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FEATURES OF THE STRUCTURAL ORGANISATION OF THE LIVER OF EXPERIMENTAL RATS 1 HOUR AFTER EXPOSURE TO THE VENOM OF THE SCORPION *LEIURUS MACROCTENUS*

Haidai O.S.  Features of the structural organisation of the liver of experimental rats 1 hour after exposure to the venom of the scorpion *Leiurus macroctenus*.

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ABSTRACT. Background. Scorpion stings are a serious threat to human health and life in almost all countries of the world. The amount and toxicity of the poison that enters the body of the victims depend on the interspecific variability of these animals. Scorpion venom usually causes the development of local, cardiotoxic, neurotoxic and vegetative effects. Depending on the predominance of one or another component in the venom, a wide range of clinical signs and symptoms can be observed from local reactions to serious consequences, including respiratory, gastrointestinal, cardiovascular or neurological complications. **Objective.** Study of the features of the microscopic organisation of the liver of experimental rats 1 hour after exposure to the venom of the scorpion *Leiurus macroctenus*. **Methods.** Experimental studies were conducted on 60 male rats (180 g±3 g), which were injected intramuscularly with 0.5 ml of the poison solution (28.8 mg/ml) ($LD_{50}=0.08$ mg/kg). For microscopic examination, liver tissue samples from animals of all groups were taken. Histological liver preparations were stained with hematoxylin and eosin. **Results and conclusion.** Microscopic studies one hour after administration of *Leiurus macroctenus* scorpion venom to rats demonstrated the appearance of minor shifts in the normal histoarchitectonics of the animal's liver. Hepatocytes were predominantly hexagonal in shape and contained one nucleus, but the presence of binucleated cells was noted. Infiltration of the portal tracts and sometimes the surrounding parenchyma of the organ with lymphocytes, histiocytes and neutrophils was stressed. Hepatocytes near the foci of infiltration underwent vacuolar dystrophy, which is a manifestation of reactive changes in response to the action of the venom.

Key words: venom, scorpions, morphology, liver, hepatocytes, rats.

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Introduction

Scorpion stings are a serious threat to human health and life in almost all countries of the world. The amount and toxicity of the venom that enters the body of the victims depend on the interspecific variability of these animals. Scorpion venom usually causes the development of local, cardiotoxic, neurotoxic and vegetative effects. Depending on the predominance of one or another component in the venom, a wide range of clinical signs and symptoms can be observed from local reactions (hyperemia, pain, oedema) to serious consequences, including respiratory, gastrointestinal, cardiovascular or neurological complications [1, 2, 3]. The severity of poisoning depends on the size and type of scorpion, the amount of venom injected, the body weight of the victim, and

the victim's sensitivity to the venom. Studies in recent decades have reported damage to the kidneys, liver, pancreas, heart, and hemolytic disorders as a result of poisoning with toxins from some scorpion species [4, 5, 6, 7].

The evolution of scorpions is approximately 400 million years, during which they have spread throughout the world. To date, more than 2,700 extant species of these animals have been recorded, numbering about 20 families. The extraordinary resilience, adaptability to changing climate conditions, and high survival rates of scorpions have contributed to their colonisation in tropical, subtropical, and temperate regions of almost all continents, except Antarctica and several Pacific islands [8, 9, 10, 11]. However, in recent years, the expansion of human civilisation and

the growth of the human population have led to a sharp reduction in the usual habitats of scorpions, but have significantly increased the frequency of poisonings due to their bites. In several regions of the world, including Central America, southern Latin America, Western Asia, North Africa, and the Middle East, scorpion stings have become a significant public health problem [12]. More than 1.2 million cases of scorpion stings are reported worldwide each year, with consequences ranging from localised pain or inflammation to severe clinical complications or death, depending mainly on the types and amounts of neurotoxins present in the scorpion venom [13, 14, 15, 16, 17]. In particular, most species of scorpions in the Buthidae family are more venomous than those in the Scorpionidae and Hemiscorpiidae families. A scorpion sting usually causes local pain that lasts for a few minutes. At the same time, neurotoxins secreted by venomous scorpions cause sympathetic excitation and release of catecholamines into the blood plasma, which leads to pronounced clinical manifestations, including high blood pressure, heart rhythm disturbances, pulmonary oedema, loss of consciousness and sometimes death [18, 19, 20].

The vast majority of scientific sources contain data on the damage to the cardiovascular, respiratory, nervous and excretory systems by scorpion toxins. A careful analysis of recent studies has shown a significant limitation of information on histological and biochemical changes in the liver under conditions of poisoning with scorpion toxins.

