DISTURBANCES OF MYOCARDIAL MORPHOLOGY IN RATS TAKING ALCOHOL FOR 20 WEEKS AND ABSTINENT FOR 6 WEEKS

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UDC 616.127-02:616.89-008.
441.13-036.11]-092.9-076

KEY WORDS: myocardial morphology; experimental alcoholization; withdrawal of ethanol.

Many studies of disturbances in the myocardium of laboratory animals after chronic alcoholization have recently been published [9, 11, 13, 14]. These have tended to ignore the question of the possible reversibility of such changes. Yet the answer to this question is of great importance for clinical practice. The results of clinical investigations have been contradictory. Cases of a gradual [3, 6-8, 10] or even a very rapid [2] recovery of patients suffering from alcoholic cardiomyopathy (ACMP) in both the initial and advanced stages, have been described; meanwhile other clinicians are skeptical of such a possibility [4, 5]. The aim of this investigation was to study the spontaneous reversibility of alcoholic damage to the myocardium in experimental animals.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats weighing initially 280-320 g, kept in the animal house and receiving a standard granulated diet supplemented with vitamins and minerals. The 20 animals of the experimental group received alcohol for 20 weeks. Half of that period was devoted to enforced alcoholization, during which a 40% aqueous solution of ethanol was given 3 times a week by gastric tube in a dose of 25 ml/kg body weight, whereas the other half was devoted to semivoluntary alcoholization, during which the animals received a 15.5% solution of ethanol with 0.08% saccharine as taste additive, as the sole source of fluid. During the period of enforced alcoholization 12 rats (60%) died from acute alcoholic poisoning. The remaining eight animals were divided into two equal groups: after 20 weeks of alcoholization the rats of group 1 were killed, whereas after the same period of alcoholization the rats of group 2 abstained from alcohol for 6 weeks. Group 3 consisted of four animals receiving water by gastric tube in a dose of 25 ml/kg body weight. Group 4 was the pure control, in which four intact rats were kept under identical conditions. The tissue was fixed by perfusion by Langendorf's method, with modifications [9]. The fixative consisted of a 1.5% solution of glutaraldehyde and a 1.5% solution of fresh formaldehyde in isotonic Krebs—Henseleit buffer, pH 7.4. Pieces from the middle part of the lateral wall of the left ventricle were postfixed in 1% osmic acid in the same buffer, dehydrated in alcohols of increasing concentration, and embedded in Araldite. Semithin sections 1 μ thick, stained with toluidine blue and with hematoxylin and eosin, were studied with an "Olympus" photomicroscope with magnification of up to 2000. Ultrathin sections 50-70 nm thick were cut on a "Reichert" ultramicrotome, stained with solutions of uranyl acetate and lead citrate, and studied in the JEM-100B electron microscope with accelerating voltage of 80 kV. Two pieces of myocardium from each animal were studied.

EXPERIMENTAL RESULTS

Examination of semithin sections under the light microscope showed that the myocardium of rats of groups 3 and 4 (water and pure control) was normal in structure (Fig. 1a). Identical morphologic disturbances were found in the myocardium of the rats of groups 1 and 2: uneven hypertrophy of the cardiomyocytes, hypertrophy of the nuclei (Fig. 1c, d), disorientation of the myofibris (Fig. 1b, c, d); multicomponent macrophages (Fig. 1b) and labrocytes can be seen in the interstitial tissue. The disturbances described above were diffuse in character. On electron-microscopic investigation of the myocardium of the rats of groups 1 and 2, accumulation of lipids associated with mitochondria (Fig.

Department of Human Cardiovascular Pathology, All-Union Cardiologic Scientific Center, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR D. S. Sarkisov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 108, No. 8, pp. 244-247, August, 1989. Original article submitted November 11, 1988.

