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The Morphological Features Of Immune System During Chronic Drug Addiction

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Absract

The aim at the present study is to find out the features of the morphological changes of the immune system organs in different development stages of chronic drug addiction.

For this study used the bodies of 53 individuals (45 men and 8 women) aged between 16 and 41, who were subjected to chronic drug addiction. Thirthy-five of them were forensic and 18 medical (people who die from various acute and chronic, relapsed infectious diseases) autopsy cases. The control group included the bodies of 15 men aged between 16 and 35, who died as a result of mechanical asphyxia. Studied histochemically and immunhistochemically metods on paraffin and selloidin sections.

All observations were divided into two groups depending on the term of abusing narcotic substances: 1st group – chronic drug addicts using narcotics for 2 years; 2nd group – chronic drug addicts using narcotics from 2 to 10 years.

The morphological changes in the immune system organs were mainly of reactive-hyper-plastic and dystrophic nature and were accompanied by acute micro-circulatory disturbances during the examinations in the 1st group. Necrotic, atrophic and sclerotic (both in parenchyma and interstition) changes along with the abovementioned pathological changes were discovered during the examinations in the 2nd group. This means the development of secondary B- and T-cell type immunodeficiency in patients.

Key words: *Chronic drug intoxication, immune system, secondary immunodeficiency.*

Kronik Madde Bağimliliği Zamani Immün Sistemin Morfolojik Özellikleri

Özet

Bu çalışmada, kronik madde bağımlılığının farklı gelişim devrelerinde immün sistem organlarında oluşan morfolojik degişikliklerin özelliklerini ortaya koymak amaçlanmıştır.

Çalışma için kronik madde bağımlısı olan 16-41 yaş arası (mean age 22,7 years), 45 erkek ve 8 kadın olmak üzere toplam 53 kişinin cesetlerinin otopsi materyalleri kullanılmıştır. Tüm vakaların 35-i adli, 18-i ise tıbbi (çeşitli akut ve kronik, rekürrens gösteren enfeksiyon hastalıklardan ölmüş şahıslara ait) otopsi vakalarıdır. Kontrol gruba mekanik asfiksi sonucu olen 16-35 yaş arası 15 kişi dahil edilmisdir. Metod olarak parafin ve selloidin kesitlere uygulanan histokimyasal ve immünhistokimyasal yontemler calışıldı.

Uyuşturucu kullanma süresine göre tüm vakalar 2 gruba ayrılmıştır. 1. grup – uyuşturucu kullanma süresi 2 yıl ve daha az olan kronik madde bağımlıları; 2. grup – aynı sürenin 2 yıldan 10 yıla kadar sürdüğü kronik madde bağımlılarından oluşmaktadır.

1. gruba ait vakalarda immün sistem organlarında morfolojik bulgular akut mikrodolaşım bozuklukların eşlik ettiği reaktif-hiperplastik ve distrofik özlü komplikasyonlardan ibarettir. 2. gruba ait vakalarda immün sistem organlarında hem parankim, hem de mezenkimal alanda nekrotik, atrofik ve sklerotik özlü morfolojik bulgular saptanmıştır. Bu gruba ait vakalarda aynı zamanda sekonder B- ve T-hücreli immün yetmezlik de izlenmiştir.

Anahtar Kelimeler: *Kronik madde zehirlenmesi, immün sistem, sekonder immün yetmezliği.*

Introduction

Today, there can be no doubt about the disturbance of immunological resistance in the patients affected with chronic drug addiction [1-3]. The organism of a sick drug addict weakened by secondary immunodeficiency easily becomes the target of chronic, relapsed infectious and inflammatory diseases, as well as oncology diseases, allergic and autoimmune disturbances and other pathologies [2, 4-8]. The long-term abuse of narcotics is accompanied by cytostatic effect, disturbance of the process of proliferation and differentiation of T- and B-lymphocytes in lymphopoetic system and other signs of disorganization of the immune system [9-11]. There are very few investigations into the characteristics of immune morphology during chronic drug addiction.

The morphological changes happened in the immune competent tissues during chronic drug addiction and the mechanisms for development of these morphological changes have not been significantly studied yet, while the results of some scientific research works differ distinctly and contradict each other. Doses of used narcotic substances, the ways of their addiction, periods of abuse, relations between the changes happened in immune tissues and the stages of formation of chronic drug sickness depending on the term of using narcotics and other important indications were not taken into consideration when conducting the research works [5, 12-14].

Considering the abovementioned, the current scientific research work aims to analyze the morphological development features of secondary immunodeficiency at different stages of chronic drug addiction and to study histological changes of lymphoid tissues.

