Structural Modifications of Colonic Transplant in Plastic Repair of the Esophagus

G. A. Lapii, Yu. V. Chikinev, I. E. Sudovykh, and R. V. Govorkov

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Structural changes in the colonic transplant were studied after esophagoplasty, carried out for post-burn cicatricial strictures of the esophagus. It was shown that artificial esophagus was liable to hypotony and deformation in delayed periods after reconstructive interventions. Regeneratory and adaptive reactions in the mucosa underlie its restructuring, while under pathological conditions proliferative catarrhal changes predominated in the artificial esophagus. The leading pathomorphological characteristics of the colonic transplant are epithelial degeneration, active, sometimes unbalanced proliferation, hyperplasia and hypersecretion of goblet cells, lymphoplasmacytic infiltration of the stroma paralleled by slight sclerosis. Modifications of the ultrastructural organization of cell populations in the Lieberkuhn crypts are determined by the intensity of pathological processes and are aimed at realization of the cytoprotective potential of the transplant mucosa.

Key Words: *esophagoplasty; colonic transplant; biopsy; electron microscopy*

Organ repair technologies are used for correction of benign pathologies of the esophagus when little invasive interventions are ineffective. Various compartments of the digestive tube are used for replacement of damaged esophagus; one of the main donor organs is the large intestine [9-12]. Colonic plasty is a prevalent method of reconstructive interventions in post-burn cicatricial strictures of the esophagus [1,8].

Important aspects of esophagoplasty are its delayed effects caused by modification of the transplant function and structure resultant from its interposition and adaptation to new conditions [5,7]. Available information on the results of esophagoplasty indicates that pathological processes can develop in the transplant, their incidence largely depending on the type of plasty. In addition to dysfunctions, a wide spectrum of diseases, including inflammatory changes, ulcers, polyps, and rare tumors were described for an artificial esophagus reconstructed from the large intestine [2-4,6]. On the other hand, the concept of the morphogenesis of artificial esophagus pathology was not developed. Complex pathomorphological study is essential for clearing out the structural basis of the pathological process in the transplant and understanding of the mechanisms of formation of delayed complications of esophagoplasty.

We studied the regularities of structural reorganization of colonic transplant after esophagoplasty, realized under conditions of benign esophageal injuries.

MATERIALS AND METHODS

The study was carried out in 65 patients (41 men and 24 women aged 23-68 years) with artificial esophagus formed from the large intestine. The

Laboratory of General Pathology, Pathophysiology, and Pathomorphology, Institute of Regional Pathology and Pathomorphology, Siberian Division of Russian Academy of Medical Sciences, Novosibirsk. ***Address for correspondence:*** pathol@soramn.ru. G. A. Lapii

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reconstructive interventions were in all cases carried out for post-burn cicatricial stricture of the esophagus; the left half of the colon was used for transplantation. The morphology and function of the artificial esophagus was evaluated by integral X-ray, endoscopic, and morphological findings for the period of 1 month to 7 years after reconstructive intervention; in 2 cases, plastic repair was carried out more than 40 years before this examination.

Complex pathomorphological analysis of the transplant, esophagocolono- and colonogastroanastomoses was carried out on biopsy specimens collected during endoscopic revision of the artificial esophagus and included light microscopy of paraffin and semithin sections and electron microscopy. Paraffin sections were stained with hematoxylin and eosin in combination with Pearl's reaction, by van Gieson's method with poststaining of elastic fibers with Weigert's resorcin-fuchsin, and by PAS method. Semithin sections (1 μ) sliced from blocks embedded in epon-araldite mixture were stained with Schiff's reagent and azur II. Ultrathin sections were contrasted with uranyl acetate and lead citrate and examined under a JEM 1010 electron microscope.

The results were statistically processed using one-way analysis of dispersions and Fisher's test.

RESULTS

X-ray examination of the artificial esophagus reconstructed from the large intestine showed symptoms of hypotony (31 cases, 47.7%), deformations (14 cases, 21.5%), and signs of reflux into the transplant (19 cases, 29.2%).

