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Research Article

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Pathomorphology of Myocardium in the Neuroleptic Cardiomyopathy: Impact of Age Factor

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Summary

By a morphometric method of research and calculation of Cohen's coefficient the force of impact of an age factor on pathomorphological changes of heart at the tissue and cellular levels of his organization at development of a neuroleptic cardiomyopathy was determined. It is established that at patients of different age crucial importance plays not an age factor, but side cardiotoxic effect of antipsychotics leading finally to development of the neuroleptic cardiomyopathy.

Keywords: Antipsychotics, Cardiotoxicity, Neuroleptic Cardiomyopathy, Pathomorphology of Heart, Tissue and Cellular Levels of Organization, Morphometry, Influence of Age.

As a result of active therapy of both the main mental and concomitant somatic pathology, the life expectancy of mental patients, in particular those suffering from schizophrenia has increased significantly [1, 2]. This process is accompanied by a significant increase in the duration of antipsychotic therapy (APT), thereby significantly lengthening the time of damaging cardiotoxic effects of antipsychotics (AP) on the heart, which is fraught with the development of severe life-threatening iatrogenic pathology – neuroleptic cardiomyopathy (NCMP) [3-6].

In parallel, natural ontogenetic involutional processes develop in the heart [7]. How these two factors interact among themselves and how their joint influence is reflected in a morphologic condition of a myocardium – this question remains open. In the special literature any information on this problem is not found.

The goal of the present study is to eliminate – at least, partially – the existing gap by studying the effect of age on structural changes in the myocardium (tissue and cellular levels of a cardiac organization) in patients with NCMP.

Materal and methods

Myocardium of 61 patients with schizophrenia (42 men and 19 women) who died at the age under 35 years and over 55 years was examined histomorphometrically. The criteria of an exception were the expressed signs of a metabolic syndrome (the increased body weight, arterial hypertension, a diabetes mellitus), a chronic pulmonary pathology with hypertension in a small circle of blood circulation, a cachexia. The final diagnosis of each deceased was verified at the autopsy.

The observations were divided into four groups: I and II were respectively 12 young and 6 elderly patients receiving AP, but had no heart disease and died of non-cardiac causes; groups III and IV included 20 young and 23 elderly patients suffering from NCMP.

Myocardium slices from various departments of the left ventricle were filled in paraffin, cuts were painted by hematoxylin and eoziny. Respective objects were studied in 10 different fields of microscope, with necessary magnifications with the help of an ocular micrometer, the point count method was also used [8-10]. Such parameters as zone of pericapillary diffusion (**ZPD**), Kernogan index (**KI**), stromal-parenchymatous ratio (**SPR**), rate of interstitial edema (**RIE**) were calculated. Karyometry and cytometry of cardiomyocytes (CMCs) were performed, the specific volumes of hypertrophied CMCs (**SVHC**), of atrophied ones (**SVAC**), and – by the method of polarization microscopy – the specific volume of dystrophic ones (**SVDC**) were determined. The above-named parameters describe a condition of three structural components of myocardium: of microvasculature (**ZPD** and **KI**), intercellular matrix (**SPR** and **RIE**), and parenchyma (**SVHC**, **SVAC** and **SVDC**).

Mathematical analysis of the obtained quantitative data included the calculation of such an index as the effect's size by J. Cohen, which in quantitative terms determines the effect of the studied factor on a particular object of study [11-13].

It is believed that the inclusion of the Cohen coefficient (**d'C**) in the mathematical data processing tool strengthens the rigor of the study and gives more weight to the analysis, conclusions and recommendations [14].

The following gradation of **d'C** is accepted: insignificant – less than 0,20; small – 0,20–0,49; average – 0,50–0,79; big – 0,80 and above [11, 13, 15]. Negative d'C values indicate the opposite direction of the effect [15].

The obtained quantitative results were processed statistically (computer program "Statistica 6.0") with the level of significance of differences of 95% and more ($p \leq 0.05$). The **d'C** calculation is performed automatically using a computer calculator [15].

Results and discussion

Quantitative results of the conducted morphometric studying of a myocardium on groups of a research and results of the calculation of **d'C** are presented in tables 1 and 2. Their analysis allows allocating the following key points.

