SOME ASPECTS OF CELL APOPTOSIS

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UDC 616-002.4-018.1-07

KEY WORDS: apoptosis; reutilization; lymphocytes

A special form of cell death, known as "apoptosis," has been widely discussed in the literature [8, 9, 14]. This form of cell death is considered to differ from necrosis and to be a feature of all types of cells. It has been postulated that apoptosis is a programmed process of active self-destruction of all types of cells with the morphological features of destruction that are inherent in this process. The biological significance of apoptosis, it is suggested, lies in a general pattern of cell death during embryogenic histogenesis, regulation of the numerical size of a cell population, in the results of exposure to hormonal, immune, chemical, and physical factors, and also in tumor growth [8]. However, no convincing evidence can be found in the literature on the factors causing death by apoptosis. There are only statements to the effect that apoptosis is the result of exposure to factors which are harmful but not strong enough to cause "coagulation necrosis" of the cell. This conclusion becomes flawed if it is recalled that so-called apoptotic particles can be found in intestinal crypts of animals irradiated in minimal as well as superlethal doses [3]. Many workers consider that apoptotic particles in the crypts of irradiated animals are the result of death of enterocytes [3]. However, there is evidence against this view [1, 2, 7] and in favor of resistance of enterocytes. Moreover, it is assumed by the authors cited that apoptotic particles in the intestinal crypts of irradiated animals are none other than breakdown products of lymphocytes which have migrated into a zone of active proliferation, and are reutilized by cells of the epithelium.

The aim of this investigation was to study relations between lymphocytes and enterocytes under the influence of ionizing radiation.

EXPERIMENTAL METHOD

CBA mice weighing 25-27 g were given ^{3}H-thymidine (specific activity 3 Ci/mmole) intraperitoneally in a dose of 1 μCi/g body weight. The thymus and spleen were taken from the animals 2 and 24 h after injection of ^{3}H-thymidine. The cell suspension prepared from these organs was injected into the caudal vein of isogenic recipient mice. The animals were irradiated with x-rays in a dose of 15 Gy 15 min and 1 and 28 h after the thymidine injection. The mice were withdrawn from the experiment under ether anesthesia after 30 min-3 h, at intervals of 30 min after irradiation. Sections through the small intestine, spleen, and thymus and films of the cell suspension for transfusion were processed autoradiographically.

EXPERIMENTAL RESULTS

The radioactive label 3 h after irradiation was found in the recipient mice in vacuoles in the cytoplasm of the epithelial cells of the intestinal crypts; clumps of different shapes, stained by Feulgen's method for DNA, were found to be labeled. The nucleus of one such cell, containing a large vacuole, was usually displaced toward its basal part (Fig. 1). In addition, intact labeled lymphocytes were observed both in the cytoplasm of the enterocytes and extracellularly. They also were found in the stroma of the intestinal wall, thymus, and spleen. Later the label was found

Laboratory of Bioregulators, S. M. Kirov Military Medical Academy, St. Petersburg. (Presented by Academician of the Russian Academy of Medical Sciences S. N. Golikov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 114, No. 8, pp. 216-217, August, 1992. Original article submitted November 28, 1991.