Fibroesophagogastroduodenoscopy showed that the colonic transplant was characterized by a twisted passage and haustral surface relief; the mucosa was covered with viscous secretion, irrespective of the period elapsed after plasty. Hypotony and deformations of artificial esophagus were associated with local leveling of haustrations, dilated segments, formation of additional loops and deviations. Signs of the transplantitis were detected in 7 cases (10.8%) and ulcerative defects in the distal part of the transplant were visualized in 3 cases (4.6%).

Intensive regeneration of the epithelium, most significant in the anastomosis zone, was detected microscopically in the transplant mucosa during the first months after esophagoplasty; this was paralleled by an increase in the number of mitoses in the upper segments of crypts, the typical cell differentiation and due balance of secreting and absorbing colonocytes being retained. Exudative reaction with foci of capillary plethora, edema, perivascular polymorphic cellular infiltration was noted in some cases.

Later, after long functioning of the artificial esophagus, the transplant mucosa retained its microarchitectonics in general, but exhibited a trend to hypertrophy of the Lieberkuhn crypts. Disproportional transformation of the epithelial stromal components, sometimes appearing near anastomoses, manifested by drawing together, compact complectation, and slight deformation of the Lieberkuhn crypts divided by narrow interstitial strata.

The colonic epithelium was characterized by proliferative changes with hyperplasia of goblet exocrinocytes. Surface epithelium looked thickened, consisted from high colonocytes, with stratification of cell nuclei in some places. Goblet cells with signs of hypersecretion predominated in the epithelial lining of the Lieberkuhn crypts; the number of column colonocytes decreased (Fig. 1, *a*).

Analysis of the epithelial compartment of the transplant mucosa showed its heterogeneous structural organization, associated with manifestation of a pathological process in the artificial esophagus. Irrespective of the period elapsed after plasty, epithelial cambial zones in biopsy specimens with the least pronounced changes were clearly limited by the Lieberkuhn crypt base, while the epithelial layer on the main territory was formed by well-differentiated goblet cells with abundant cytoplasm overfilled with PAS-positive secretion (Fig. 1, *b*).

The ultrastructure of goblet exocrinocytes reflected high secretory function and was characterized by high polarity of intracellular structure. The major part of the cytoplasm was filled by large electron-transparent globules of mucus, fusing in conglomerations; cells with granulated globules were seen (Fig. 1, *c*). Flattened nuclei with narrow zone of marginal heterochromatin were located basally. Elements of the Golgi complex, cytoplasmic reticulum tubules, few mitochondria could be differentiated in the perinuclear compartment of the cytoplasm. Dilatation of intercellular spaces with the lateral plasmalemma processes protruding into them were seen in some places because of intercellular edema (Fig. 1, *d*).

In other biopsy specimens, the mucosa had signs of active unbalanced epithelial proliferation. Pronounced elongation of the cambial zones, filled by numerous poorly differentiated epitheliocytes, was observed (Fig. 2, *a*). The percentage of young colonocyte forms increased in Lieberkuhn cell population; individual oligomucous cells were virtually everywhere seen in the epithelial lining between mature goblet exocrinocytes (Fig. 2, *b*).

The ultrastructure of poorly-differentiated colonocytes was characterized by nuclei containing predominantly euchromatin and large nucleoli of gra-

