EXPERIMENTAL METHODS FOR CLINICAL PRACTICE

Role of Microcirculatory Disorders in the Morphogenesis of Fissured Ulcers in Children with Terminal Ileitis

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 128, No. 7, pp. 76-77, July, 1999
Original article submitted October 10, 1998

Structure and ultrastructure of ileal biopsy specimens were studied in 6 children with Crohn's disease in order to investigate the morphogenesis of fissures. Microcirculatory disorders lead to the formation of microinfarctions which are shaped as long fissures due to tissue vascular architectonics and peristaltic movements of the intestine.

Key Words: *Crohn's disease; microcirculation; ulcerogenesis*

Patho- and morphogenesis of Crohn's disease (CD) is still insufficiently known, and therefore there are plenty of concepts and interpretations, and hence, approaches to its therapy [10,11]; however, the efficacy of treatment and prevention of complications of CD depend on the solution of these problems.

MATERIALS AND METHODS

Biopsy specimens (n=6) from children aged 5-14 years with histologically diagnosed terminal ileitis and clinically diagnosed latent form of CD during infiltration phase were fixed in 2% buffered glutaraldehyde (pH 7.2-7.4) at 4°C for 1 h, washed in a buffer, stained with osmium tetroxide, and embedded in epon. Ultrathin sections were prepared from each block and examined under an EMB-100 electron microscope.

Parallel biopsy specimens from the same patients were embedded in paraffin for histological and histochemical studies after staining with hematoxylin-eosin, alcyan blue 8GX, periodic acid Schiff (PAS) reagent, and according to Van Gieson.

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RESULTS

All three stages of inflammation (alterative, vascular mesenchymal, and proliferative), differently expressed, were observed in different sites of the same block, which is in line with other reports [4-6].

Alterative stage was characterized by cascade changes in the basal membranes of lymph and blood capillaries (Fig. 1, *a*): mucoid, fibrinoid, and finally necrotic degeneration. Stasis (Fig. 1, *b*) [3], endothelial degeneration, hyperchromatic endothelial nuclei, accumulation of PAS-positive material (necrosis) in the vascular walls, and leukocyte adhesion were seen in the vessels [2,8-10].

Vascular mesenchymal stage was associated with the blockade of lymph and blood capillaries resulting in multifocal intestinal infarctions [11]. These zones were surrounded by abundant anastomosing capillaries with unevenly thickened deformed walls (Fig. 1, *c*).

The proliferative stage was incomplete, i. e., lamina propria of the intestinal mucosa (LPIM) consisted of immature connective tissue, as was confirmed by Van Gieson's staining.

Unlike other authors [4,7], we examined endoscopically unaltered mucosa (without fissures), and therefore it can be concluded that capillary injuries in

0007-4888/99/0007-0725$22.00

CD are primary, developing in minimal infiltration of the intestinal wall by inflammation cells.

Further disorders of the blood and lymph circulation lead to chronic local hypoxia, disorganization and paravital changes in the LPIM, epithelial desquamation, and, finally, to ulceration.

Medium-sized arterioles branch into smaller vessels (capillaries) within the muscular layer of the intestine by the arch principle [1], corresponding to the site of the mesentery afferents (longitudinally). Therefore, every arch delivers blood to a longitudinal strip of the intestine. All layers of the intestinal wall are involved in CD, including the muscular layer where the arterioles branch. When the peristaltic wave passes along the intestine in CD patients, the stenosed arterioles are compressed at the sites of branching. The blood flow in the longitudinal part of the intestine is more disturbed than in ulcerative colitis, when only LPIM, but not the muscular layer is involved. Thus, in CD hypoxia involves longitudinal segments of the intestine and determines the formation of longitudinal fissures. In CD, ulceration in involved spastic segment depends on vasculitis and peristalsis, while in ulcerative colitis it depends only on vasculitis.

At later stages of CD, when the intestinal wall is fibrosed and peristalsis does not affect ulcer formation, ulcers acquire an irregular shape.

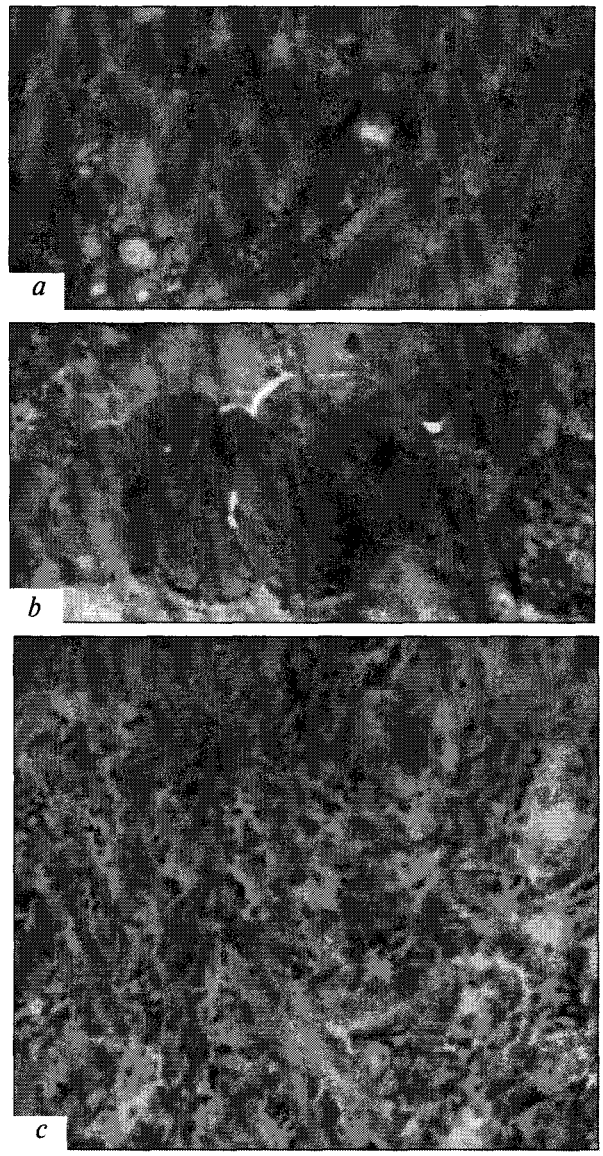

Fig. 1. Microcirculatory disturbances in Crohn's disease. *a*) alterative and vascular stages of the inflammatory reaction. Pinocytic vesicles and fenestration of the laminar membrane of vascular endothelium, perivascular edema. Electron microscopy, ×1800; *b*) erythrostasis. Electron microscopy, ×2400; *c*) peculiar anastomoses in dense capillary network in the lamina propria of the intestinal mucosa. Light microscopy, hematoxylin-eosin staining, ×120.

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