Material and Method

The autopsy materials of bodies of 53 individuals aged between 16 and 41 (mean age 22,7 years), who were subjected to chronic drug addiction, were studied. Thirty-five of them were forensic medicine (21 – acute intoxication with narcotic substances, 6 – injuries with guns and sharp tools, suicide, car accident, etc.); 18 – were the pathological-anatomic examinations of individuals died of various acute and chronic, relapsed infectious diseases (7 – septic endocarditis, 5 – sepsis, 4 – lung tuberculosis, bilateral relapsed pneumonia, etc.). The bodies of 45 men and 8 women were examined. It became evident during the examination of bodies as well as on a basis of the conditions for occurrence of incident and catamnestic data that all these individuals abused narcotic substances (opium preparations) for a long period.

All observations were divided into two groups depending on the term of abusing narcotic substances: 1st group – chronic drug addicts using narcotics for 2 years; 2nd group – chronic drug addicts using narcotics from 2 to 10 years.

In most cases, the period between of death and examination of body was not more than 24 hours. In all cases, the antibodies of HBsAg and hepatitis-C virus in blood serum was examined by the method of immune ferment. The antibody of hepatitis-C virus was discovered in blood serum in 21 cases, while the antibody of HBsAg and HIV was not discovered.

The control group included the bodies of 15 men aged between 16 and 35, who died as a result of mechanical asphyxia (drowning or hanging). The facts of using narcotic substances and alcohol including anamnestic data were negated in all bodies. No pathological changes were discovered in the inward parts of the bodies in the comparison group, while dimensions and weights of immune competent organs and their microscopic views were normal.

The samples of tissues taken from the organs and tissues including the organs of immune system (thymus, spleen, lymph nodes, Peyer's aggregates) were reflected in 10% neutral formalin solution and consolidated in paraffin (and/or in selloidin). The micro preparations prepared from lymphoid organs were stained with picrophucsin by the method of hematoxylin, eosin, orsein, and van Gieson, as well as Perls reaction and PAS reaction were set. Immune morphological examinations were conducted by using the panel of standard monoclonal antibodies (CD3, CD4, CD8, Ki-67, IgA, IgM and IgG) with a view to determining T- and B-lymphocytes. The prepared preparations were examined in the "LEICA DMLB" (Germany) light microscopes. Computer analyzers (the complex includes a microscope, a digital video-camera and a computer) of images were used for examinations.

Results and Discussions

A great number of signs of infection of different periods were determined in the weak hypodermic fat layer and along superficial veins in the elbow hollow of most bodies during external examination. Inflammatory and sclerotic changes in the wall of superficial veins and the hotbed of hemorrhage of different periods are seen during the microscopic examination.

Narcotic substances were determined in the blood serum and tissues of the deceased through forensic-chemical examinations. The components of morphine and heroine were discovered in 14 cases, while marijuana preparations were discovered in blood in 6 cases. Medicinal preparations (barbiturates, amphetamine and methamphetamine preparations, etc.) along with the components of morphine and heroine were determined during 7 autopsies.

Common asfictics symptoms – limpid blood in vessels and heart cavities as well as acute venous hyperemia, edema, diapedesis hemorrhages with small hotbed in organs and tissues were discovered during the autopsy of bodies of 21 individuals died of acute drug intoxication (overdose). Histological changes extremely differing from the norm were determined in the immune competent organs of all patients during the microscopic examination. On the other hand, these changes had various natures and development degrees in separate autopsy materials.

The morphological changes were of hyperplastic and alterative nature and accompanied by acute microcirculator disturbances in the examined immune competent organs of chronic drug addicts, who abused narcotic substances less than 2 years.

Besides weakly developed changes, more obviously striking necrotic, atrophic and sclerotic changes were determined in the patients included in the 2nd group.

The re-division of T-lymphocytes, strengthening of apoptosis of lymphocytes and average activeness of B-lymphocytes were determined in the immune system organs of the patients included in the 1st group. Accidental involution was discovered in thymus at the background of changes of age. Hyperplasy and lymphocyte rows were registered in parenchyma atrophied, intralobule perivasculary areas. The volume and quantity of Hassal's bodies increased and kistozis variants make up majority (picture 1, a). In most cases, large-diameter lymphoid follicles possessing bright multiplication centers consisting of blast cells are seen in the spleen (picture 1, b). Mainly, plazmositys and eozinophill's make up majority in both pulps. Hotbeds of diapedesis hemorrhage of different periods are often observed in the red pulp at the background of venous hyperemia. Inactive follicular hyperplasy and obliteration of borders of lymphoid follicles are seen in the lymph nodes. The hyperplasy of cells is

discovered in the paracortical zone, while accumulation of T-cells in the outside sinus. The gleams of sinuses and exit lymphatic vessels are stuffed with dilated lymphocytes (in connection with rapid emigration of lymphocytes) and monocytes.

