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Study of the Influence of Hypothyrous and Thyrotoxicosis on the Morphological Structure of the Spleen in Experimental Animals with Implanted Akatol Tumor

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Abstract:
Currently, the problem of combating malignant neoplasms is not only one of the most urgent in medicine, but also affects many aspects of the social life of society. The high rates of mortality from malignant neoplasms and the associated significant socio-economic losses make it possible to reasonably consider the fight against malignant neoplasms as a state problem.

Keywords: AKATOL, thyroid hormones, apoptosis, thyrotoxicosis, melanoma, proliferation of reticular tissue.

INTRODUCTION

In the last decade, the question of the relationship between thyroid and other non-thyroid pathologies has become very significant. Its importance has increased in the situation of improving the diagnosis of thyroid diseases and increasing the incidence of them (Abduvaliev, Ismayilova, Gildieva & Saatov, 2010; Abduvaliev, Gildieva & Saatov, 2006). In addition, the significance of the issue under consideration was actualized in connection with the receipt of new data on changes in thyroid status in non-thyroid diseases (Abduvaliev, Gildieva & Saatov, 2005; Agol, 1996; Appay, Sauce & Prelog 2010; Bazarov, Rajamuradov, 2020). Violation of the secretion of thyroid hormones in the body often leads to the emergence of a number of cancers (thyroid cancer, breast cancer, skin melanoma, etc.), (Azimova, 2008; Akramova, Umerov, Saatov, 2002). However, at present, the mechanisms of action of thyroid hormones on the development and suppression of the tumor process still remain unclear. Disclosure of the peculiarities of the mechanism of interrelation of the endocrine and immune systems will allow using the obtained results in order to inhibit the proliferation of tumor cells, search for new targets for chemotherapeutic agents capable of influencing the molecular mechanisms occurring in tumor cells and leading to inhibition of their proliferation or apoptosis (Axel, 2006; Artykbaeva, 1993; Babaeva, Gevorkyan, Zotikov, 2009).

MATERIALS AND METHODS

For histological examination, 1 cm^3 of a tumor sample was taken. This site was fixed in 10 % normal formalin. Then the tissue was embedded in paraffin and sections of histological preparations with a thickness of 4-5 μm were prepared, staining them with a mixture of hematoxylin + eosin and in them cells in the apoptosis stage were counted under a microscope according to the following signs: blebbing of the plasma membrane, condensation of nuclear chromatin along the periphery of the nucleus, a decrease in its size (pycnosis), the formation of DNA fragments with a high molecular

weight (karyorexis), DNA cleavage into oligonucleosomal fragments (ladder type), densification of cell organelles, a decrease in the volume of cytoplasm, a bubbly appearance of the cell membrane, budding of cell fragments with the formation of discrete apoptotic bodies surrounded by membrane and containing compacted remains of organelles and nuclei (Baryshnikov, 2003; Bueverov et al., 2000; Vasiliev, 1997; Vasiliev, 1997). The number of apoptotic cells was expressed as a percentage relative to the total number of counted cells (Volyansky et al., 2008; Granov, Shutko, 2002).

In an in vivo experiment on the model of a tumor strain of adenocarcinoma of the large intestine AKATOL, the effect of hypothyroidism and thyrotoxicosis on morphological changes in the spleen of BALB / c mice was studied. The experimental animals were divided into 4 groups: Group I - the animals underwent thyroidectomy (removal of the thyroid gland), which caused hypothyroidism, i.e. lack of T_4 in the body; Group II - animals received T_4 per os in a high (5 mg / kg) dose, which led to the development of thyrotoxicosis, i.e. an excess of T_4 in the body; Group III - tumor-bearing animals were not exposed to any effect; Group IV - control, intact healthy animals that did not undergo tumor implantation (Ivchenko et al. 2005; Ismailov, 2007; Ipatov, 2003; Karpova et al. 2000).

Statistical processing of the data obtained was carried out using the Student-Fischer method in relation to biological research (Lakin, 1990). Differences at the level of significance $p < 0.05$ were considered significant.

RESULTS AND DISCUSSION

Table 1 shows the results of changes in the weight of the spleen in the experimental groups. The greatest increase in the spleen mass was observed in group II, where thyrotoxicosis was modeled - the organ mass increased by 108.69 % compared to the control group IV.