0007-4888/89/0008-1197$12.50

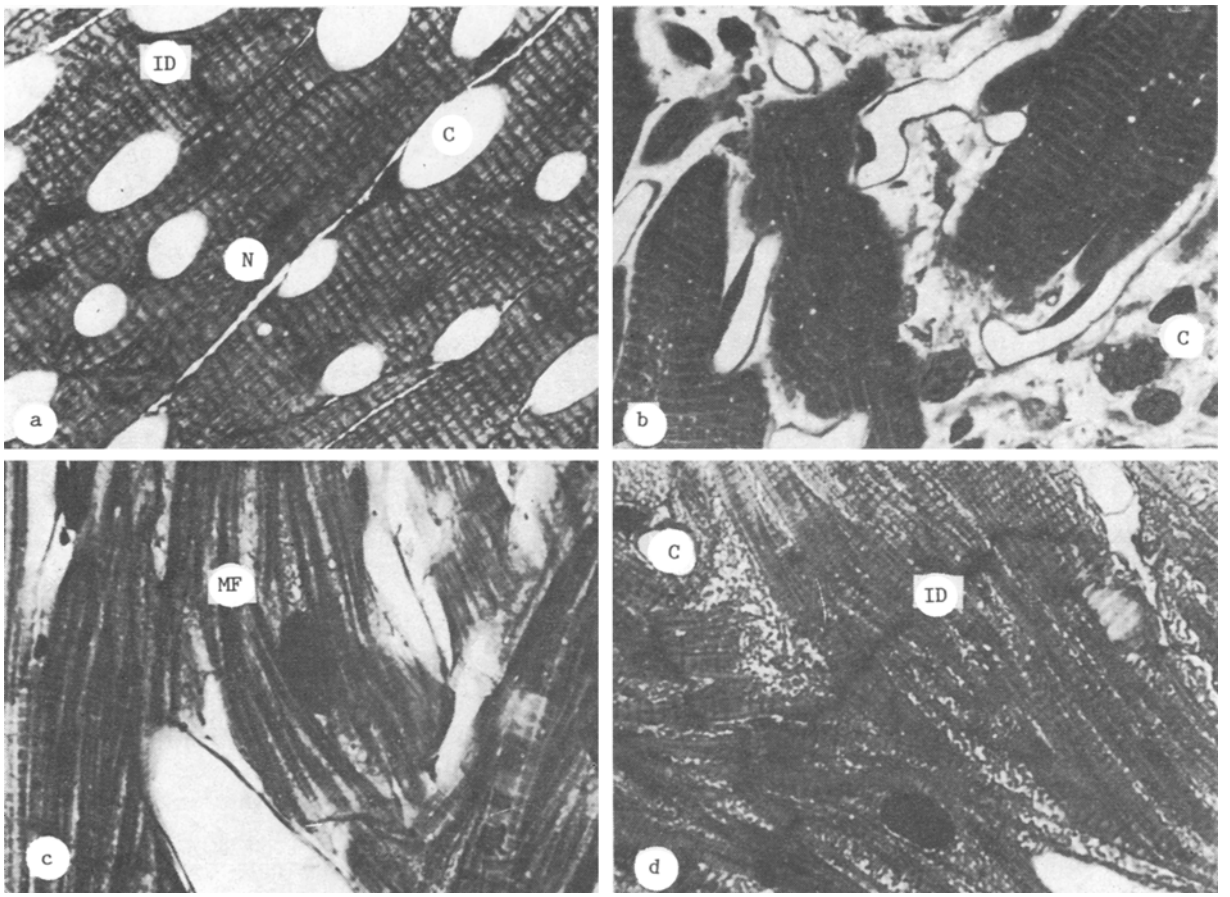

Fig. 1. Changes in myocardium of rats after chronic alcoholization and withdrawal. Hematoxylin and eosin, 1000×. a) Control, normal structure; C) capillary, ID) intercalated disks; b) myocardium of rats of group 1; infiltration by macrophages (M), myofibrils turned through a right angle in cell lying just below center; c, d) myocardium of rat of groups 1 and 2 respectively; hypertrophy of nucleus (N) of cardiomyocytes, myofibrils (MF) disoriented.