Thus, the morphological changes of the immune system consists of “acute atrophy” – acceleration of emigration of lymphocytes and their re-division and partial lymphoid evacuation of thymus and spleen in connection with their apoptosis – in the early stages of chronic drug intoxication.

The morphological changes of atrophic and sclerotic nature were usually registered in the immune system organs of older drug addicts (the individuals died of infectious diseases at the background of chronic drug addiction), who abused narcotic substances intravenously more than 2 years. These changes show the exhaustion of compensatory potentials and the development of secondary B- and T-cell type immunodeficiency conditions in both systems. The atrophy of lymphoid tissues gets more progressive due to the extinguishment of proliferation of lymphocytes and activeness of apoptosis at this late stage of chronic drug addiction.

Morphological changes, which are characteristic for acute accidental transformation, are registered in the thymus of these patients. Diffuse lymphocyte evacuations happen in the cortics of the thymus due to the acceleration of the migration of thymosyts, weakening of limphopoesys as well as limphositolys realized by macrophages. The area of the medulla of thymus grew significantly larger, consequently changing relativity between the areas of cortecs and medulla. Atrophy, sclerosis of vessels and strengthening of macrophage reaction are registered (picture 2, a). A great quantity of vacuolar appears in the cytoplasm of epitelioreticulosit’s. Calsinoz and hialinosys are seen in Hassal’s bodies subjected to grave dystrophic changes.

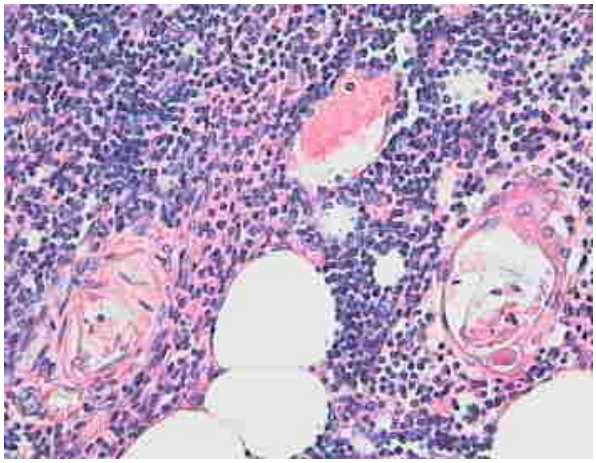
The most characteristic morphological changes in the spleen and lymph nodes in all cases of intravenous use of narcotic substances for a longer period were the increase in the size and number of lymphoid follicles, the significant diminution of their reactive centers, namely breakdown of T- and B-zones (“subatrophy and atrophy”) of specific parenchyma. The center of white pulp in the spleen covers a small area around the artery; its borders are not distinguished exactly and mainly comprised of lymphocytes with apoptosys, eozinophill’s, macrophage and reticular cells. Hyalinoz and perivascular sclerosis is discovered in the central arteries. The acute decrease in the number of lymphocytes is registered in the hyperemia red pulp. The cortecs and paracortical zone became deserted in lymph nodes and plasmatic cells were seen in lymphoid follicles. T-suppressors and separate T-helpers are mainly seen in T-zones during the immune morphological investigations conducted (picture 2, b). The disappearance of bright multiplication centers in the lymphoid follicles, the increase in the number of mitosis and the total delimphatitation of lymph nodes can be mentioned as the characteristic sign of the secondary T- and B-cell type immunodeficiency that is under formation. In most cases, masses like hyaline and sclerosis areas are registered in the bright multiplication centers of some of the lymphoid follicles. The atrophy of lymphoid tissue of lymph nodes are accompanied by the gradual intensification of “histiositosys” of sinuses and sclerotic changes.

These involutive changes discovered during the morphological researches of immune competent cells, the disturbances of the histological structure determined in the immune system organs and the conclusions attained show the development of the secondary immunodeficiency during long-term drug intoxication [7, 9, 11].

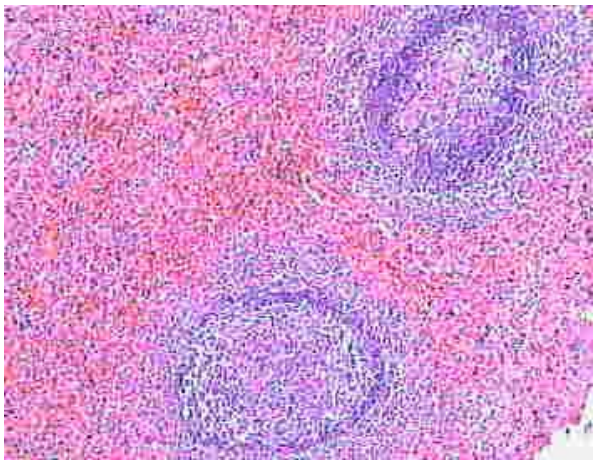
The necrosis (apoptosis) and atrophy of specific parenchyma, sclerosis of parenchymatose elements and interstitation and other morphological changes are also discovered in the endocrine system of the individuals, who abused narcotic substances for a long period [13, 14].