Fetaih H. A. et al. in experiments on mice studied histopathological changes in the structure of the liver under the influence of *Androctonus amoreuxi* scorpion venom. 6 hours after the introduction of $\frac{1}{4}$ LD₅₀, significant blood stasis was found in the vessels of the organ. On the 4th day, hydropic degeneration of hepatocytes, karyolysis and karyorrhexis of nuclei were noted. An increase in the concentration of the poison, namely $\frac{1}{2}$ LD₅₀, after 9 hours of observation showed the appearance of extramedullary hematopoiesis islands in the liver and dilation of sinusoidal capillaries. Already on the 4th day of the study, at the indicated dose of poison, dilation of blood vessels, fibrinoid degeneration, and deposition of weakly basophilic homogeneous material in the portal zones of the organ were detected [21].

The study aims to study the features of the microscopic organisation of the liver of experimental rats 1 hour after exposure to the venom of the scorpion *Leiurus macroctenus*.

Materials and methods

The study was carried out in accordance with the scientific research plans of the O. O. Bogomolets National Medical University and is a fragment of the scientific research works of the Department of Descriptive and Clinical Anatomy: "Morphological Features of Rat Organs under Experimental Exogenous Influence" (state registration number 0122U000491).

The study was conducted on 60 male rats (180

g \pm 3 g), which were injected intramuscularly with 0.5 ml of a solution of venom (28.8 mg/ml) (LD₅₀=0.08 mg/kg) of the scorpion *Leiurus macroctenus* dissolved in saline (0.9%) [22]. The control group (13 rats) was injected with only 0.5 ml of saline (0.9%).

The studies were conducted in accordance with the regulatory documents regulating the organisation of work with experimental animals and compliance with the principles of the "European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes" [23, 24]. Also, all work with animals was conducted in accordance with the Law of Ukraine No. 3447-IV of February 21, 2006, "On the Protection of Animals from Cruelty and Ethical Norms and Rules for Working with Laboratory Animals".

For microscopic examination, liver tissue samples were taken from animals of all groups. The pieces were fixed in 10% formalin solution for 1 day. Then the pieces were dehydrated in alcohols of increasing concentration and embedded in paraffin blocks. Histological preparations of rat livers were stained with hematoxylin and eosin [25]. Histological preparations were studied using a SEO SCAN light microscope and photographed using a Vision CCD Camera with an image output system.

Results and conclusions

Microscopic studies one hour after administration of *Leiurus macroctenus* scorpion venom to rats demonstrated the appearance of minor shifts in the normal histoarchitectonics of the liver. Hepatocytes were predominantly hexagonal in shape and contained one nucleus, but the presence of binucleate cells was noted. The cytoplasm of hepatocytes was oxyphilic and contained numerous inclusions. Their nuclei had 1-2 nucleoli, and the chromatin occupied a marginal position under the nuclear envelope. Hepatocytes formed hepatic plates that were ordered and located radially from the central vein (Fig. 1).

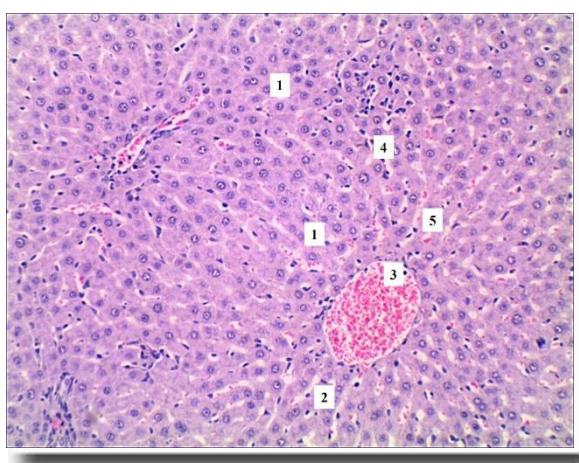


Fig. 1. Microscopic organisation of the liver of an experimental rat 1 hour after administration of the venom of the scorpion *Leiurus macroctenus*. Hepatocytes (1), hepatic laminae (2), lumen of the central vein (3), space of Disse (4), lumen of the sinusoidal capillary (5). Staining with hematoxylin and eosin. $\times 100$.

Sinusoidal capillaries between hepatic beams were somewhat dilated, and their lumen was mainly filled with erythrocytes. Endothelial lining of capillaries – without signs of desquamation from the basement membrane. Their endothelial cells are somewhat flattened and contain fenestrae in the cytoplasm. The presence of perisinusoidal Kupffer cells in the space of Disse was observed, which had an irregular shape and were distinguished by the presence of processes. They were characterised by elongated hyperchromic nuclei and weakly oxyphilic cytoplasm with numerous inclusions and a well-developed Golgi complex (Fig. 1, 2).

