FORENSIC STUDY OF THE MORPHOLOGICAL CHANGES IN THE BRAIN TISSUE OF DECEASED WITH HISTORY OF DRUG ABUSE

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ABSTRACT

The modern concept of illicit drugs includes a diverse group of chemicals that are harmful to the body, cause dependence and are included in special lists in each country which are constantly updated. One of the target organs of drug influence is the central nervous system. Materials and methods: For the period 2011-2014 in the Department of Forensic medicine and deontology, Sofia, 3945 autopsies of deceased with full forensic analysis were performed, including the gathering of preliminary data, internal and external forensic examination of the body and chemical analysis of blood, urine samples and internal organ parts. In 156 of the cases the chemical analysis showed the presence of illicit drugs. A histological examination of brain tissue was performed in each of the cases and compared with a control group. Results: Frequent macroscopic and microscopic findings were brain edema, engorgement of cerebral vessels, atrophy of the cerebral cortex, cerebral hemorrhages, vasculitis, changes in the cerebral vessels, infectious diseases, etc. Conclusion: Some of the observed changes were not specific – they were seen in both of the examined groups, while others were observed only in the group of drug addicts. These neuropathological changes play a significant role in the genesis of death and should draw the attention of clinicians of probable drug abuse.

Key words: brain, morphological changes, drug abuse

INTRODUCTION:

The modern concept of illicit drugs includes a diverse group of chemicals harmful to the body, that cause dependence and are included in special lists which are constantly updated (EMCDDA, 2014, Караджов, 2003). The main researches carried out are related to morphological changes in the cardiovascular and respiratory systems, given their frequent involvement in different pathological processes, associated directly or indirectly in the genesis of death. Other affected organs mentioned in such researches are the liver, skin, kidney, etc. The brain tissue is very briefly studied, mostly by MRI analysis. This is the major target organ of the impact of psychoactive substances and the observed effects of the drugs.

The aims and objectives of the present study are to determine the main macroscopic and histological changes in the brain tissue and to clarify their involvement in the genesis of death.

MATERIALS AND METHODS

Between 2011-2014 in the Department of Forensic Medicine and deontology, Medical faculty, Medical University Sofia, Bulgaria, a total of 3945 deceased were examined, of which in

156 cases death was associated with the use of illicit drugs. This study used data from chemical and toxicology analysis of biological fluids (blood, urine, aqueous humor) and internal organ parts taken during autopsy, macroscopic and microscopic examination of brain tissue and the results were compared with all preliminary data available for each individual case. Necropsy material was fixed in 10% formalin solution. Paraffin blocks were prepared by the classic method and the tissues were stained with hematoxylin and eosin. According to initial histological findings in some of the cases we carried out further staining with Elastica and van Gieson. Microscope MCX 300 made of Micros-Austria was used to observe the histology. For photographing we used a digital camera Canon-Power Shot A650 IS, with basic technical features 12.1 megapixels, 6x optical zoom.