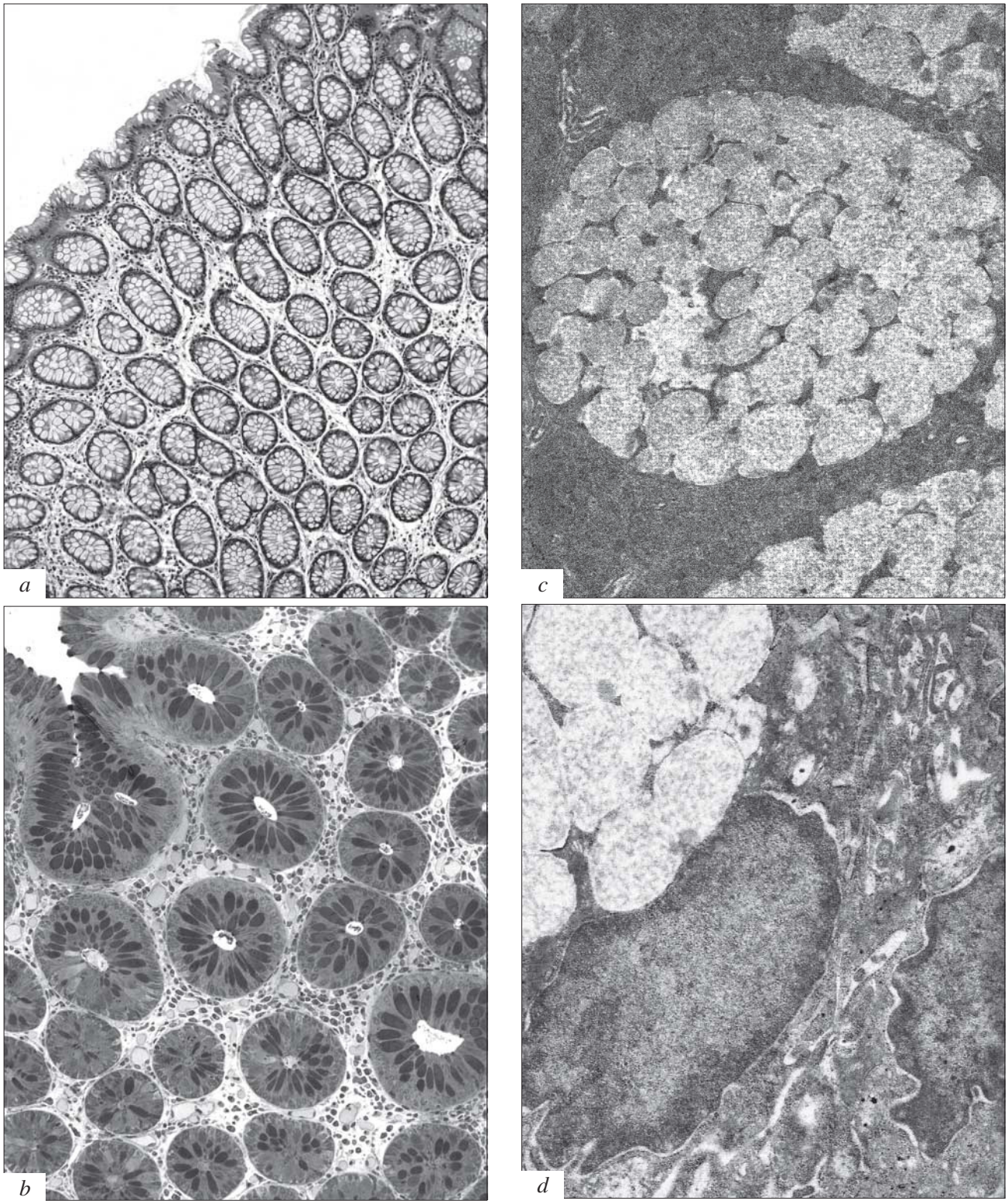

Fig. 1. Photooptic and ultrastructural characteristics of colonic transplant in delayed periods after esophagoplasty. *1*) Lieberkuhn crypt epithelium with goblet cell hyperplasia, ×70; *b*) high secretion of mucus by goblet cells, lymphoplasmacytic infiltration of stroma, ×140; *c*) numerous globules of mucus in the cytoplasm of goblet exocrinocytes, ×5000; *d*) fragment of epithelium, dilatation of intercellular spaces, ×8000. *a*) hematoxylin and eosin staining; *b*) semithin section, PAS reaction; *c*, *d*) electronograms.

