A CYTOCHEMICAL STUDY OF THE EFFECT OF HYDROCORTISONE ON PHAGOCYTOSIS OF QUARTZ DUST

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UDC 616.24-003:662-085.357.
453-07:616.155.3-008.
13-07

The effect of hydrocortisone on phagocytosis was investigated in albino rats, 24, 48, and 72 h after intraperitoneal injection of 100 mg quartz dust, using cytochemical tests for certain mitochondrial (NAD-diaphorase and succinate dehydrogenase) and lysosomal (acid phosphatase) enzymes. On the basis of the results obtained it is postulated that hydrocortisone probably stabilizes lysosomal and mitochondrial membranes, and thus delays death of the coniophage. The material is discussed in the light of earlier results indicating the inhibitory effect of hydrocortisone on collagen formation in the lungs in experimental silicosis and other findings indicating different mechanisms of action of hydrocortisone on the cell.

Death of the coniophage is at present regarded as the initial trigger mechanism of development of the pathological process in the pneumoconioses. The writers' earlier cytochemical investigations showed that quartz causes injury to the mitochondria of the coniophage and disturbs the integrity of the lysosomal and phagosomal membranes, liberating into the cytoplasm the lysosomal hydrolytic enzymes, thus accelerating and completing the process of death of the cell.

The object of the present experiment was to determine whether hydrocortisone exerts a protective action against injury to cells by quartz.

EXPERIMENTAL METHOD

The material for the investigation consisted of peritoneal macrophages of albino rats. Cytochemical tests for NAD-diaphorase, succinate dehydrogenase, and acid phosphatase were used as indicators of the state of the mitochondria and lysosomes. Impression films were made 24, 48, and 72 h after injection of 100 mg quartz dust intraperitoneally into each of the control and experimental animals. Each group of experimental animals throughout the period of the experiment received additional injection of hydrocortisone, to a total dose of 60 mg. The control animals received pure physiological saline.

EXPERIMENTAL RESULTS

High NAD-diaphorase activity and moderate succinate dehydrogenase activity were observed after 24 h in the coniophages. As a rule the deposition of the reaction product (diformazan) was diffuse in character. Only at the periphery of the macrophages, against the background of the dissuse staining, was diformazan localized as large, polymorphic granules. At this same period, a slightly less marked activity of the oxidation-reduction enzymes was observed in the macrophages under the influence of hydrocortisone.

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The reaction end-product was distributed mainly as small and larger polymorphic granules; diffusion of the enzymes in the cytoplasm was not so conspicuous. Tests for acid phosphatase in the control showed uniform pinpoint deposits of lead sulfide granules in the lysosomes and also larger deposits of the reaction product, sometimes confluent, in the phagosomes. Meanwhile, in the experimental specimens the deposits of lead sulfide in the lysosomes was mainly discrete in character, and the number of lysosomes in the cells was noticeably reduced. In some coniophages, however, deposition of the reaction product was of approximately the same character as that observed in the control tests.

The harmful action of quartz on the mitochondrial membranes after 48 h was manifested as virtually complete diffusion of the reaction product, diformazan, in the cell cytoplasm. As before, diformazan in the coniophages under the influence of hydrocortisone was mainly localized as large, polymorphic granules, sometimes confluent, and on the whole diffusion of the formazan was less marked than in the coniophages in the control tests, even after exposure to quartz for 24 h. Acid phosphatase in the control tests was detected mainly as aggregating granules of lead sulfide. In the experimental coniophages this tendency toward fusion of the granules, like the activity as a whole, was somewhat less marked.

Coniophages with sharply reduced NAD-diaphorase and succinate-dehydrogenase activity and with solitary polymorphic granules of diformazan in the dying cells appeared after 72 h. Many of the coniophages, after additional treatment with hydrocortisone, as before possessed high activity of oxidation-reduction enzymes although the character of the diformazan deposits was predominantly diffuse. In the series of control investigations complete diffusion of acid phosphatase in the coniophages was observed, followed by disintegration and autolysis of the cells. In the experimental series a picture of fusion of granules was mainly observed in the coniophages, just as after exposure for 48 h to quartz alone, but sometimes the picture was more clearly defined. Cells with complete diffusion of the enzyme and dying forms were rare.

It can be postulated from the analysis of these results that, under the influence of hydrocortisone, quartz on the whole causes less injury to membranes of the mitochondria and lysosomes, such important organelles for the basic functions of the cell. Probably it can be assumed that the protection of the membrane resulting from the action of hydrocortisone prevents or postpones death of the coniophage, the initial trigger mechanism of the sclerotic process.

There is extensive evidence in the literature of delayed development of experimental and clinical silicosis under the influence of steroid therapy. In combined histochemical and biochemical investigations the writers have previously demonstrated the inhibitory effect of hydrocortisone on the development of experimental silicosis [1].

The role of hydrocortisone in phagocytosis is probably not limited to its ability to stabilize mitochondrial and lysosomal membranes, but it can evidently also prevent the fixation of dust particles on the surface of macrophages [4], reduce acid phosphatase activity [3], inhibit collagen formation [1], and so on.

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