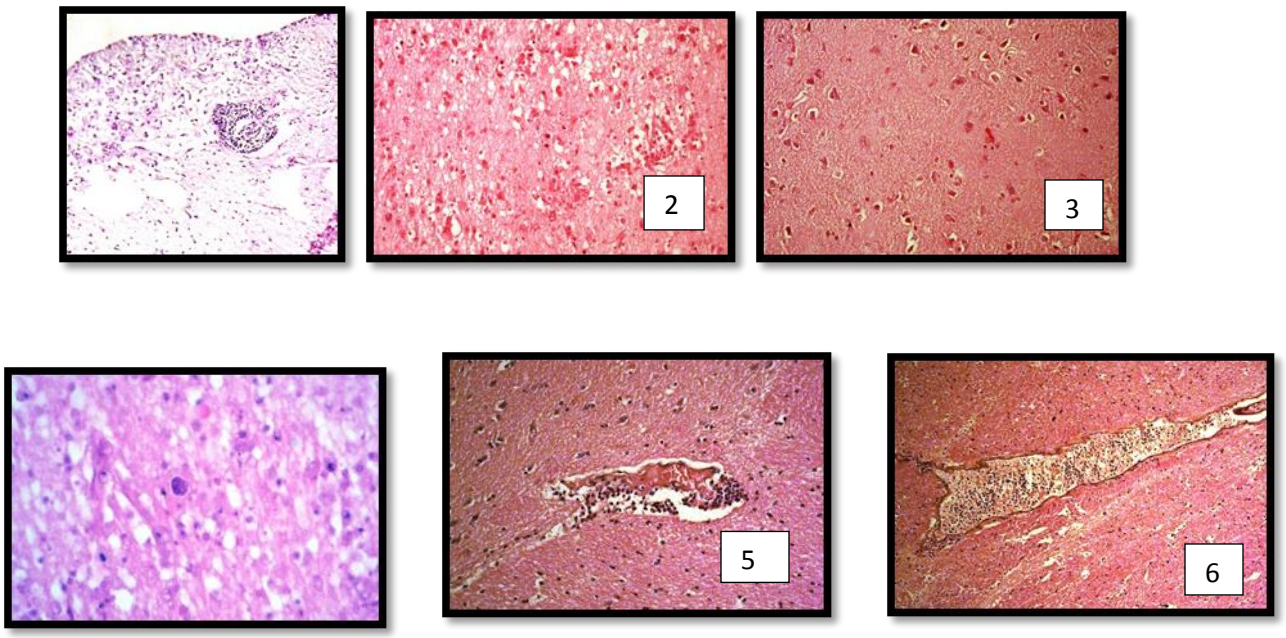
The objects of examination were divided into two groups:

- The first group included 134 deceased with history of drug abuse or people that at the time of their death were under the influence of illegal psychoactive substances, all subjects of examination in the Department of Forensic Medicine and deontology Sofia for the period 2011-2014 (cases with traumatic injuries involving the central nervous system /CNS/ were excluded);

- The second group (case-controls) included 46 deceased between the ages of 21-40 years without data at the time of their death or in the past of drugs abuse with a non-violent or violent cause of death (cases without traumatic injuries of the CNS), chosen randomly.

RESULTS

We observed macroscopic and microscopic data for the development of brain edema in varying degrees depending on the cause and the rate of death in people with a history of substance abuse. Its development is due to the severe circulatory and metabolic disturbances occurring in the brain tissue, and in particular at the level of the blood-brain barrier (Donkin et al, 2010). Brain edema is found in 92.5% of cases. In over 40% of them is less expressed, as this type of swelling occurs predominantly in cases with "an overdose" or acute intoxications (mainly after using drugs from the group of the opioids - heroin, methadone, either alone or in combination with each other or with other substances), as well as some of them occur in cases of mechanical asphyxia caused by aspiration of gastric contents and subsequent rapid death. We registered a case of acute intoxication with a "designer drugs" from the group of stimulants in which we observed strong cerebral edema - the mechanism that is not yet understood. Middle and high degree of cerebral edema is seen most often in cases of death due to an illness as a result of prolong drug abuse after a longer period of agony. When we examined the controls the percentage of cases with cerebral edema was higher - 95.6%, mainly represented by medium and strong cerebral edema in 60% of the studied cases. Brain edema was observed in both studied groups of drug addicts and case-controls, which defines it as uncharacteristic sign that can be seen in rapid deaths by different mechanisms. Based on that, it can be concluded that isolated cerebral edema cannot be defined as a characteristic morphological change in the brain showing drug abuse.



