ACTION OF IMMUNOMODULATORS ON THE ADRENALS OF MICE OF DIFFERENT STRAINS

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The adrenals play an important role in adaptation to many types of stress, such as severe infectious diseases, toxic conditions, and so on. The mechanism of action of the adrenals in these complex processes is not clear, but the importance of many hormonal, nervous, and alimentary factors for adaptation is only just beginning to be understood.

Differences in hormonal regulation of metabolic processes under the influence of different preparations, including immunomodulators, determine the direction of their action.

Cortisol is the principal member of the glucocorticoids and it acts on different spheres of metabolism, but predominantly it regulates the metabolism of organic compounds. Clearly disturbances of cortisol metabolism have a profound effect on the ability of the body to adapt itself to real life, and for that reason this hormone was chosen as our test object.

The aim of this investigation was to study the functional morphology of the adrenals and the blood cortisol level in mice of different strains, under the influence of immunomodulators of bacterial origin, using a combination of morphological, histochemical, and biochemical methods.

EXPERIMENTAL METHOD

Experiments were carried out in the fall and winter on male mice aged 3 weeks, belonging to the following lines: CBA, C57BL/6, BALB/c, and (CBA × C57BL/6)F_1 hybrids. Intact mice of the same lines served as the control. Immunomodulators of bacterial origin were used: Salmozan, a polysaccharide from *Salmonella typhi abdominalis* (obtained at the N. F. Gamaleya Research Institute of Epidemiology and Microbiology, Academy of Medical Sciences of the USSR, under the direction of Professor M. A. Tumanyan), and staphylococcal enterotoxin A, an immunomodulator of protein nature with mol. wt. of 29,000 (from the Ufa Research Institute of Vaccines and Sera). Salmozan (S) and staphylococcal enterotoxin A (SE) were injected subcutaneously in a dose of 100 and 1 μg/mouse respectively. During the first day after injection of the immunomodulators the blood cortisol level was determined by a fluoroimmunometric method (DELFA). The functional morphology of the adrenals was evaluated by means of a combination of morphological and histochemical methods.

EXPERIMENTAL RESULTS

The morphological and histochemical investigations indicate that immunomodulators cause considerable changes in the endocrine status of the animal, the character and severity of which depend on the line of mice and the chemical nature of the immunomodulators.

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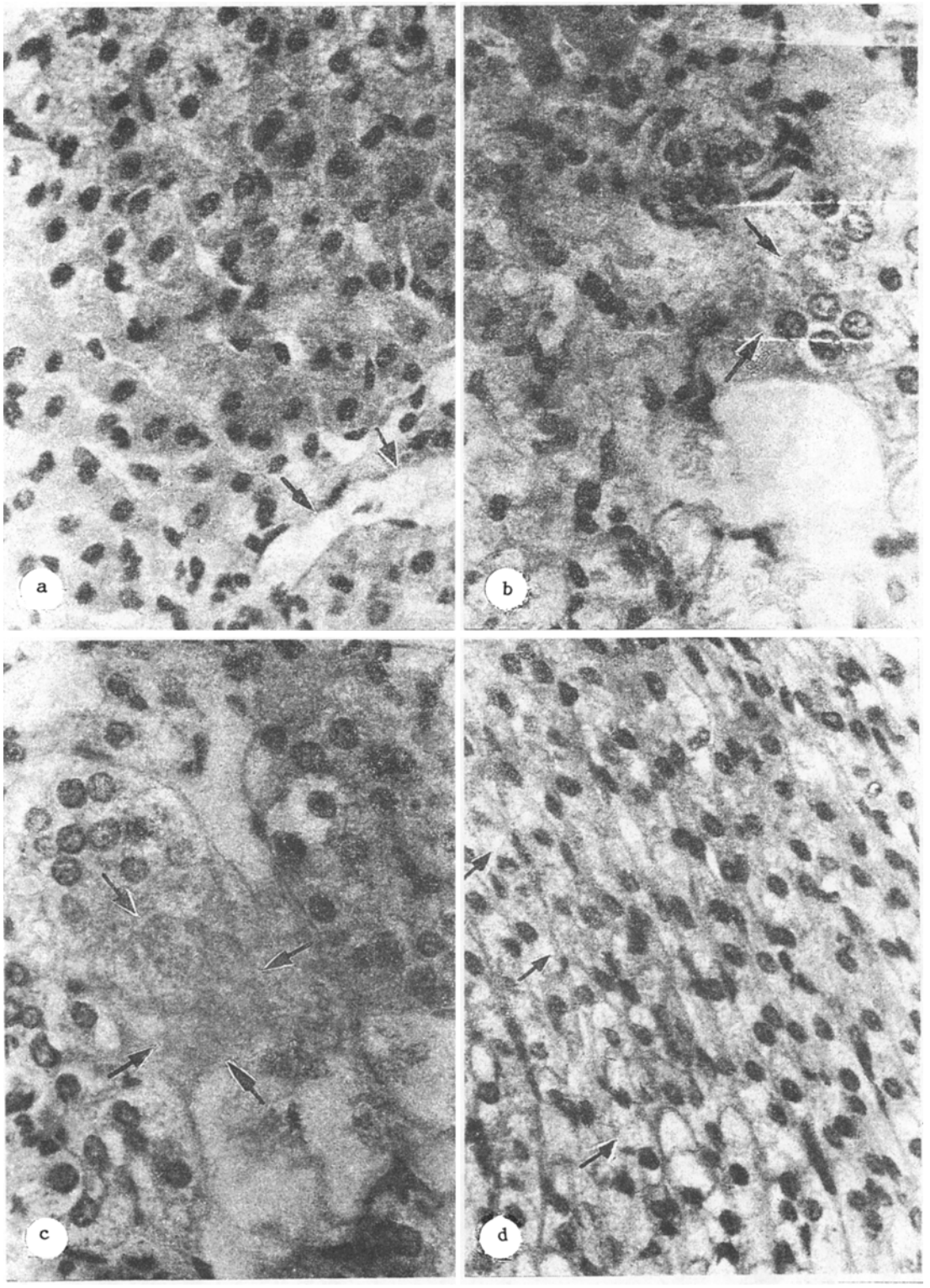

