ULTRASTRUCTURE OF LYMPHATIC CAPILLARIES OF THE HUMAN MYOCARDIUM IN MITRAL STENOSIS

M. V. Danilenko, D. D. Zerbino, and V. P. Olefir

UDC 616.126.421-07:616.423-091.8-031:611.127

Electron-microscopic investigations showed marked edema and sclerosis in the lymphatic system and stroma of the myocardium in mitral stenosis, due to general stasis of the lymph associated with generalized venous hypertension. Changes in the pathways of the microcirculation and the attendant hypoxia play an important role in the mechanism of the heart failure in mitral stenosis.

Microscopic investigation of the myocardium of persons dying from decompensation of the heart following rheumatic defects reveals more or less severe sclerosis and edema of the interstitial tissue. It was shown previously that in mitral stenosis the right ventricular failure is followed by generalized venous hypertension and general stasis of lymph [4]. It can accordingly be postulated that microcirculatory disturbances, including stasis of lymph in the lymphatic capillaries and vessels of the myocardium, play an important role in the genesis of the contractile weakness of the myocardium [3].

EXPERIMENTAL METHOD

The ultrastructure of the lymphatic capillaries of the left ventricle was investigated in 15 patients with mitral stenosis in its various stages. During mitral commissurotomy with a transventricular access a strip of myocardium not more than 0.5 mm wide and thick was taken from the edges of the operation wound. As a control the ultrastructure of the microcirculatory pathways of the normal myocardium of four persons killed in road accidents was investigated (the material was taken 1.5-2 h after death). The pieces of tissue were fixed in the cold for 2 h in a 2% buffered solution of osmium tetroxide; they were stained with a 2% aqueous solution of uranyl acetate for 2.5 h, rinsed in sucrose solution, dehydrated in increasing concentrations of ethanol, and embedded in the epoxy resin Epon 812. After polymerization the blocks were sharpened by hand under the MBS-2 stereoscopic binucular microscope. Sections under 1 μ in thickness were cut on the LKB 8802A ultramicrotome from the whole area of the piece of the tissue (1 mm^2), applied to grids coated with Formvar film, and examined under the minimal power of the UÉMV-100B electron microscope. To examine a lymphatic capillary its position was chosen in the block, which was then tapered to a pyramid, and ultrathin sections were cut to a thickness of 400-600 Å. The sections were then treated with lead nitrate to reduce contrast.

EXPERIMENTAL RESULTS

The general structure of the lymphatic capillaries of the myocardium in mitral stenosis differs greatly from normal. The marked tortuosity and corrugation of the walls of the lymphatic capillaries were particularly pronounced (Fig. 1a). These changes were due to several causes: interstitial edema, an increased number of connective-tissue elements in the stroma of the myocardium, and hypertrophy of the muscle cells. In some cases the corrugation of the capillary wall was so marked that it was difficult to detect the points of contact between the endothelial cells. The pericapillary space and the lumen of the lym-

Department of Thoracic Surgery and Anesthesiology, and Department of Pathological Anatomy, L'vov Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR A. I. Strukov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 77, No. 6, pp. 104-107, June, 1974. Original article submitted April 3, 1973.