Photos 1-6: Photo 1: Vasculitis; Photo 2: Encephalitis; Photo 3: Atrophy of the cerebral cortex; Photo 4: Changes in the cerebral blood vessel wall; Photo 5: Venous congestion; Photo 6 Toxoplasmosis

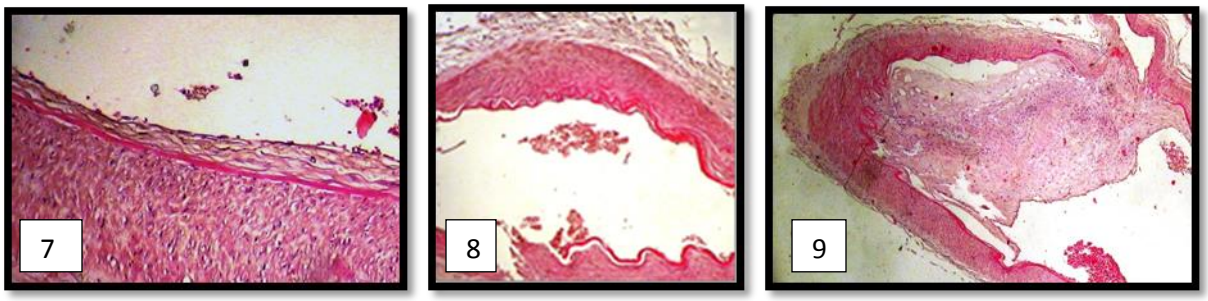
Venous stasis in cerebral vessels is observed at 97.76% of the deceased with history of substance abuse, and in controls this rate is slightly smaller - 84.782%. However, in the first group the strongly expressed venous stasis is twice more observed compared to controls, while the less marked stasis is almost identical in both groups. Nevertheless, acute venous stasis, as well as brain edema, is seen in most of the cases of deaths (excluding those with expressed anemia), and therefore cannot be used as a characteristic morphological sign of illicit drug abuse.

In 14.18% of the cases we observed atrophy of the cerebral cortex (macroscopically and histologically proven), represented by areas of thinning of the gray matter of the brain, reducing the number of nerve cells, and in some areas we have found only "shadows " of cells, as well as change in the architectonic of the cortex with random location and orientation of different neurons. These morphological changes were detected in people in the age range 27-33 years with no evidence of neurodegenerative diseases that used for a long time heroin, methadone, cocaine and marijuana, alone or in combination with each other. A reason for that could be the development of oxidative stress to the neurons caused by narcotics. We did not register a single case of cerebral atrophy in the case-control group (age range 21-40 years).

Cocaine, amphetamines and other illegal stimulants, given to one of their effects vasoconstriction, with temporary and significant rise in blood pressure, can cause intracerebral and subarachnoid hemorrhages in individuals without evidence of arterial hypertension (Pozzi et al., 2008). It affects young people. In two cases we observed massive intracerebral hemorrhage

with bleeding in the lateral ventricular system and subarachnoid space. In other cases we found focal bleeding with light microscopy. In the case-controls the cerebral bleeding developed as a complication of longstanding arterial hypertension. The presence of intracerebral, focal, subarachnoid hemorrhage in young persons should draw the attention of clinicians and morphologists for possible use of illegal substances, mainly from the group of stimulants. The pathogenesis of cerebral bleeding is not fully understood.

In the present study the results have shown changes in the vascular wall of cerebral blood vessels – lamina elastica interna is thickened and curled in cases of people using stimulants. Konzen et al. (1995) define this as a possible marker for cocaine-induced vasospasm. More recent studies have shown that cocaine damages the vascular endothelium and activates the coagulation system (Hobbset al., 2013, Treadwellet al, 2007, Konzen et al., 1995). It acts on von Willebrand factor - high molecular weight glycoprotein that promotes the adherence of platelets to the injured vessel wall, as well as the aggregation of blood platelets to each other. In Hobbs and al. study it is described that besides cocaine, its metabolites, such as cocaethylene and benzoylecgonine, stimulate the same clotting factor, which explains the cases where the cocaine was not detected in plasma, but are observed thrombotic events in individuals with evidence of use of this stimulant. Thus, in addition to cocaine sympathomimetic effect leading to increased need for oxygen to tissues (increased heart rate, increased blood pressure, contractility and metabolism) and reduced supply of oxygen (vasoconstriction), cocaine and its metabolites likely contribute to ischemic events by promoting platelet aggregation on the endovascular surfaces (Sáez. et al, 2011, Yaoet al. 2011, Bhattacharya et al, 2011).



