ULTRASTRUCTURAL CHANGES IN THE RAT CEREBRAL CORTEX DURING THE EARLY PERIOD OF ACUTE RADIATION SICKNESS CAUSED BY NEUTRON IRRADIATION

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In view of the relatively few recent investigations in this field [2, 3, 5-7] it is impossible to present a complete picture of the early ultrastructural changes in nerve cells and the microcirulatory bed of the brain after exposure to high doses of ionizing radiation and, particularly, of neutrons. In particular, the role of injury to the microcirculatory system in the development of early irradiation pathology of the CNS has not been fully explained. The problem of the specificity of neutron-induced damage likewise remains unsolved.

This paper gives an analysis of the time course of ultrastructural changes in neurons and blood capillaries in the rat sensomotor cortex during the first 24 h after whole-body irradiation with fast neutrons.

EXPERIMENTAL METHODS

Experiments were carried out on male Wistar rats weighing 180-210 g. The animals were subjected to whole-body all-round neutron irradiation in the vertical channel of a VVR-M reactor in a dose of 10 Gy, with a total dose rate of 0.35 Gy/min. The gamma-component did not exceed 30%. The mean energy of the neutrons was 0.85 MeV. Dosimetry was carried out by means of ionization chambers [3]. The animals were decapitated 15 min and 1, 3, 6, and 24 h after irradiation. Control animals were subjected to "mock" irradiation. Material for electron-microscopic study was processed by the usual method. Sections were examined in the field of vision of Hitachi H-300 and Tesla BS-613 electron microscopes.

RESULTS

An increase in electron-optical density of the majority of mitochondria was observed in the cytoplasm of the neurons 15 min after irradiation. Slight dilatation of the tubules of the endoplasmic reticulum (ER) was observed. The number of free ribosomes and polysomes was increased. Presynamptic endings of axons contained numerous syamptic vesicles and mitochondria with high electron-optical density. At this stage changes in ultrastructure of the blood capillaries were negligible.

Swelling of the mitochondria took place in the nerve cells 1 and 3 h after exposure. Diltation of the tubules of ES and framentation of individual tubules, whose membranes were without ribosomes, were observed. The lamellar apparatus showed hypertrophy. The number of free ribosomes and polysomes in the cytoplasm was reduced. The diameters of pores in the nuclear membrane and the perinuclear space were enlarged. The matrix of the nucleus and cytoplasm of the neurons were translucent. The number of synaptic vesicles in the presynaptic axon endings was reduced. The matrix of the endothelial layer of the capillaries gradually become more translucent. In the perivascular space swelling of processes of astrocytes was noted.

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Further swelling of the mitochondria, many of which showed fragmentation of the cristae and vacuolation, was observed in the neurons 6 h after irradiation. The lamellar apparatus consisted of large vacuoles. ER consisted of separate short fragments, although in some neurons small areas of this reticulum and polysomes in the cytoplasm of the cells was very small, but there was an increase in the number of lysosome-like bodies. The perinuclear space and the diameters of the pores in the nuclear membrane were considerably enlarged. The number of vesicles in synaptic endings was reduced, and at the same time the quantity of electron-dense granular material increased. Active zones of synapses were poorly defined. Swelling of the capillary walls took place and the number of swollen mitochondria with fragmentation of their cristae increased in the capillary endothelium. The number of micropinocytotic vesicles was less than at previous times of observation. Meanwhile in the endothelial layer large vacuoles with pale contents were frequently found. The width of individual intercellular spaces in the endothelium was increased. The matrix of the basement membrane was translucent. In the perivascular space zones of electron-translucent material were often observed. Processes of astrocytes were considerably swollen.

