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Thymus Atrophy

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Abstract. The article is devoted to thymus atrophy. It was revealed that from the morphological point of view, atrophy is similar to age-related involution: the division into cortex and medulla disappears, the thymus is replaced by connective and adipose tissue, and the number of mitoses decreases, according to bromodeoxyuridine staining. A significant difference between atrophy and age-related involution is the fact that when the factor causing induced atrophy is eliminated, the thymus is restored, while in age-related involution, reverse restoration of the thymus is not observed.

Key words: thymus, atrophy, influencing factors, characteristic signs.

INTRODUCTION.

. There is such a thing as thymus atrophy, and unlike age-related involution, it is not related to age. For example, thymus atrophy that occurs during pregnancy is not related to age, but rather to the importance of reducing the immune response to the fetus. Thus, the thymus is the most sensitive of the lymphoid organs to various influences. Provoked by various factors, induced atrophy is observed in inflammatory reactions, infections of various etiologies, thymomas, allergic reactions, physical overloads and psychological stress. The thymus is sensitive to toxins, pharmacological agents. For example, chemotherapy, especially glucocorticoid hormone therapy, causes strong changes. Thymus atrophy has also been established during hibernation in some animals [6,13].

The study of thymic atrophy in humans is limited to noninvasive methods such as chest computed tomography and autopsy or post-thymectomy thymus examination. Therefore, many animal models of atrophy induced by the administration of various substances or mechanical effects have been developed [2,10].

In his experiments, Selye induced atrophy by administering morphine, formaldehyde, atropine, and noradrenaline. The adaptive syndrome was accompanied by hypertension, which in turn was caused by the release of adrenaline and noradrenaline into the blood. The sizes of the thymus and adrenal glands changed in mutual proportion. Selye suggested that atrophy was not caused by adrenaline itself, and this was confirmed experimentally when no atrophy was observed after resection of the adrenal glands and administration of adrenaline. The same result was obtained when other drugs were administered instead of adrenaline. If the drugs themselves do not directly cause atrophy, then it follows that atrophy of lymphoid organs is caused by corticosteroid hormones. The release of corticosteroid hormones by the adrenal cortex occurs under the influence of adrenocorticotropic hormone (ACTH), synthesized by the pituitary gland. It should be noted that the thymus is subject to atrophy more than all other lymphoid organs, the spleen and lymph nodes are less susceptible, and the bone marrow is least susceptible [11,12].

Henry Jaffe found that secondary hyperplasia of the thymus was observed in rabbits and rats when both adrenal glands were removed. During the operation in the experimental group, the thymus in the control animals showed signs of involution. That is, the size of the cortex decreased, and fatty infiltration was observed. In the experimental group, the thymus structure resembled the thymus of young, immature animals with a fairly wide cortical zone and densely packed thymocytes. The most valuable experiment was one in which Jaffe removed one lobe of the animal's thymus and left the other, but completely removed the adrenal glands. After 13-17 days, the second lobe was removed during autopsy. The difference in the structure of the lobes of the same animal was striking. In the first, control, lobe, signs of involution were clearly expressed, while in the second, experimental, hyperplasia and regeneration of lymphoid tissue were observed [9].

Glucocorticoids are a group of steroid hormones and are derivatives of cholesterol. In this they are similar to sex hormones, which affect age-related involution of the thymus. In humans, the main glucocorticoid hormone is cortisol, and in mice, it is corticosterone. Stress is the strongest stimulus for the secretion of ACTH, which in turn causes the release of glucocorticoid hormones. Glucocorticoid receptors are cytoplasmic receptors that are complexed with heat shock proteins and contain a DNA-binding domain. This complex, having bound to a ligand, moves to the nucleus, where it binds to certain transcription factors or directly to DNA. According to some studies, glucocorticoid hormones have a stronger effect on T cells than on B cells. Glucocorticoid hormones cause atrophy of the cortex, and drugs such as cyclosporine and tacrolimus lead to atrophy of the medulla [16].

Glucocorticoids can affect the thymus both negatively and positively. Depending on the age of the animal, the concentration of glucocorticoid hormone and the sensitivity of thymocytes. Therefore, the role of glucocorticoid hormones in regulating thymopoiesis is also ambiguous and may differ in normal conditions and under stressful conditions [15].