Table 1: Micromorphometric parameters of the myocardium in the study groups

Indicators / Groups	Microvasculature		Intercellular matrix		Cardiomyocytes		
	ZPD	KI	SPR	RIE	SVHC	SVAC	SVDC
I	**105,5**	**1,17**	**6,5**	**4,0**	**5,7**	**1,9**	**1,3**
	±8,4	±0,05	±1,7	±0,9	±1,1	±0,3	±0,5
	2–4	2–4	2–4	2–4	2–4	2–4	2–4
II	**122,8**	**1,33**	**11,4**	**13,3**	**19,3**	**10,6**	**4,0**
	±10,4	±0,07	±2,1	±1,6	±1,7	±0,9	±0,7
	1,3,4	1,3,4	1,3,4	1,3,4	1,3,4	1,3,4	1,3,4
III	**238,3**	**1,51**	**56,1**	**58,8**	**24,6**	**32,7**	**24,3**
	±14,2	±0,12	±3,7	±2,9	±1,9	±3,2	±1,3
	1,2	1,2	1,2	1,2	1,2	1,2	1,2
IV	**253,6**	**1,69**	**61,1**	**62,3**	**26,8**	**37,3**	**26,1**
	±11,8	±0,15	±4,1	±3,3	±2,7	±3,4	±1,9
	1,2	1,2	1,2	1,2	1,2	1,2	1,2

Note: 1-4 – statistically significant differences between the groups

Table 2: Cohen's coefficient (d'C) micromorphometric parameters of the myocardium in the study groups

Indicators / Groups	Microvasculature		Intercellular matrix		Cardiomyocytes		
	ZPD	KI	SPR	RIE	SVHC	SVAC	SVDC
I	0,653	0,981	0,914	2,923	3,679	6,237	1,657
I–III	2,551	0,794	3,735	5,362	2,719	2,771	4,978
II–IV	2,567	0,563	3,36	3,486	0,649	1,851	2,738
IV	0,262	0,287	0,28	0,246	0,203	0,306	0,237

Comparison of all studied indicators in groups I and II (table 1) reveals the pronounced and statistically significant ontogenetic changes expressed to varying degrees, but having the identical focus on ascending.

This indicates that as the body ages the all structural components of the heart muscle – microvasculature, stroma (intercellular matrix), and parenchyma (CMCs) – are deeply damaged. During ontogenesis the processes of microcirculation in the myocardium and collagen genesis in its extracellular matrix are gradually disturbed, which is accompanied by the development of interstitial edema and myofibrosis, which, in turn, lead to parenchymatous damages.

At the same time, along with the phenomena of compensatory-adaptive nature, a dystrophic-degenerative and an atrophic changes that significantly reduce the contractile reserves of the myocardium and cause an age-related increase in manifestations of myocardial dysfunction are deployed at an advanced rate.

The calculation of **d'C** in the compared groups I and II (table 2) confirms the strong influence of an age factor on the structure of the heart muscle in persons without cardiac pathology. On the contrary, with the development of NCMP (group III and IV) its leveling effect on the degree of severity of ontogenetic shifts in the myocardium is observed (table 1). That is NCMP causes so deep morphological injuries of a myocardium that the age changes on such pathological background are practically not caught.

This is also evidenced by the monotonic values of **d'C** for each compared indicator (table 2) which are near the lower limit of the gradation interval designated as "small". This suggests that the strength of the influence of age on the state of a cardiac muscle in patients suffering from NCMP is extremely small, and all the identified changes are due to the development of specified iatrogenic pathology.

The results of a comparative analysis of the dynamics of indicators in paired groups I–III and II–IV, that is in persons of the same age respectively without NCMP and with the development of such, confirms this thesis once again convincingly.

In both pairs of the compared groups, NCMP is accompanied by deep and statistically significant pathomorphological shifts in the

myocardium, affecting all its structural components (Table 1). It is important to note that "size effect" of the development of NCMP at any age for the vast majority of the studied quantitative indicators is very high (Table. 2).

Conclusion

Thus, the carried-out analysis of the dynamics of the morphometric parameters of a myocardium in the aspect of ontogenesis and the development of NCMP shows the absence of any significant influence of an age factor on the condition of the heart muscle in mentally ill patients in the presence of NCMP.

Generalizing everything told, it is possible to note that at the development of NCMP in patients of different age the crucial importance in the genesis of various pathological changes of the myocardium has not an age factor, but the side cardiotoxic effect of AP leading eventually to the development of NCMP.

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