure of BS differed from that observed at the previous term only by the degree of maturation of the granulation tissue that formed the BS bottom (Fig. 3, *b*). In the distal part of BS, the mature fibrous connective tissue alternated with focal clusters of lymphocytes and macrophages. Later, only the organ-specific differentiation of BS tissues developed. At delayed terms (3, 6, and 12 months), the structure of BS did not significantly change.

Thus, both MS and HOS provoked pronounced inflammatory infiltration in BS, which spread to the peribronchial tissues and was accompanied by local hemorrhages and necrosis in all the layers of bronchial wall. After HOS, the acute inflammatory reaction was more severe with the development of purulent foci

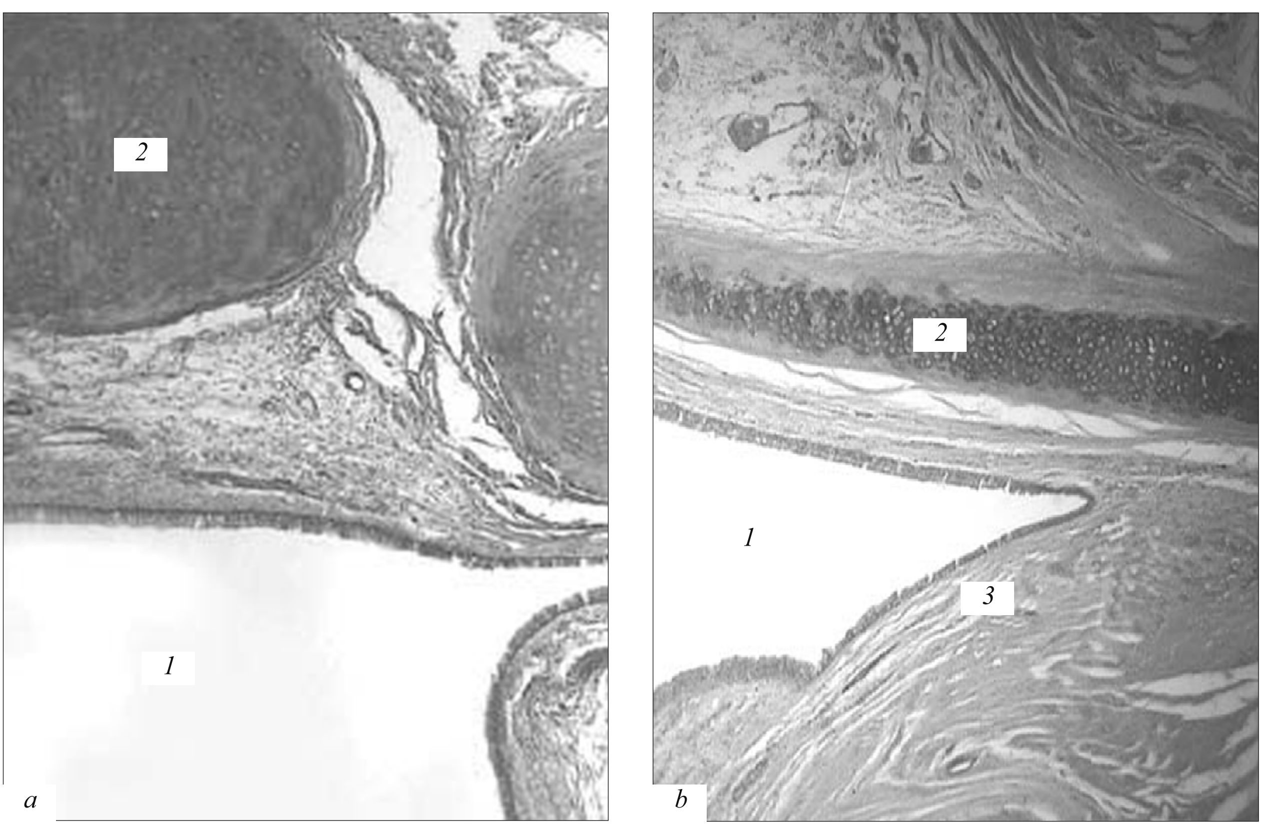

Fig. 3. Compression suture. Hematoxylin and eosin staining, ×80. *a*) postoperation day 7. Edema of mucosa at the compression site, the normal structure of hyaline cartilage; *b*) postoperation day 30. Continuous epithelium on BS bottom. 1) BS lumen; *2*) chondral region; *3*) membranous region.

near the ligatures and at a distance from them. By day 30, we observed restoration of the multilayer epithelium in BS bottom and formation of connective tissue capsule around the staples and ligatures. In some cases, gap-like cyst with epithelial lining developed in the distal region of BS. The bronchial wall regenerated by the process analogous to secondary intention. The formation of cyst-like structures in BS lined with epithelium should be considered as disadvantage of the piercing procedures employed in both suture technique examined here, because the cyst can be infected via the ligature channels, which can lead to suppurative inflammation in BS and to the late inefficiency. It seems that these reasons can explain the appearance of bronchial fistulas long after pneumonectomy despite a favorite course of immediate postoperative period.

Assessment of morphological alterations in BS on day 30 after compression suture revealed the development of the successive phases of aseptic inflammation and restoration of typical epithelial lining of the airways at the bottom of BS. The destructive and degenerative alterations of the cartilages accompanied by replacement of all the layers in the bronchial wall with connective tissue took place in the compression area and in the distal segment of BS. The connective tissue developed between the elements of the device and formed a capsule around them. Microscopic examination indicated healing of BS by primary intention.

It can be concluded that the compression suture provides more favorite conditions for BS healing in comparison with the routine MS and HOS characterized by healing via secondary intention. In this case, healing is promoted by the nonpenetrating character of the suture, better adaptation of the mucosa, and fixation of the BS borders due to prevention of the action of elasticity of the chondral semirings. As a result, the inflammatory process was short, aseptic, and moderately expressed. The healing process was characterized with the development of a small amount of cell-tissue detritus and its early disappearance resulting in early and complete reparation of the affected tissues.

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