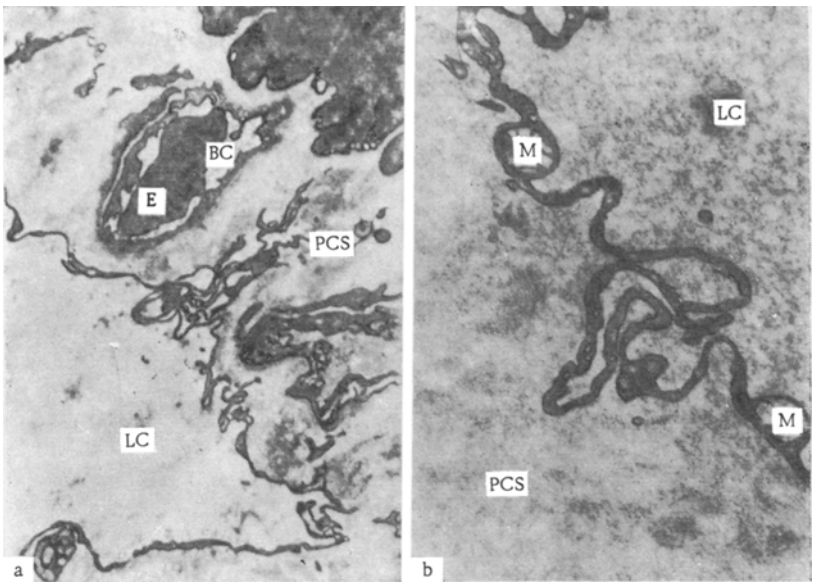

Fig. 1. Second stage of mitral stenosis in a woman aged 36 years: corrugation of wall of lymphatic capillaries and interstitial edema: a) corrugation of walls of lymphatic capillaries (LC), at its side a blood capillary (BC) with an erythrocyte (E) can be seen, 5500 ×; b) lumen of capillary and pericapillary space (PCS) contain identical protein substrate; degenerative changes in mitochondria (M) of endothelium, 11,000 ×.

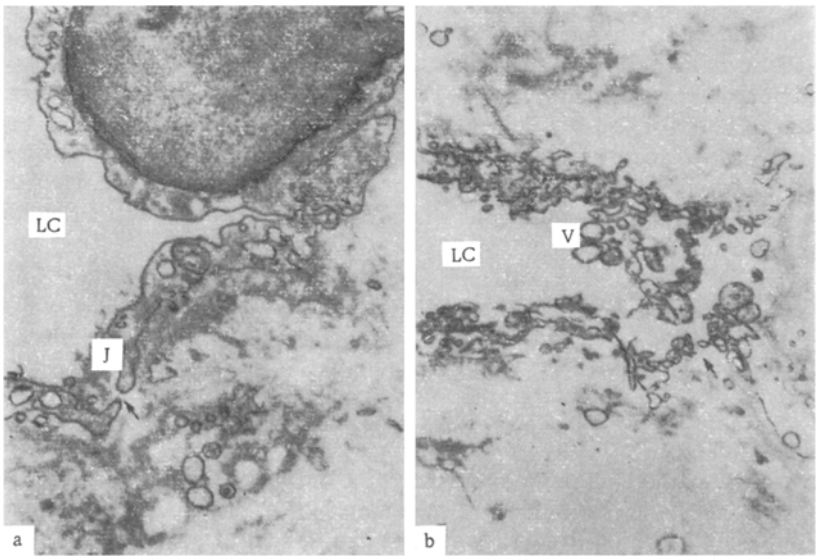

Fig. 2. Third stage of mitral stenosis in a woman aged 40 years. Passage (arrow) of protein and debris into lumen of lymphatic capillary (LC) through open junctions (J); a) passage of protein, 16,000 ×; b) passage of protein and vacuoles, 10,000 ×.

phatic capillaries contained the same protein substrate (Fig. 1b). Open contacts (joints) between the endothelial cells through which masses of protein pass from the lumen of the lymphatic capillary into the interstitial space or vice versa were very frequently seen. The direction of the movement of the protein (lymph) was difficult to determine. Only in a few specimens could the transport of the protein substrate be clearly seen through the closed junctions into the lumen of the lymphatic capillaries (Fig. 2a). The zones of many junctions sometimes were more complex: several appendages were in contact with the edges of a neigh-

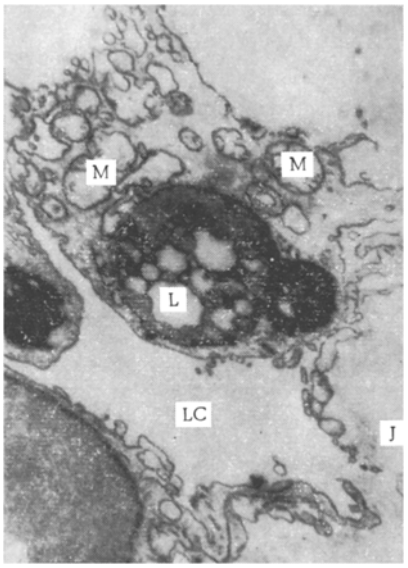

Fig. 3. The fourth stage of mitral stenosis in a patient aged 34 years: open junction (J) between endothelial cells containing secondary lysosomes (L) and degeneratively changed mitochondria (M); 8,000 ×.

boring endothelial cell or the junction between the endothelial cells was open and the appendages did not make contact. A finely granular mass of protein, debris, and vacuolated structures passed through the open junctions (Fig. 2b).