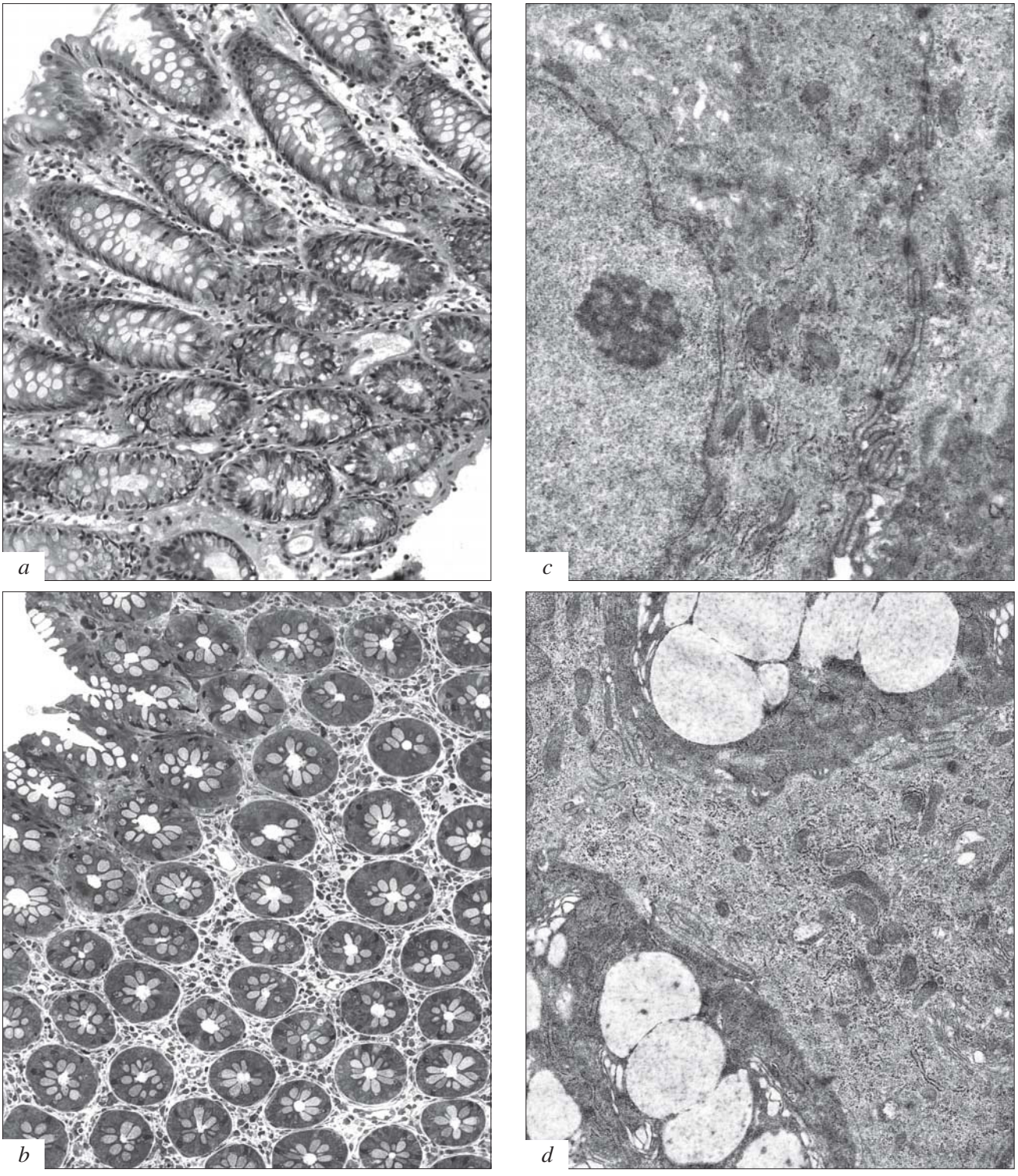

Fig. 2. Proliferative catarrhal changes in colonic transplant in delayed periods after esophagoplasty. *a*) degeneration and active proliferation of Lieberkuhn crypt epithelium, edema and lymphoplasmacytic infiltration of stroma, ×140; *b*) goblet cells of different differentiation degree in Lieberkuhn crypt epithelium, ×140; *c*) fragment of poorly-differentiated colonocyte, nucleus with a large nucleolus, narrow profiles of granular cytoplasmic reticulum in the cytoplasm, numerous polysomes, small vacuoles, ×6000; *d*) fragment of colonic epithelium, oligomucous cells with scanty globules of mucus and large elements of Golgi complex, ×6000. *a*) hematoxylin and eosin staining; *b*) semithin section, azur II staining; *c*, *d*) electronograms.

nular fibrillar structure. The cytoplasmic compartment included numerous cisterns of granular cytoplasmic reticulum, numerous polysomes and free ribosomes, polymorphic mitochondria, and small vacuoles (Fig. 2, *c*). Solitary large globules of mucus, hyperplastic Golgi complex, well-developed tubules of the cytoplasmic reticulum were seen in moderately dense cytoplasm of oligomucous cells (Fig. 2, *d*).

The progress of pathological process in an artificial esophagus was paralleled by predominantly degenerative changes in the epithelium, associated with disorderly location of colonocytes, blurred contours of cells, cytoplasm vacuolation, and uneven secretion. Foci of dysplastic transformation of the Lieberkuhn crypt epithelium were detected in 2 cases. Atrophic changes in the mucosa were extremely rare. Pronounced bacterial contamination of the transplant was seen in some cases with deformations.

Diffuse lymphoplasmacytic infiltration was detected in the lamina propria in the majority of biopsy specimens; lymphoid follicles were seen. Focal microcirculatory disorders were most often detected in the distal compartments of the esophagus, in some cases with an admixture of leukocytes in the infiltration. Sclerotic changes in the stroma, irrespective of the time elapsed after plastic repair, were rare and as a rule were not intense. The muscle plate was predominantly intact or slightly sclerosed.

