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Influence of Heavy Metal Salts on the Morphology of the Spleen

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Abstract: The spleen exhibits a high level of reactivity with cytological restructuring of its immunocompetent structures under the influence of various endo- and exogenous factors, including heavy metals. Currently, it is known that the adaptive immune function, which determines the cellular and humoral homeostasis of the organism, is carried out by the organs of the immune system. Its morphological basis is lymphoid tissue, organized into functional formations, the largest of which is the spleen. This article presents a review of the literature on the influence of heavy metal salts on the morphology of the spleen.

Keywords: heavy metal salts, white pulp, red pulp, spleen, morphology, morphometry.

Introduction

The spleen is a complex and largest multifunctional peripheral organ of the immune system, in which the intensity of immune and filtration processes is closely related to the architectonics of its white and red pulp, the ratio of the areas occupied by functionally different departments to the quantitative composition of their cellular compartments. At the same time, the spleen exhibits a high level of reactivity with cytological restructuring of its immunocompetent structures under the influence of various endo- and exogenous factors, including heavy metals. Currently, it is known that the adaptive immune function, which determines the cellular and humoral homeostasis of the organism, is carried out by the organs of the immune system. Its morphological basis is lymphoid tissue, organized into functional formations, the largest of which is the spleen [Volkov V. P., 2015].

The study of the structural and functional properties of the spleen is an urgent problem, since the immune apparatus of the spleen, according to many researchers, has a much more complex structure than other peripheral organs of the immune system. It is characterized by its specificity, determined by the specific interaction of lymphoid cells and stromal cells, which creates a special microenvironment of each area of the spleen and ensures the formation of an adequate immune response [Bashina S.I., 2022].

The high sensitivity of the spleen to the effects of factors of various origins and the ability to respond to adaptive changes in morphological organization, one of the first in the body, have been experimentally proven [Arlashkina O., 2016]. These facts determine the possibility of using the spleen as an experimental object for assessing the immunomodulatory effect of external factors.

According to the International Registry of Metabolic Disorders (Fifth IFSO Global Registry Report 2019), it can be concluded that the combined effects of heavy metal compounds, in particular, base metal pollutants, cause significant disorders in the body, which differ in the

degree of damage from the effects caused by each element separately. In many studies, an increase in the process of lipoperoxidation plays an important role in the pathogenesis of chronic heavy metal poisoning [Gorbachev D.O., 2024].

Methodology

Lipid peroxidation products cause secondary damage, primarily to the formation of cell membranes, reduce the function of enzymes, regenerative processes, and from a certain point serve as the main pathogenetic factor in the development of intoxication syndrome. The effects of dioxins and a number of heavy metals reduce the phagocytic activity of macrophages, the proliferation and maturation of thymocytes. Many heavy metals (lead, mercury, cadmium, cobalt, thallium, titanium, tungsten), dioxins, polychlorinated and polycyclic hydrocarbons have a suppressive effect on local and systemic immunity [Елизарьева Е. Н., 2016].

According to Ермолина Е. В., et al. (2012), the effect of chromium on spleen morphology was studied. During the observation period, the spleen of animals showed a fullness of trabecular and pulp vessels, as well as an increase in the volume of lymphoid follicles. The hyperplastic reaction of the germinal zones is combined with the accumulation of plasma cells and macrophages in them. A large number of siderophages were found in the red pulp of the organ in the spleen. The appearance of such cells and their increase in their number indicate a high infiltration of the intercellular structures of the spleen with hemosiderin. In some areas of the spleen, small foci of necrosis and diapedetic hemorrhages were noted around sharply dilated pulp vessels. In reactive areas, cells with signs of karyopyknosis and karyorrhexis were noted against the background of activation of plasmacytic-macrophage elements. As a result of immunocytochemical studies of the immune system of rats on days 45 and 90, apoptotic thymocytes and lymphocytes with characteristic changes in their nuclei and cytoplasm were detected in the T-dependent areas of the spleen and lymph nodes [Ермолина Е. В., 2012].

It should be noted that the content of cells prone to apoptosis (measured by the expression of p53 protein synthesis) and cells showing apoptosis (caspase 3-positive) increased when chromium was administered to animals. It can be concluded that the chromium mixture has an enhancing effect on the expression of proapoptotic genes in immunocompetent cells. The appearance of such apoptotic cells and their groups probably indicates intracellular induction of programmed cell death. Taken together, the data indicate a decrease in the activity of T-lymphocytes, which clearly reflects the state of T-cell immunodeficiency. This probably occurs against the background of immunocyte dysfunction, which is consistent with previously obtained data on a decrease in the relative and absolute content of lymphoid cells in the spleen of rats on days 45 and 90 [Zhevlakova S.I., 2022].

Results and discussion

Cadmium occupies a special place among heavy metals as the most dangerous element [Gonokhova M. N., 2019]. The toxic effect of cadmium salts is enhanced by its high ability to accumulate. The ability of cadmium to accumulate for a long time in living organisms, due to the nature of the effect of this element on the human body, goes beyond the competition among ecotoxic metals [Drozdova, L.I., 2018].

Cadmium enters the body mainly with food and water. Then, through the portal vein, it enters the liver, where it partially accumulates, and then, possibly, with the help of blood and lymph exosomes (microvesicles), it spreads to other target organs, including the spleen [Danielyan G.A., 2020].