Photos 7-9: Photo 7 Normal internal elastic membrane; Photo 8: Curled internal elastic membrane; Photo 9: Thrombosis with recanalization

Another reason for cerebrovascular accidents are inflammatory changes of the cerebral vessels - vasculitis. The basic data for vasculitis of the brain blood vessels is due to changes identified by angiography of the vessels, but in a minority of cases the diagnosis is confirmed histologically (Fredericks et al., 1991). In our study, we found that in 3.73% of the cases there was the presence of inflammatory changes in the cerebral vessels (vasculitis) with lymphocytic infiltrates, thickening of the walls of the vessels with small or medium caliber and in some places they was partial destruction. Vasculitic changes were observed mainly in cases of stimulant abuse with cocaine, amphetamines and methamphetamines. It is assumed that the reported changes in the vascular wall are due to still unknown mechanisms of direct toxic effect of the psychoactive

substance (Fredericks et al., 1991).

The failure to comply with the basic principles of aseptic and antiseptics while injecting drugs leads to an increased risk for bacteria, viruses, parasites or adulterants and unfiltered particles to enter the blood vessels. In some cases they can reach the central nervous system and lead to inflammation. One of the most common complications observed in injection type of drug addicts is AIDS (Garcés, 1989, Martinez et al., 1995; Mossakowski and Zelman, 1997), viral infection that, due to a decrease in immunity, is associated with the development of numerous opportunistic infections. Cases of AIDS encephalitis, meningitis, and infection with Toxoplasma Gondi were observed. In the group of case-controls there was not a single case of inflammation of the meninges as the cause of death (table 1).

Table 1. Morphological changes in the brain tissue

Morphological findings	Number of cases of drug addicts	proportion N = 134	Number of cases of persons without evidence of drug use	proportion N = 46
Swelling of brain cells	14	10,447%	6	13,043%
Brain edema - slight	56	41,791%	9	19,565%
Brain edema - moderate	16	11,940%	19	41,304%
Cerebral edema - strong	38	28,358%	10	27,739%
Venous congestion - slight	77	57,462%	30	65,217%
Venous congestion - strong	54	40,299%	9	19,565%
Atrophy of the cerebral cortex	19	14,179%	0	0%
Intracerebral hemorrhage and focal	9	6,716%	3	6,521%
Subarachnoid hemorrhage	1	0,746%	0	0%
Encephalitis	3	2,239%	0	0%
Meningitis	1	0,746%	0	0%
Cerebral toxoplasmosis	1	0,746%	0	0%
Inflammatory changes of cerebral vessels	5	3,731%	0	0%
Other changes of brain blood vessels	6	4,478%	0	0%

CONCLUSIONS

On the basis of everything stated it can be concluded that we observed mainly unspecific and less specific changes in the brain tissue, which on one hand are a result of direct toxic action of the illicit drugs, and on the other a result of the reduced immunity or accompanying diseases. Although the non-specificity of the main and most common morphological changes in brain tissue, these changes considered together with the preliminary data and the toxicological analysis, and studies of other tissues and organs can be described as typical in individuals abusing with illicit drugs.

To clarify the cause of death in each case, a complex approach is important with collection of preliminary information (targeted general and medical information about deceased from the family, friends, acquaintances or casual eyewitnesses, data from the inspection of the scene - the presence of drugs, devices for intake, the specific environment where the death occurred, etc.), forensic autopsy of the corpse and chemical analysis of blood, urine, internal organ parts of the first and second routes. Thus it becomes possible to create the most accurate and complete picture of the changes taking place in the human body, leading to death.

Performed to date researches worldwide, their results and data for the characteristics, effects and impact of drugs on the human body show that the CNS is the main target anatomically-physiological structure of different drugs. The examination of the bodies of deceased in the Department of Forensic Medicine and deontology - Sofia, with data or suspicion of drug abuse, showed various pathological changes in the brain tissue that directly or indirectly play a role in the genesis of death.

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