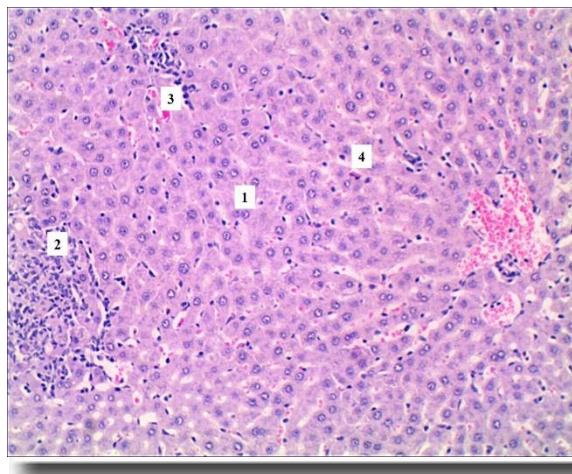


Fig. 2. Histological structure of the liver of an experimental rat 1 hour after administration of the venom of the scorpion *Leiurus macroctenus*. Hepatocytes (1), lymphohistiocytic infiltration (2), lumen of the sinusoidal capillary (3), space of Disse (4). Staining with hematoxylin and eosin. $\times 100$.

The bites of scorpions, *Leiurus quinquestriatus*, have been proven to cause changes in the morphological organisation of the rat liver. Histological examination of the organ after injection of the poison in animals at a dose of 0.03 mg/kg revealed pronounced oedema of hepatocytes, which led to a change in the shape of the cells and the "disappearance" of most sinusoidal capillaries. The cytoplasm of hepatocytes underwent vacuolization and the appearance of areas that did not respond to staining with hematoxylin and eosin. Hypochromia of the nuclei and their pyknotic changes were noted. Degenerative changes in individual nuclei and chromatin margination were also observed. In some fields of view, hepatocyte necrosis and stagnant phenomena in the portal vein branch were present [26, 27]. The lumen of the central vein in most histological samples was dilated. The endothelial cells of the inner lining of the vascular wall were elongated, and their nuclei were hyperchromic. Stasis of formed blood elements, mainly erythrocytes, was noted in the lumen of the central vein (Fig. 1).

A characteristic feature of the structural organisation of the liver, one hour after the start of the experimental study, was pronounced histiocytic and

lymphocytic infiltration of the portal tracts, sometimes with the presence of neutrophilic leukocytes. Lymphocyte accumulations were detected around the portal vein and bile ducts. However, in some fields of view, partial infiltration of the surrounding parenchyma was also observed. It should be noted that in these areas, individual hepatocytes had signs of vacuolar dystrophy. These structural changes can be regarded as initial reactive changes in response to the action of scorpion venom toxins. The walls of the bile ducts under these conditions did not undergo pronounced changes. They were lined with a single row of cubic cells. Their nuclei occupied a central position and contained one nucleolus. Chromatin had a marginal location, formed clumps or was diffusely scattered. The hepatic artery was distinguished by the presence of elongated endothelial cells of the inner membrane with round or oval hyperchromic nuclei. Some endothelial cells protruded into the lumen of the vessel in the form of palisades. The lumen of the hepatic vein was dilated, sometimes with erythrocyte stasis (Fig. 3, 4).

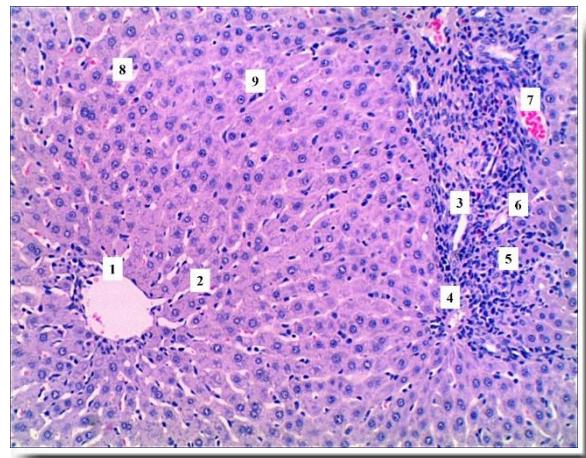


Fig. 3. Morphological organisation of the liver of an experimental rat 1 hour after administration of the venom of the scorpion *Leiurus macroctenus*. Central vein lumen (1), hepatic lamellae (2), bile duct lumen (3), hepatic artery (4), lymphohistiocytic infiltration (5), portal vein (6), hepatic vein (7), sinusoidal capillary lumen (8), Disse's space (9). Hematoxylin and eosin staining. $\times 100$.