Table 1: Spleen weight in BALB / c mice with induced hypothyroidism and thyrotoxicosis under experimental carcinogenesis

Group	Spleen weight, mg
Group I. Hypothyroidism	211,0±14,6*
Group II. Thyrotoxicosis	384,0±32,18*
Group III. Intact tumor-bearing animals	236,0±17,7*
Group IV. Healthy animals without tumor implantation	184,0±17,0

Note: * - $p < 0.05$ (in comparison with group IV)

The smallest set of spleen mass was in group I (hypothyroidism) - the organ mass increased by 14,67 % compared to the control group IV. In group III, in tumor-bearing mice without any effect, the spleen mass increased by 28,26 % compared to the control. Histological examination of the spleen of group IV mice showed its normal structure. Trabeculae of the spleen departed from the connective tissue capsule inside, which anastomosed each other in its deep parts. The ratio of the red and white pulp is shifted towards the red pulp, consisting of reticular tissue with cellular elements of the blood located in it and numerous blood vessels, mainly of a sinusoidal type, which indicates a normal blood filling of the organ. In the pulp cords located between the sinuses, foci of plasmacytogenesis were revealed. Lymphoid tissue (white pulp of the spleen) was located in the adventitia of its arteries in the form of globular clusters or elongated lymphatic sheaths (lymphatic follicles) (Fig. 3). They passed the central arteries, which were located eccentrically. Hemocapillaries departed from the lymphatic follicles towards the marginal sinuses of the red pulp. In lymphatic follicles, three indistinctly demarcated zones can be distinguished: periarterial (center of reproduction), mantle layer and marginal (marginal). In the field of view, 3-4 follicles with blurred boundaries were observed. The number of cellular elements is average, the megakaryocytic reaction is weak – 13,5 ± 6,38%, tissue proliferation is average (Appay et al. 2010).

In the spleen of mice of group III (tumor-bearing animals without exposure), the pulp prevailed over the red, which indicates irritation of the lymphoid tissue with antigens. Spleen trabeculae, extending

from the connective tissue capsule inward and in its deep parts, anastomosing to each other, were mainly represented by elastic fibers, since the capsule and trabeculae constitute the spleen's musculoskeletal system. The red pulp, occupying a relatively small area, contained a large number of hemocapillaries. In the field of view, 3-4 follicles were observed without a center of reproduction, with blurred edges (Fig. 1). The number of cellular elements is average, the megakaryocytic reaction is expressed – 28,0 ± 8,93%, tissue proliferation is low.

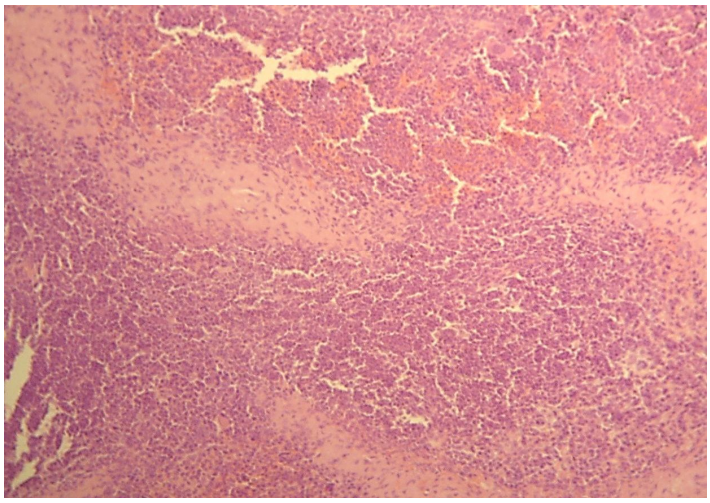

Figure: 1: Spleen. Group IV (control). White and red pulp. Staining with hematoxylin and eosin. Uv. OK. 10x, rev. 10x.

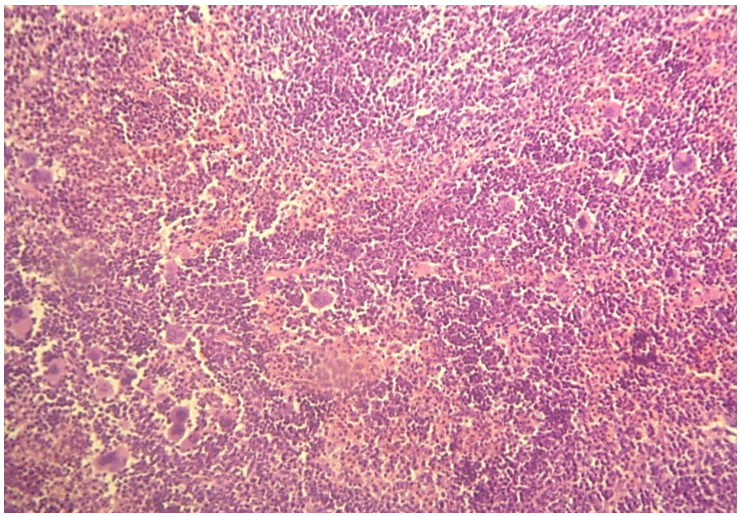

Figure: 2: Spleen. Group III (tumor-bearing animals without exposure). High megakaryocytic response. Staining with hematoxylin and eosin. Uv. OK. 10x, rev. 10x.