Fig. 1. Characteristic changes in adrenals of mice of different lines under the influence of immunomodulators of bacterial origin. Stained with hematoxylin and eosin. 900×. a) Adrenal medulla of CBA mice during first 10 h after injection of SE: marked congestion, irregular vasodilatation, blood vessels packed with sludged cells; b, c) the same group. Structures revealing degenerative (b) and necrotic (c) changes visible in adrenal medulla toward 24 h of the experiment; d) adrenal cortex of C57BL/6 mouse receiving injection of S. Cells of zona fasciculata in a state of increased functional activity.

A study of morphological changes in CBA mice revealed sharp changes in the hemodynamics of the adrenals, which showed a weak focal tendency to return to normal 24 h after injection of SE and S. The clearest reaction was observed in cells of the zona fasciculata and zona glomerulosa: the changes were mosaic in character and the cells were polymorphic and heterochromic. The adrenal cortex was reduced in thickness and deprived of lipids. The medulla during the first 10 h after injection of SE was highly congested and the blood vessels were packed with sludged cells (Fig. 1a). By 24 h the morphological features of adrenal functional stress were mild and some evidence was obtained of degenerative changes and foci of necrosis in the medulla (Fig. 1b, c). The adrenals of C57BL/6 mice receiving an injection of S were in a state of increased functional activity (Fig. 1d), with a moderate decrease in the lipid content of the cortical cells and focal degeneration of the medullary cells.

Injection of the immunomodulators into mice of different lines was accompanied by marked changes in their blood cortisol level. Interlinear differences were observed in the character of the change of the blood hormone level. These differences were greatest in CBA and C57BL/6 mice.

In C57BL/6 mice injection of S and SE caused uniform changes in blood cortisol: a sharp rise in the concentration of the hormone during the first 10 h after injection followed by a fall until 24 h, below the control level. In CBA mice, changes in cortisol in response to injections of S and SE were similar in character only during the first 10 h of the investigation, and thereafter they differed sharply.

It can be tentatively suggested that interlinear differences in the character of the effect of immunomodulators on hormonal activity are determined by the particular features of their action on the enzyme balance in mice of different lines, and they depend on the initial endocrine status of the animal. For instance, CBA and C57BL/6 mice differ with respect to their initial blood cortisol and corticosterone levels, they are opposite as regards the action of ACTH [2], and they also exhibit significant differences in adrenal morphology.

On the basis of these results it is possible to devise a scientifically based tactics for the use of immunomodulators and their individual selection which will take into account the original endocrine status of the recipient.