Thus, stage-by-stage changes happen in the immune system of the organism during chronic drug addiction. At the first stage, the immune system becomes active in order to remove the stressor

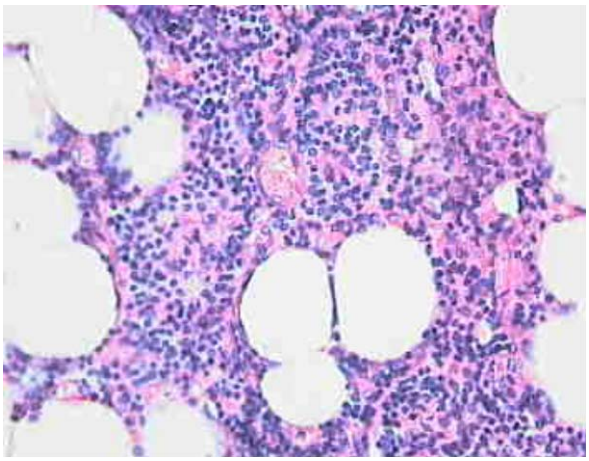
situation. In chronic drug addicts, this stage is mainly characterized with the formation of the T-cell type immunodeficiency from the immunological aspect and called the stage of compensation of the immunodeficiency situation. The compensation takes place due to the temporarily surplus activeness of the B-lymphocyte (humoral) part of the immune system and has a latent pace in clinic.



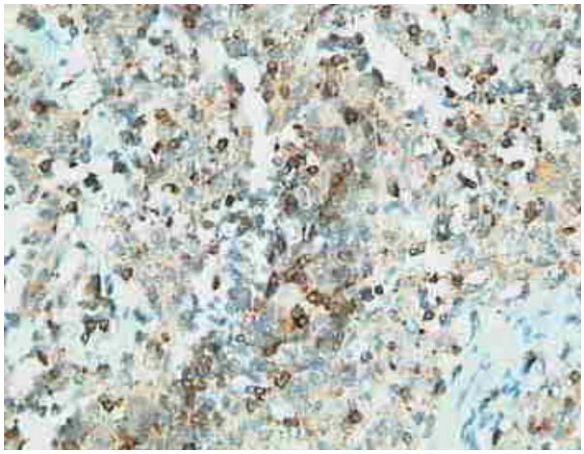
Picture 1, a. Secondary immunodeficiency, compensation stage in chronic drug addicts (up to 2 years). Thymus. Kistosys changes in Hassal's bodies. Paint: hematoxyllin and eosin. x 180.



Picture 1, b. Secondary immunodeficiency, compensation stage in chronic drug addicts (up to 2 years). Spleen. Great lymphoid follicle with bright multiplication center. Evacuation of T-zone, hyperplasy of B-zone. Paint: hematoxyllin and eosin. x 120.



Picture 2, a. Secondary immunodeficiency, decompensation stage in chronic drug addicts (up to 10 years). Thymus. Atrophy of parenchyma. Paint: hematoxyllin and eosin. x 180.



Picture 2, b. Secondary immunodeficiency, decompensation stage in chronic drug addicts (up to 10 years). Lymph node. Accumulation of T-suppressors. Paint: monoclonal antibodies against CD8 antibodies. x 180.

Like in the patients of the 1st group, the formation of the T-cell type immunodeficiency is mainly manifested with the progressively accidental evacuation of the thymus, the delimphatization of its cortecs and the acute decrease in the cortico-medular relativity as well as with the strengthening of blast transformation of lymphocytes in T-zones and plazmatization of the peripheral organs of the immune system.

The combined T- and B-cell type immunodeficiency starts in the long-term chronic drug addicts after the first stage. Morphologically, this process is characterized with appearance of a great number of cells subjected to dystrophic and destructive changes; destruction of the specific lymphoid tissue; disappearance of bright multiplication centers; development of subatrophic and atrophic changes in the lymph follicles in the peripheral organs of the immune system; the decrease in the relative volume of their parenchyma; and sclerosis of parenchyma and stroma of lymph tissues. As a consequence of all this, the clinical signs of immunodeficiency develop in the organism.

These morphological changes discovered during chronic drug addiction are, most probably, the results of the immunepathogenic effect of narcotic substances with too toxic doses. The abovementioned differences between the morphological changes determined in the lymph tissues in separate investigation groups much depend not only on the period of drug addiction but also, most probably, on the various effects of narcotic substances with different doses and the individual features of chronic drug addicts – sick people.

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