In the spleen of mice of group I, where hypothyroidism was simulated, histological examination revealed changes characteristic of inflammatory reactions: plethora, exudation and leukocyte infiltration of the spleen pulp, proliferation of B-lymphoblasts in the centers of follicular reproduction; clusters of macrophages with phagocytosed lymphocytes or their fragments in the form of chromophilic bodies; degenerative and necrotic changes in the tissue elements of the pulp and follicles (Fig. 2). In the field of view, 2-3 follicles were observed without a center of reproduction, with clear boundaries. The number of cellular elements is average, the megakaryocytic reaction is expressed – 31,0 ± 7,81%, tissue proliferation is low.

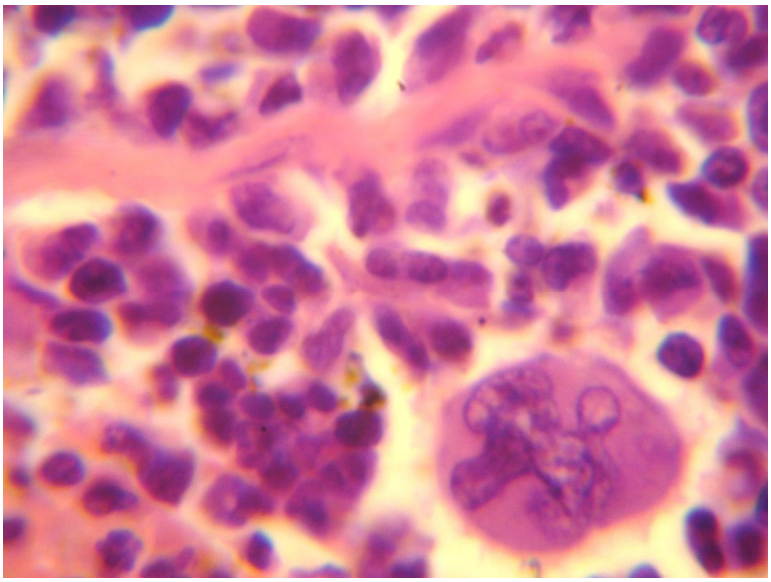

Figure 3: Spleen. Group II (thyrotoxicosis). Megakaryocyte (arrow). Staining with hematoxylin and eosin. Uv. OK. 10x, rev. 100x.

In the spleen of mice of group II, where thyrotoxicosis was simulated, changes characteristic of inflammatory reactions were also revealed: plethora, exudation and leukocyte infiltration of the spleen pulp, proliferation of B-lymphoblasts in the centers of follicular reproduction; clusters of macrophages with phagocytosed lymphocytes or their fragments in the form of chromophilic bodies.
At the same time, in the histological preparations of the spleen of this group, signs of normalization of the structure of this organ were established. Numerous lymphatic follicles were distinguished: periarterial zones (centers of reproduction), occupying small areas of the follicle near the arteriole; the mantle layer with a layered arrangement of small T- and B-lymphocytes, which form a "crown", stratified by circularly directed thick reticular fibers; the marginal zone, which is a transitional area between the white and red pulp. Follicular proliferation centers consisted of reticular cells and proliferating B-lymphoblasts. Small clusters of macrophages were also found here. The red pulp predominated over the white. The basis of the pulp was the reticular tissue, which forms its stroma.
In the adventitia of the arteries penetrating the spleen, lymphoid tissue was determined in the form of round or oval clusters - lymphatic follicles. In the field of view, 3-4 follicles with blurred boundaries were observed. The number of cellular elements is average, the megakaryocytic reaction is weak – 19,83 ± 2,6%, tissue proliferation is low (Fig. 3).

CONCLUSION

Thus, the lack of thyroid hormones leads to degenerative and necrotic changes in the tissue elements of the pulp and spleen follicles, while the norm or excess of T4 induces the normalization of the structure of this organ under conditions of experimental carcinogenesis.

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