MORPHOLOGICAL CHANGES IN THE ADRENALS IN EXPERIMENTAL BURNS

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UDC 617-001.17-092.9-07:616.45-091-07

After an interval of 48-72 h a burn of the dorsal skin in rabbits gave rise to hyperplasia of the adrenal cortex, and the concentration of 17-hydroxycorticosteroids in the urine was lowered on the first day after burning. On the 3rd-4th day the normal concentration of 17-hydroxycorticosteroids was restored.

Changes in the adrenals after burns have frequently been studied experimentally and clinically, but aspects of this problem still await an explanation. Some workers [2, 3, 10, 12] have observed an increase in the glucocorticoid function of the adrenals on the first day after burning, while others have observed periodic fluctuations in the secretion of glucocorticoids after burns: a transient increase 10-30 min after burning, followed by a period of marked inhibition, which could last for 6-7 days [4, 5, 7, 11].

In this investigation the state of the adrenals was studied after burns by the use of morphological and biochemical methods of analysis.

EXPERIMENTAL METHOD

Severe burns of the skin (20-30% of the body surface) were inflicted on 50 rabbits with the flame of a blowlamp for 40 sec: 5 healthy rabbits acted as the control.

The parameters studied included the arterial pressure, body temperature, erythrocyte count, hematocrit index, circulating plasma volume (using the dye T-1824), and mean length of survival.

The animals were sacrificed 3, 8, 24, 48, and 72 h and 8 days after burning. The adrenals were weighed and then fixed in neutral formalin. Some of the tissue was fixed in 10% silver nitrate solution for the determination of ascorbic acid by the method of Giroud and Leblond. Sections were stained with hematoxylin-eosin and with Sudan III for lipids. Cholesterol was studied in a polarization microscope. Alkaline phosphatase activity was determined by Gomori's method and the concentration of 17-hydroxycorticosteroids in the urine was determined on the 1st-7th days after burning by Metcalf's method as modified by Norymberski and Few [9].

EXPERIMENTAL RESULTS

Thermal burning was followed by a rapid motor response for the next 5-10 min. In this period the arterial pressure rose by 20-30% compared with initially, the pulse quickened, respiration quickened and its amplitude increased, and the body temperature rose by 3-4°.

Later the arterial pressure fell by 20% compared with its initial values, and the body temperature fell by 5°.

During the first few hours after burning no hemoconcentration was observed. The circulating blood volume fell below its initial level as the result of a decrease of 20% in the circulating plasma volume.

A. V. Vishnevskii Institute of Surgery, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR S. A. Sarkisov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 69, No. 6, pp. 113-116, June, 1970. Original article submitted November 24, 1969.

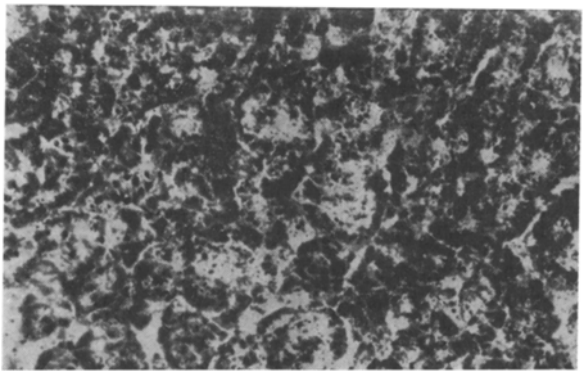

Fig. 1. Accumulation of lipids in zona fasciculata of adrenal cortex of a rabbit dying on the 8th day after burning. Sudan III, 200×.

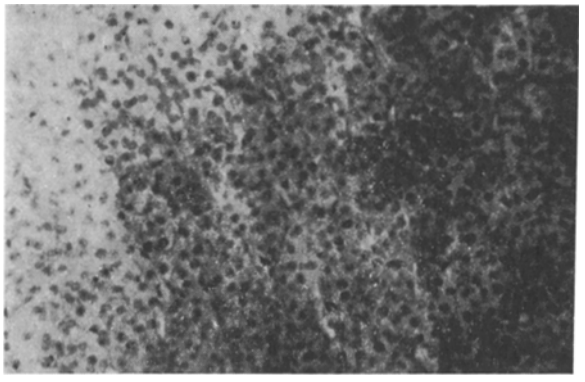

Fig. 2. High alkaline phosphatase activity in adrenal of a rabbit dying on the 8th day after burning. Gomori's reaction for alkaline phosphatase, 200×.