The pericapillary space contained a granular protein mass – the interstitial fluid. This fluid displaced the collagen fibers far from the walls of the lymphatic capillaries, and only in a few places were the fibers close to the lymphatic capillaries. In some places the fibers appeared to be connected with the outer plasma membrane of the endothelium of the lymphatic capillaries.

A very characteristic finding was that the cytoplasmic matrix of the endothelium of the lymphatic capillaries during hypoxia developing in association with a heart defect was much denser electron-microscopically than in the normal heart. Meanwhile fewer organoids, micropinocytotic vesicles, and vacuolated structures were observed in the matrix of these cells. "Swollen" mitochondria were encountered. The cisterns of the endoplasmic reticulum were dilated. The matrix of some endothelial cells was translucent. The Golgi complex was clearly visible in only a few endothelial cells, but its cisterns were wider than usually. In some cases manifestations of intercytoplasmic edema and degenerative changes in the organelles, especially swelling of the mitochondria, could be clearly seen (Fig. 1b).

One characteristic feature was observed: resorption of the elements of the disintegrated cells by the lymphatic capillaries. The entry of debris into the lumen of the lymphatic capillaries through the widely open contacts between the endothelial cells was visible on these electron micrographs (Fig. 2b). It was impossible to determine precisely the cells from which these elements came. This debris was possibly from the destroyed endothelial cells of the capillaries themselves, but it is more likely that, because of the increasing hypoxia, the material resorbed was from distintegrated histiocytes or muscle cells, located alongside the lymphatic capillaries.

The second stage of mitral stenosis was characterized by some degree of edema of the stroma and an increase in the quantity of protein metabolites entering the lumen of the lymphatic capillaries; the lymphatic capillaries were dilated and filled with lymph. In stage III of mitral stenosis the cell organelles, especially the mitochondria, were swollen, the matrix of the endothelial cells was translucent, and cell debris was resorbed by the lymphatic capillaries. In this same period not only the lymphogenic edema but also the sclerosis started to progress. The processes of sclerosis were more marked still in stage IV. The parenchyma (myocytes) became widely separated from the blood and lymphatic capillaries, increasing the hypoxia and stimulating fibrillogenesis. Meanwhile secondary lysosomes of the phagocytoma and cytolysosome type appeared (Fig.3). This phenomenon has also been noted by other workers studying the ultrastructure of the myocardium in patients with mitral stenosis [1, 2, 5].

The electron-microscopic investigations of the myocardium in mitral stenosis thus show marked edema and sclerosis in the lymphatic system and stroma of the heart. These changes are due largely to general stasis of the lymph in connection with the generalized venous hypertension. Changes in the pathways of the microcirculation and the attendant hypoxia play an important role in the mechanism of heart failure in mitral stenosis.

LITERATURE CITED

1. B. V. Vtyurin, Arkh. Pat., No. 6, 51 (1968).
2. B. V. Vtyurin, The Importance of Lysosomes in Degenerative and Regenerative Intracellular Processes [in Russian], Vol. 3, Moscow (1971), p. 51.
3. M. V. Danilenko, D. D. Zerbino, and R. I. Orach, Proceedings of the Twelfth Plenum of the All-Union Society of Surgeons [in Russian], Moscow (1971), p. 196.

4. D. D. Zerbino, Pathological Anatomy and Pathogenesis of Certain Types of Failure of the Lymphatic Circulation, Author's Abstract of Doctoral Dissertation, [in Russian], L'vov (1965).
5. A. I. Strukov and V. S. Paukov, Arkh. Pat., No. 4, 12 (1969).
6. E. S. Reynolds, J. Cell Biol., 17, 208 (1963).