It is known that the spleen, in addition to its special importance in the body as one of the peripheral organs of the immune system, plays an important role in the mechanism of blood coagulation, the destruction of damaged blood cells and foreign particles, the formation of lymphoid elements and macrophages. It is known that lymphoid cells of the spleen are morphologically differentiated into small, medium and large lymphocytes, lymphoblasts,

immunoblasts and plasmablasts. On the 7th and 14th days of cadmium intoxication, Alekseeva N.T. (2021) showed that the relative weight of the spleen in white rats increased by 15% and 21%, the number of lymphoid nodes in it increased by 17% and 19%, respectively, compared to control values. The T- and V-dependent areas of the white pulp are clearly distinguished, the cells in them are represented by small and medium lymphocytes. On days 7 and 14, the number of nodes with light centers of proliferation increased by 15% and 17%, which indicates an immune response of the rat body to the effects of cadmium chloride [Alekseeva N.T., 2021].

The sinuses of the red pulp of the spleen were filled with blood, numerous small hemorrhages were visible. Diffuse small lymphocytes, as well as plasma cells, were observed. On day 21, the weight of the rats increased by 36%, and the number of lymphoid nodes and light centers of proliferation in them increased by 25%. In smaller nodes, only the T-dependent area was often detected. The central artery of the node was filled with blood, its wall was thickened. The sinuses in the red pulp of the spleen remained filled with blood, among which there were a large number of erythrocytes and plasma cells. The formation of small dark lymphocyte islands scattered throughout the spleen parenchyma was observed. The red pulp became full. The sinuses were dilated, filled with blood, and there were areas of hemorrhage. Several small clusters of plasma cells were noted. On the 30th day, the relative weight of the spleen remained at the same level, the lymphoid follicles in the white pulp increased in size, but their number did not differ significantly from the parameters of the previous period. The number of nodes with light-colored proliferation centers decreased slightly compared to the previous periods of the experiment. The formation of small dark lymphocyte islands scattered throughout the spleen parenchyma was also observed. The red pulp became full. Several small clusters of plasma cells were noted [Kvaratsheliya A. G., 2016].

In the dynamics of experimental chronic cadmium intoxication in mice, morphofunctional disorders in the spleen were revealed, which were characterized by a change in its mass, an increase in the number of red and white pulp, an increase in the number of lymphoid nodes of the white pulp, and nodes with centers of light proliferation in them, a pronounced plasma cell reaction of the red pulp. Together, they indicated the toxic effect of cadmium on the spleen and the implementation of immunity to the effects of cadmium chloride. The above allows us to classify the spleen not only as an organ of development of the immunotoxic effect of cadmium ions [Lastkov D. O., 2019].

Chromium belongs to the group of heavy metals, the specificity of which in the environment is determined by their stability, bioavailability and the possibility of negative effects at very low doses. Boron metalloid is a natural element of the earth's crust, widely distributed in nature in the form of boric acid, borates and borosilicates. People are exposed to boron primarily through the consumption of vegetarian foods, drinking water, mineral supplements and various consumer products. Boron is an essential element for plant growth. For humans, low levels of boron are beneficial for bone structure and normal brain function; high concentrations of boron can be toxic. Chemical compounds of chromium and boron worsen the ecological situation [Umbetov T. Zh., 2016].

Conclusion

As a rule, an increase in adverse anthropogenic factors leads to a significant increase in pathological conditions associated with immunity and allergies. If the immune defense of the human and animal body is mainly carried out by lymphoid tissue, the spleen is the largest collector of lymphoid tissue and, as the largest peripheral organ of immunogenesis, is responsible for the effectiveness of both innate and acquired immunity, cellular and humoral immunity. The content of lymphocytes in the white pulp of the spleen reaches 85% of the total number of cells, which is almost 25% of all lymphocytes in the body, and almost 50% of B lymphocytes in the white pulp of the spleen. Thus, the spleen, together with the lymph nodes, is an organ that provides humoral immunity. If the relative area of the lymphoid periarterial sheath in the white pulp tends to be 59.71±6.14% (57.06±5.17% in the control group), then the relative

area of the lymphoid nodes decreases slightly to 40.29±3.95% (42.94±4.23% in the control group). Changes are observed in the relative area of the functional areas of the lymphoid nodes of the white pulp. A significant decrease is observed in the relative area of the germinal center to 0.71±0.06% (0.83±0.08% in the control group). The area of the periarterial zone decreases to 1.61±0.09% (1.85±0.17% in the control group). The area of the mantle zone decreases to 4.81±0.39% (5.57±0.51% in the control group). The area of the marginal zone decreased by 0.97±0.08 (in the control group 1.28±0.07). In general, the area of lymph nodes in the experiment was significantly reduced to 8.1±0.79% (in the control group 9.53±0.97%). It should be noted that despite sufficiently large doses of combined poisoning of the body with potassium dichromate and sodium tetraborate, no obvious fatal changes were detected in histological sections. As a result of subacute combined poisoning of the body with chemical compounds of chromium and boron, the relative weight of the spleen decreases relative to the body weight of the animal, which leads to a decrease in the spleen weight coefficient to 2.85±0.29. (in the control group 4.09±0.41). The red / white pulp index increases significantly to 3.2±0.31 (in the control group 2.72±0.21). In studies, high concentrations of potassium dichromate and sodium tetraborate lead to a decrease in weight and spleen index [Мельникова О. В., 2016].

Taking into account the systemic nature of the reaction of lymphoid (immune) organs to the combined effects of potassium dichromate and sodium tetraborate, Lastkov D. O. (2019) suggests the possibility of developing functional insufficiency of all organs of immunogenesis and a decrease in the immune status of animals [Lastkov D. O., 2019].

As can be seen from the above literature analysis, the effect of heavy metal salts on the human body, especially on spleen morphology, has not yet been fully studied, which once again requires further scientific research in this direction.

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