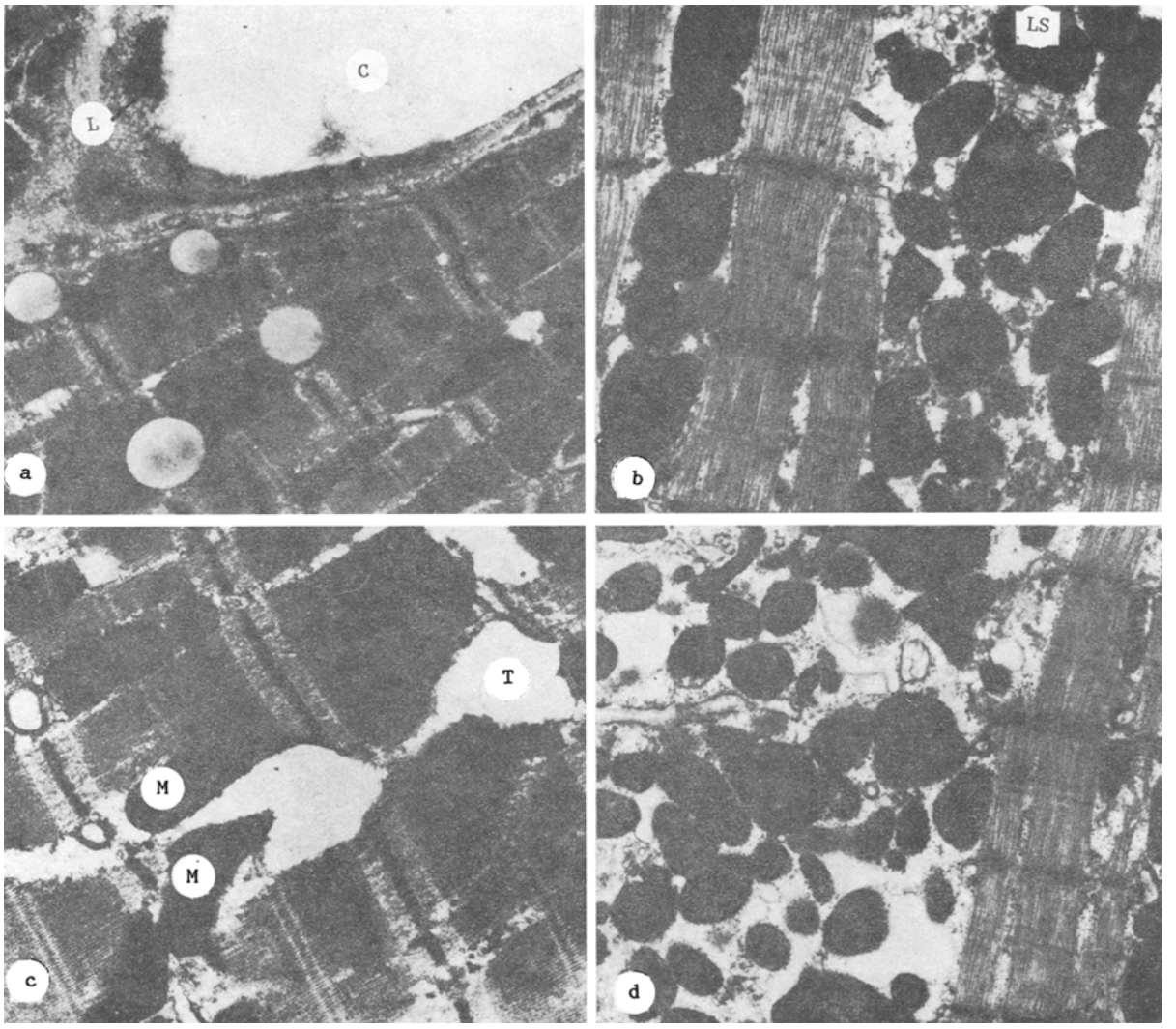

Fig. 2. Ultrastructural changes in rat myocardium after chronic alcoholization and withdrawal. a) Myocardium of rat of group 1; lipid granules (L) associated with mitochondria can be seen; C) capillary; b) myocardium of rat of group 1; four phagolysosomes (LS) can be seen; c) myocardium of rat of group 2; rupture of outer membrane of mitochondrion (M); T) tubules dilated; d) myocardium of rat of group 2; hypertrophy of T system and of sarcoplasmic reticulum. Magnification: a, d) 10,000×, b, c) 12,000×.