When their level increases excessively over a long period, glucocorticoids can cause harm, but in general they play a key role in the processes of adaptation to stress. Apoptotic death of thymocytes via the mitochondrial pathway is stimulated by glucocorticoid hormones. This effect is tissue-specific and is characteristic to a greater extent of myeloid cells. In connective tissue cells and in the epithelium of the mammary gland, ovarian follicles, and liver, they have the opposite effect - a protective effect. An endogenous increase in the concentration of glucocorticoids during the formation of an immune response provides protection of the body from the harmful effects of cytokines, histamine and nitric oxide, due to their excessive amount. In the thymus, the concentration of glucocorticoids is normally maintained at one level due to the fact that the epithelial cells of the thymic stroma themselves produce a certain amount of glucocorticoid hormones. However, sensitivity to this hormone at different stages of thymocyte development is different, since the density of receptors for this hormone in thymocytes changes due to the passage of different stages of their development [3].

The thymus also atrophies when exposed to non-specific stress factors, such as immersion under water or movement restriction in mice. This effect is observed due to an endogenous increase in the level of glucocorticoid hormones against the background of stimulation of the hypothalamic-pituitary system and adrenal glands. Methoxychlor (insecticide) imitates the action of estrogens and leads to thymus atrophy. Thymus atrophy is also observed with a deficiency of certain vitamins and minerals, such as

zinc and iron. In the case of zinc, atrophy is associated with apoptosis of thymocytes in the cortical zone. However, in the case of iron, it has been shown that it is necessary for lymphocyte proliferation, so with a deficiency of this metal, thymus atrophy is more likely associated with a decrease in proliferation. Magnesium deficiency leads to thymus atrophy due to an increase in the intensity of apoptosis [5].

After the introduction of bacterial lipopolysaccharide to mice, apoptosis of thymocytes is also observed, which is most likely also mediated by glucocorticoid hormones, since apoptosis was not observed in animals after adrenalectomy. The immunosuppressive effect of progestins is known, which was described in patients after hormonal therapy for endometrial and breast cancer. When rats were given the synthetic progestin medroxyprogesterone acetate, pronounced thymus atrophy was observed with a decrease in the thickness of the cortex and the number of thymocytes in it, as well as with impaired lobulation and a decrease in the number of lobules. The growth hormone somatotropin, when administered in high doses, also leads to pronounced thymus atrophy [1].

In malignant neoplasms, thymus atrophy may or may not be observed depending on the tumor type. Thus, of three breast adenocarcinoma cell lines, only one resulted in pronounced thymus atrophy [7].

Since a huge range of anti-inflammatory drugs needed to treat thousands of people contain glucocorticoid hormones, the study of their effect on the immune system is of great practical importance. In cases of malnutrition and acute infections (AIDS, malaria, rabies, etc.), especially in children, the thymus is also subject to severe atrophy due to mass apoptosis of lymphocytes in the cortex, sometimes the cortex practically disappears. The thymus has even been called a "barometer of malnutrition." This should be taken into account when treating such children, since when proper nutrition is prescribed, the structure of the thymus is restored within 2 months [4,14].

Stress-induced atrophy is a reversible process. From a histological point of view, the restoration of the thymus in mice begins 2-3 days after the administration of 0.5 mg of hydrocortisone, but the organ weight continues to decrease, especially in males. Similar results were obtained in experiments with the administration of cyclophosphamide to immature mice: in the early stages, pronounced atrophy with inversion of the cortex and medulla and a decrease in the thymus weight is observed, by the 30th day, the histological structure is restored, and the difference in organ weight between the experimental and control animals is only 9.9%, as opposed to 30.2% on the 1st day. When glucocorticoid hormones are administered at a dosage of 0.5 mg, the restoration of the thymus after atrophy in mice takes approximately 2 weeks [8].

Leptin may act as an agent protecting against stress-induced atrophy. Its positive effect on atrophy caused by the introduction of lipopolysaccharide has been experimentally demonstrated. Presumably, the mechanism of leptin action is associated with its inhibitory effect on the synthesis of glucocorticoid hormones [17].

Conclusion. Thus, from the morphological point of view, atrophy is similar to age-related involution: the division into cortex and medulla disappears, the thymus is replaced by connective and adipose tissue, and the number of mitoses decreases, according to bromodeoxyuridine staining. An essential difference between atrophy and age-related involution is the fact that when the factor causing induced atrophy is eliminated, the thymus is restored, while in age-related involution, there is no reverse restoration of the thymus.

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