Electron microscopy of blood capillary endotheliocytes showed mainly signs of high functional activity. The cell luminal plasmalemma formed an intricate relief with short microvilli, folds, and invaginations. Short profiles of cytoplasmic reticulum were seen in the perinuclear zone; numerous pinocytous vesicles were differentiated in the peripheral compartments of the cytoplasm. Pericytes were characterized by well-developed cytoplasmic processes, in which solitary microvesicles, small mitochondria, Golgi complex elements, and cytoplasmic reticulum cisterns were discernible.

Hence, the study showed an intricate complex of restructuring in the colonic transplant after esophagoplasty, caused by regeneratory and adaptive processes aimed at realization of the defense potential of the organ under conditions of performing an atypical esophageal function. Proliferative catarrhal changes predominated in the artificial esophageal mucosa after long functioning. The leading pathomorphological characteristics of the colonic transplant are epithelial degeneration, active (sometimes unbalanced) proliferation with hyperplasia and hypersecretion of goblet cells, diffuse lymphoplasmacytic infiltration, and slight sclerotic changes in the stroma. Modifications of ultrastructural organization of the Lieberkuhn crypt cell populations are caused by formation of a pathological process in the transplant and reflect intensification of cytoprotective properties of the mucosa.

It is noteworthy that hyperplasia of the colonic epithelial secretory elements, providing effective cytoprotection, is paralleled by minimization of the mucosal absorption function. In addition, the proliferating epithelial tissue seems to provide a low level of sclerogenesis, a peculiar feature of the epithelial stromal integration of the colonic transplant mucosa under conditions of esophagoplasty. Presumably, destabilization of the compensatory adaptive reactions or their inadequacy to new conditions of functioning can induce a disease of the artificial esophagus.

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