2a), many phagolysosomes (Fig. 2b), ruptures of the outer mitochondrial membrane (Fig. 2c), and dilatation of the T-tubules and canaliculi of the sarcoplasmic reticulum (Fig. 2d) were observed. Most of the myofibrils appeared intact, but they were less compact in some cells. Disorientation of the myofibrils was not so marked as when examined under the light microscope, because of the smaller field of vision. The myocardium of groups 3 and 4 (control) was normal in its ultrastructure.

The morphological changes discovered experimentally in the myocardium of the rats agree in certain features with those observed in ACMP [1], but do not completely reproduce them. The results of the present investigation showed that a 6-week period of abstinence is not sufficient to reverse the structural changes arising in the rat myocardium as a result of 20 weeks of alcoholization. We found no data in the literature on the reversibility of the morphological disturbances in experimental ACMP. Segel et al. [12] studied alcohol-induced disturbances of the hemodynamics and of calcium binding by the sarcoplasmic reticulum. Experimental alcoholization in their experiments lasted 10 months; in this case the response of the heart to β-adrenergic stimulation was reduced and binding of Ca^{++} by the microsomal fraction was delayed. After abstinence for 15-24 weeks the parameters returned to normal. Reichert et al. [15], in the course of intensive alcoholization (14 g ethanol/kg body weight daily for 8 weeks), discovered a gradual lowering of the level of mitochondrial respiration and of contractility of isolated cardiomyocytes. During the subsequent 8 weeks of abstinence, these workers observed recovery of all the parameters studied. Contradictory results such as these

necessitate a combined morphological and biochemical investigation, with the use of different periods (and methods) of alcoholization and withdrawal.

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IMMUNOHISTOCHEMICAL CHARACTERIZATION OF CHRONIC EROSIONS OF THE GASTRIC MUCOSA

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UDC 616.33-018.73-002.44-036.
12-092.18

KEY WORDS: gastric erosions; formation of chronic erosive defects; gastric biopsy; immunohistopathology; cytometry.

Chronic erosions are a special form of lesion of the gastric mucosa the verification and study of which has become possible as a result of progress in endoscopic techniques [1, 5, 10-12]. Endoscopic features and the histopathology of acute ("incomplete") and chronic ("complete") gastric erosions have now been sufficiently well studied, but the mechanisms of transformation of erosive defects into the chronic state remain unexplained [1]. The presence of a special form of fibrinoid necrosis, an essential component of erosions, its unusual relations with leukocytes [1, 12], the discovery of viruses [11, 12] and of bacteria [7] in the zone of erosive defects, and also the positive therapeutic effect of local application of leukocytic concentrate [7] are all evidence of the possible involvement of immunopathological reactions in the pathogenesis and morphogenesis of erosions.

The aim of this investigation was to study local immunity of the gastric mucosa in order to establish the role of an immunopathological component in the formation and chronic transformation of erosion lesions.

EXPERIMENTAL METHOD

Biopsy specimens from the stomach, taken during fiberoptic gastroscopy with direct vision biopsy from 85 male patients aged between 30 and 49 years, were studied by methods of light and electron microscopy and immunohistochemistry. In 36 patients with endoscopically diagnosed erosive gastritis, biopsy material was taken from the zone of erosions and the body and pyloric canal of the stomach. The comparison group consisted of 35 patients with

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(Presented by Academician of the Academy of Medical Sciences of the USSR Yu. I. Borodin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 108, No. 8, pp. 247-250, August, 1989. Original article submitted October 21, 1988.

0007-4888/89/0008-1200$12.50