On the first day after burning 50% of the rabbits died in a state of burn shock.

From 3 to 8 h after burn trauma focal vasodilatation developed in the adrenal cortex of the rabbits, and was especially marked in the zona reticularis and in the inner layers of the zona fasciculata of the cortex. Cells of the zona fasciculata were filled with lipids and cholesterol crystals.

Only a small amount of lipids was found in the zona glomerulosa and zona reticularis. Numerous granules of ascorbic acid were visible in the upper and middle layers of the zona fasciculata. Alkaline phosphatase activity in the cells of the zona fasciculata and zona glomerulosa was very low. Substantial activity of this enzyme was found only in the zona reticularis of the adrenal cortex.

Considerable circulatory disturbances were found in the adrenals 24 h after burning and the capillaries in all zones of the cortex were dilated and congested. The content of lipids and cholesterol crystals was slightly lower than in the adrenal cortex of intact animals and of animals sacrificed 3-8 h after burn trauma. In a few cases lipids were present in the cells as fine granules, whereas in the adrenals of healthy animals they occurred mainly as large drops. Granules of ascorbic acid were detected only in the upper layers of the zona fasciculata.

Alkaline phosphatase activity was negligible in the zona glomerulosa and zona fasciculata of the adrenals, just as in the healthy animals.

Hyperplasia of the adrenal cortex was observed 48-72 h after burning. The weight of the adrenals increased to 995-1050 mg (normal weight 500-700 mg). The thickness of the cortical layer was 1.08 mm (normally 0.72-0.78 mm). Numerous "compact" cells, i.e., cells containing no lipids or cholesterol and with cytoplasm densely stained with eosin, were found in the zona fasciculata. High alkaline phosphatase activity was present in these parts of the cortex. The appearance of compact cells in the adrenal cortex has been attributed to an increase in the glucocorticoid function of the adrenals [1, 13].

A marked decrease in the content of ascorbic acid in the adrenal cortex took place 48-72 h after burning. Its granules became thinner and were located in a narrow band of cells, under the zona glomerulosa. Just as in the preceding experiments, the capillaries were congested, but to a greater degree.

A considerable increase in weight of the adrenals (to 1500 mg) was found 8 days after burning, on account of widening of the cortical layer to 1.2 mm. Congestion of the capillaries was severe, and in some parts of the cortex stasis was observed. In the zona fasciculata lipids and cholesterol had accumulated once again (Fig. 1). In the inner layers of the zona fasciculata and in the zona reticularis high alkaline phosphatase activity was detected (Fig. 2). The ascorbic acid content in the adrenal cortex 8 days after burning was variable; in some cases only a few ascorbic acid granules were observed in the zona glomerulosa and the upper layers of the zona fasciculata, while in others the ascorbic acid content in the adrenal cortex was high.

Investigation of the concentration of 17-hydroxycorticosteroids in the urine showed a decrease 24 h after burning to 0.14 mg% (normal level 0.36-0.40 mg%). On the 2nd day the concentration of 17-hydroxycorticosteroids in the urine rose again to the normal level. Some animals had anuria on the 1st and 2nd

days after burning. In these cases a low concentration of 17-hydroxycorticosteroids was found in the urine on the 2nd and 3rd days after burning. The steroid level rose on the 3rd and 4th days after burning.

Considerable depression of adrenal cortical function was thus established in the period of burn shock, as shown by the decrease in concentration of 17-hydroxycorticosteroids in the animal's urine on the 1st day and, in the case of anuria, on the 2nd and 3rd days after burning. This inhibition of secretion of glucocorticoids evidently did not take place as a result of the development of destructive changes in the adrenal cortex, for morphological investigations revealed absence of any marked degenerative changes in the cortical cells. The most useful hypothesis to account for this phenomenon is that of Knigge [11], who claimed that in the torpid phase of burn shock the hypothalamic control of the adrenocorticotropic function of the pituitary is inhibited and, as a result, the liberation of ACTH into the blood stream stops. Lowering the ACTH content sharply depresses adrenal cortical function. An increase in the level of hydroxycorticosteroids to the normal level and, in some cases, above it evidently took place when the animal emerged completely from the state of shock. Hyperplasia in the adrenal cortex, a feature of the adaptation reaction, developed 48-72 h after burning. Similar histological pictures have been found during the investigation of the adrenals of patients dying from burn shock and in the stage of acute burn toxemia [6, 8]. It thus follows that there are many common features in the pathogenesis of experimental burn shock and of shock observed in clinical practice.

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