Clinical observations of patients after scorpion stings and experimental studies demonstrate cases of toxic hepatitis and coagulopathy. Biochemical studies under these conditions show an increase in ALT, AST, and LDH, and rarely hyperbilirubinemia. The mechanisms of liver damage caused by scorpion stings remain unclear, although the hypothesis of direct hemolytic and cytotoxic effects of the venom prevails. In addition, stimulation of neurotransmitters, catecholamines and the release of cytokines and inflammatory mediators are usually associated with hepatotoxicity and haematological disorders. In addition, intravascular hemolysis, coagulopathy, and thrombocytopenia are characteristic, which may act as indirect factors of liver damage [28, 29, 30].

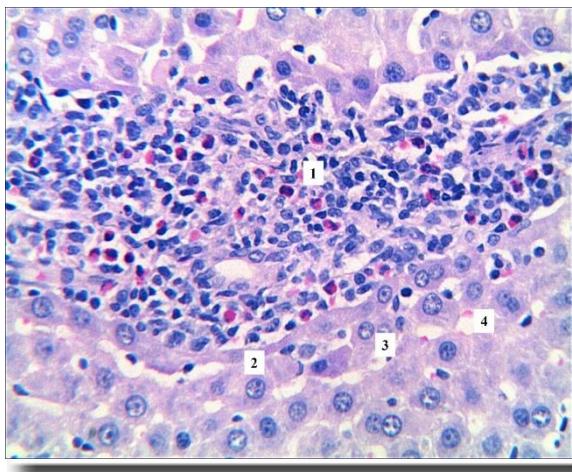


Fig. 4. Microscopic structure of the liver of an experimental rat 1 hour after administration of the venom of the scorpion *Leiurus macroctenus*. Lymphohistiocytic infiltration (1), hepatocyte (2), Disse's space (3), lumen of the sinusoidal capillary (4). Staining with hematoxylin and eosin. $\times 100$.

Summary

Administration of *Leiurus macroctenus* scorpion venom to rats did not cause the development of pronounced changes in the structural organisation of the liver of experimental rats. Infiltration of the portal tracts and sometimes the surrounding parenchyma of the organ with lymphocytes, histiocytes and neutrophil leukocytes was noted. Hepatocytes near the foci of infiltration underwent vacuolar dystrophy, which are reactive changes in response to the action of the venom.

Prospects for further development are related to studying histological changes in the rat liver under the influence of *Leiurus macroctenus* scorpion venom at later stages of the experiment.

Information on conflict of interest

There are no potential or apparent conflicts of interest related to this manuscript at the time of publication, and are not anticipated.

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Гайдай О.С. Особливості структурної організації печінки експериментальних щурів через 1 годину після впливу отрути скорпіонів *Leiurus macrosternus*.

РЕФЕРАТ. Актуальність. Укуси скорпіонів є серйозною загрозою для здоров'я та життя людей майже в усіх країнах світу. Кількість і токсичність отрути, яка потрапляє до організму постраждалих залежить від міжвидової мінливості цих тварин. Отрута скорпіона зазвичай спричиняє розвиток місцевих, кардіотоксичних, нейротоксичних і вегетативних ефектів. Залежно від переважання в складі отрути того, чи іншого компоненту можна спостерігати широкий спектр клінічних ознак і симптомів від локальних реакцій до серйозних наслідків, включаючи респіраторні, шлунково-кишкові, серцево-судинні або неврологічні ускладнення. **Мета.** Вивчення особливостей мікроскопічної організації печінки експериментальних щурів щурів через 1 годину після впливу отрути скорпіонів *Leiurus macrosternus*. **Методи.** Експериментальні дослідження проводили на 60 щурах-самцях щурів (180 г±3 г), яким внутрішньом'язово вводили 0,5 мл розчину отрути (28,8 мг/мл) ($LD_{50}=0,08$ мг/кг). Для мікроскопічного дослідження забирали зразки тканини печінки тварин всіх груп. Фарбування гістологічних препаратів печінки здійснювали гематоксиліном та еозином. **Результати та підсумок.** Мікроскопічні дослідження через одну годину після введення щурам отрути скорпіонів *Leiurus macrosternus* продемонстрували появу незначних зрушень нормальної гістоархітектоніки печінки тварин. Гепатоцити мали переважно шестикутну форму, містили одне ядро, однак відмічали наявність двоядерних клітин. Відмічали інфільтрацію порталних трактів та подекуди оточуючої паренхіми органу лімфоцитами, гістіоцитами та нейтрофільними лейкоцитами. Гепатоцити поблизу вогнищ інфільтрації зазнавали вакуольної дистрофії, що є проявом реактивних змін у відповідь на дію отрути.

Ключові слова: отрута, скорпіони, морфологія, печінка, гепатоцити, щури.