A tendency for recovery of the ultrastructure of the greater part of the organelles was observed in the neurons 24 h after exposure to radiation. Both in the cytoplasm and in the processes of the neurons the mitochondria were in a typical condensed state, although some of them showed signs of swelling and fragmentation of the cristate. Single disintegrating mitochondria with oncentric myelin-like structures also were found. Tubules of the rough ER had mainly even outlines, but in individual neurons there were regions with local dilatations. Small areas of membranes forming tubules contaed no ribosomes. The number of free ribosomes and polysomes in the cytoplasm was greater than at the previous time of observation. The lamellar apparatus consisted of collapsed cisterns, but individual cisterns in some neurons were considerably enlarged and had the appearance of large vacuoles. Close to the lamellar apparatus multivesicular bodies were frequently seen. The number of lysosome-like bodies was translucent. The nuclear membrane had the typical ultrastructure. Chromatin was distributed irregularly in the nucleus, Translucent zones could be seen in the nucleoplasm. In the dendrites local flask-shaped expansions of individual microtubules were noted. The number of synaptic vesicles in the axon endings was increased a little. The considerable widening of the intercellular spaces in the neurophil must be specially emphasized. At this time of observation the microvessels were characterized by further swelling of all components of the vascular wall. Enlargement of the perivascular space was observed, and in it, besides swollen processes of astrocytes, there were many large, pale vacuoles, bounded by an elementary membrane. Numerous vacuoles of different sizes also appeared in the processes and perikaryon of the astrocytes.

A complex temporal pattern of postradiation changes in the structure of the neurons and blood capillaries of the sensomotor cortex was thus observed. Ultrastructural changes in the nerve cells immediately after irradiation can be interpreted as an indication of their increased functional activity. Signs of inhibition of the nerve cells were observed after 6 h, and toward the end of the first day activation of intracellular compensatory processes could be identified. This interpretation of the time course of the changes in neuronal ultrastructure is in agreement with results obtained by investigators whoe studied early ultrastructural changes in intracellular organelles under the influence of various injurious factors [1]. The results now obtained suggest that the time course of postradiation changes in cortical neurons in the first 6 h is mainly determined by the direct action of ionizing radiation on them, for the vascular changes at this period are limited to the development of mild perivascular edema only. The after-effects of damage to the microcirculatory bed evidently aggravates this pathology later. The results also are evidence that ultrastructural changes in neurons and blood capillaries associated with neutron irradiation do not differ qualitatively from the analogous changes caused by low-frequency ionizing radiation, which other investigators have used [5-7]. The problem of how the high relative biological effectiveness of neutrons is manifested in the CNS at the ultrastructral level requires special study.

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ULTRASTRUCTURE OF THE AIR–BLOOD BARRIER OF THE LUNGS IN DOGS TREATED FOR ACUTE HYPOXIA BY EXTRACORPOREAL MEMBRANE OXYGENATION

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Treatment of acute respiratory failure (ARF) still remains an urgent problem in modern medicine [2, 5, 10]. The high mortality from ARF and the limited possibilities of methods of intensive treatment of respiratory failure make the development of new methods of oxygenation of the patient, one of which is extracorporeal membrane oxygenation (ECMO), particularly important. Accounts of experimental [3, 7, 8] and clinical [1, 11, 12] investigations and survey articles [4, 6, 9, 13], giving the results of the use of membrane oxygenators (MO) in the treatment. Yet the effect of new gas-exchange systems of membrane type on the structure of the lungs and other organs, which is particularly important in connection with the evaluation of the functional properties and qualities of MO, has received totally inadequate study.

The aim of this investigation was to study the ultrastructural changes in the air–blood barrier (ABB) of the lungs under conditions of severe hypoxia and treatment with MO.

EXPERIMENTAL METHODS

Experiments were carried out on 10 mongrel dogs of both sexes weighing 15-20 kg. Severe hypoventilation hypoxia was induced in all the animals by reducing the respiratory minute volume suddenly to 30% of normal. In five dogs of the control series, 40-90 min after the beginning of hypoxia, under general anesthesia (pentobarbital) and muscle relaxation (succinylchlorine), left thoractomy was performed and pieces of the lung removed for electron-microscopic investigation. In the main series of experiments (on five dogs) hypoxic animals were connected to a Soviet Sever-OMR membrane oxygenator, on the vein–oxygenator–vein principle. After the MO had been in operation for 3-3.5 h, under hypoventilation conditions material was taken for morphologic investigation in the same way as from animals of the control series. Material for electron microscopy of the lungs was treated by the usual method. Ultrathin sections were studied in the IEM-100CX electron microscope. In each series 10 samples of the lungs were studied. The lungs of four healthy intact dogs also were investigated electron-microscopically.

RESULTS

Electron-microscopic study of the lungs of dogs of the control series with severa hypoxia revealed considerable changes in all components of ABB, the most severe being disturbances of the microcirculation (Table 1). In 70% of lung samples studied the blood capillaries in the alveolar septa were grossly dilated and contained agglutinated erythrocytes (Fig. 1a), with at the same time unchanged erythrocytes and erythrocytes with a

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