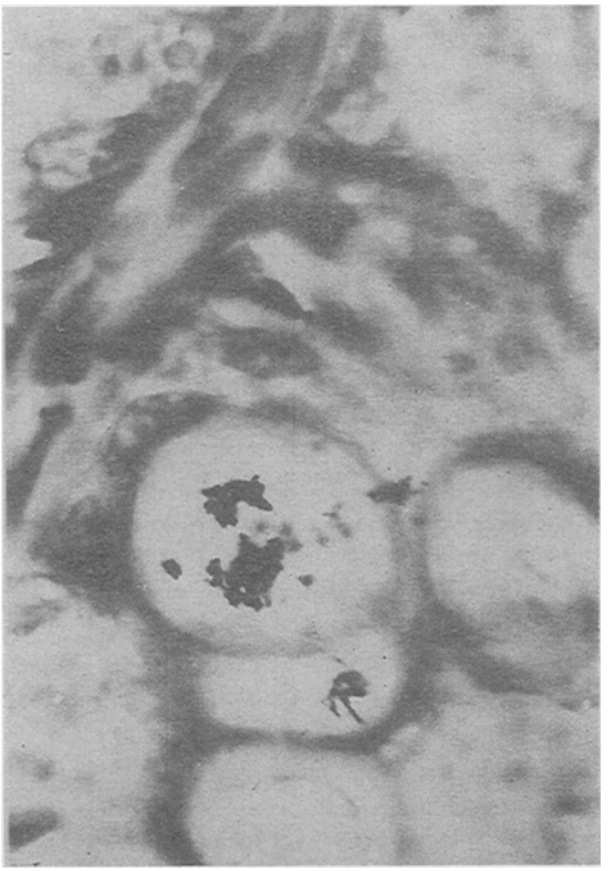

Fig. 1. Crypt of small intestine of recipient CBA mouse irradiated in a dose of 15 Gy. ^{3}H-thymidine label visible in giant vacuole in cytoplasm of epithelial cell whose nucleus is displaced toward its basal part. Iron-hematoxylin. 900×.

above nuclei of the epithelium of the crypts. Spherical inclusions in the cytoplasm of the enterocytes, containing fragments of lymphocyte nuclei (as shown by labeling with ^{3}H-thymidine), however, create the false impression of destruction of enterocytes, and are the result of endocytosis of nucleoproteins from lymphocyte nuclei and confirm the radioresistance of the intestinal epithelium.

Thus the trophic function of lymphocytes, universally described in the literature [4-6, 10], is effected through their destruction, i.e., their apoptosis, a process typical only of lymphoid cells and no others, as some investigators consider [8, 9, 14]. Morphologically this process is always represented by the presence of pycnotic figures in the cytoplasm of the epithelium, reticular cells, and various malignant cells, taking up essential nucleoproteins [11, 13, 15]. This phenomenon also has been described in the literature as "apoptosis." In fact, only lymphocytes undergo apoptosis, and their breakdown products are taken up by cells of many tissues and organs, and once they are in the cytoplasm of these cells, usually in the composition of a large vacuole, they create the false impression of pycnotic changes in these cells. Analysis of data in the literature and our own findings leads to the conclusion that the phenomena observed reflect a physiological process of plastic provision for growth, regeneration, and functional activity of the tissues taking place in the body and achieving maximal expression under extremal conditions.

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MECHANISM OF ACTION OF CHORIONIC GONADOTROPHIN ON LACTATE DEHYDROGENASE ACTIVITY

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UDC 612.015.1:577.152.1].06:577.175.327].08

KEY WORDS: chorionic gonadotrophin; lactate dehydrogenase

Proliferation and differentiation of all cells in the body are under the control of many different mechanisms involving the biologically active compounds of protein nature. A special place among these compounds is occupied by chorionic gonadotrophin (CG). It is considered that any nonendocrine tissue in which intensive cell proliferation takes place may be a source of CG [2]. There is some evidence that CG is involved in prostaglandin synthesis, and in intracellular protein synthesis [6]. The study of its effect on the liver has shown that this hormone is closely connected with the liver, as is shown by stimulation of regeneration and reversibility of pathological changes in the structure and function of that organ [7]. The number of normal hepatocytes increases rapidly under these circumstances, the number of degenerating cell forms decreases, normal lipid metabolism is restored, and the quantity of excessively growing connective tissue and activity of lysosomal enzymes are reduced. Meanwhile, in the liver tissue, activity of organ-specific enzymes (urokinase, frustose-1-phosphate aldolase) and of alanine aminotransferase is increased, evidence of intensification of enzyme synthesis [1, 3, 4].

Thus CG, by reducing the intensity of catabolism in the pathologically changed liver, makes hepatocyte destruction less likely and promotes acceleration of regeneration in the organ and in that way affects the activity of various intracellular enzymes. The mechanism of action of CG on enzymes has not yet been finally settled.

Our aim was to study the effect of CG on the catalytic properties of lactate dehydrogenase in vitro.

EXPERIMENTAL METHOD

Preincubation of CG in a dose of 5 mg/ml (50 U/ml) with a solution of the enzyme lactate dehydrogenase (LDH) from porcine muscle ("Reanal") was carried out in vitro for 10 min. LDH activity was then determined [5]. To

Medical Institute, Nizhnii Novgorod. (Presented by Academician of the Russian Academy of Medical Sciences Yu. A. Romanov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 114, No. 8, pp. 217-218, August, 1992. Original article submitted January 28, 1992.