ECRONICON OPEN ACCESS

EC CLINICAL AND MEDICAL CASE REPORTS

Research Article

Neuroleptic Cardiomyopathy: Morphometric Approach to the Determination of the Beginning of the Development

Volkov VP*

Tver Center of Judicial Examinations, Russia

***Corresponding Author**: Volkov VP, Tver Center of Judicial Examinations, Russia.

Received: June 13, 2019; **Published:** August 22, 2019

Abstract

By a morphometric method of research the pathologic changes of the myocardium in the process of antipsychotic therapy and in neuroleptic cardiomyopathy as a whole, and at various stages of the disease was determined. The analysis of the obtained results shows that the development of neuroleptic cardiomyopathy in its latent stage begins gradually after 10 years of psychotropic treatment. Clinical manifestations of the disease occur after 20 years of taking antipsychotics due to the compensatory-adaptive processes occurring during this period in the myocardium.

Keywords: *Antipsychotics; Cardiotoxicity; Duration of Antipsychotic Therapy; Neuroleptic Cardiomyopathy; Clinical Stages of Disease; Pathomorphology of Myocardium; Morphometry*

Introduction

Neuroleptic (antipsychotic) cardiomyopathy (NCMP) is one of serious complications of psychotropic therapy caused by side cardiotoxic effect of antipsychotic preparations [1-4].

As showed my researches, in its development NCMP passes three clinical stages: 1) a latent one, it is clinically fully compensated, 2) a full-scale (developed. manifesting) one, when cardiac disorders are clearly detected, but without the expressed signs of CHF, and 3) a terminal one, when the clinical picture of CHF comes to the foreground [5,6].

Demonstration NCMP occurs usually after prolonged treatment with antipsychotics [7-9]. However, in general, the timing of the onset of the disease is still not precisely defined.

According to my preliminary unpublished data obtained by correlation analysis, the NCMP begins after 10 years of APT. The latent stage of the disease is quite long, and only after 20 years of taking antipsychotic drugs comes its clinical manifestation.

Purpose of the Study

The purpose of this study is to verify these preliminary data by morphometric study of myocardial microstructure at different stages of NCM and at different time of APT, followed by a comparison of the results.

Materials and Methods

To characterize cardiac changes in NCMP at the microscopic (tissue and cellular) level, morphometry of myocardium was performed in 58 deceased patients with schizophrenia (38 men and 20 women; age from 16 to 77 years), who suffered during the life of NCMP, verified at autopsy. In general, without separation by stages of the disease, the material is collected in group I.

In 24 of dead patients the disease was in the latent stage (group II), in 13 patients it was in the full-scale stage (group III), and in 21 patients it was in the terminal stage (group IV).

In addition, autopsy protocols of 70 patients with schizophrenia (41 men and 29 women) who died at the age from 22 to 77 years were analyzed. The final diagnosis of each deceased was verified at the autopsy.

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.

During their lives the patients received various antipsychotic in quantities corresponding to the therapeutic standard; these medicines are not rarely received in combination with each other. The duration of APT ranged from six months to 30 years or more.

Depending on the duration of the APT material is divided into four groups (V-VIII): V - up to 10 years (20 dead); VI - from 11 to 20 years (25); VII - from 21 to 30 years (19); VIII - over 30 years (6).

Microscopy and micromorphometry of the myocardium (tissue and cellular levels) are carried out according to the proposed for this purpose own algorithm [10,11].

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 [12-14]. 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 (CMC) were performed, the specific volumes of hypertrophied CMC (SVHC), of atrophied ones (SVAC), and - by the method of polarization microscopy - the specific volume of dystrophic ones (SVDC) were determined.

The method of polarization microscopy was used to detect dystrophic-degenerative changes in CMC. It is believed that the combination of this type of study with conventional histological and histochemical techniques allows to obtain and evaluate much more complete information about the state of CMC and their myofibrillar apparatus, which is a very sensitive indicator of myocardial damage [15]. This makes the polarization microscopy method most suitable for detecting early stages of CMC damage [15].

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).

The obtained quantitative results were processed statistically (computer program "Statistica 6.0") with the level of significance of differences of 95% and more ($p \leq 0.05$).

Results

In table 1 presents the data obtained in the course of the study.

Discussion

Analysis of the results of the study, conducted in the direction of the purpose of the work, showed the following.

In a sequential comparison of changes in the microstructure of the heart muscle in the NCMP (group I) with changes in different periods of APT (group V-VIII), it was established that the differences between groups I and V are statistically significant for all indicators. The marked differences between groups I and VI relate to four of the seven indicators, which characterize the state of the CMC. However, in group I there are no differences in the vast majority of parameters compared to those in subsequent groups of observations (VII-VIII). In other words, the morphometric changes of the heart muscle observed in the morphogenesis of NCMP and after 20 years of APT are almost identical.

Indicators	Microvasculature		Intercellular matrix		Cardiomyocytes		
Groups	ZPD	KI	SPR	RIE	SVHC	SVAC	SVDC
I	246.5 ± 70.8	1.62 ± 0.18	58.8 ± 5.3	60.7 ± 5.1	25.8 ± 4.9	35.2 ± 5.3	25.3 ± 4.7
II	189.3 ± 51.8	1.54 ± 0.21	39.2 ± 6.2	36.4 ± 6.1	37.3 ± 6.1	23.6 ± 5.4	12.8 ± 4.2
III	282.5 ± 82.2	1.61 ± 0.18	70.7 ± 5.7	75.8 ± 5.8	20.1 ± 6.6	36.6 ± 6.1	27.7 ± 5.1
IV	289.0 ± 79.1	1.70 ± 0.17	73.7 ± 4.7	78.8 ± 4.6	16.5 ± 6.4	46.9 ± 5.4	37.4 ± 4.6
V	128.5 ± 24.0 1.2.3.4	1.32 ± 0.11 1.3.4	10.3 ± 5.8 1.2.3.4	9.8 ± 5.6 1.2.3.4	16.9 ± 7.2 1.2	8.4 ± 5.3 1.2.3.4	5.7 ± 4.4 1.2.3.4
VI	179.7 ± 46.7 3.4	1.51 ± 0.19	41.8 ± 8.6 3.4	37.7 ± 8.2 1.3.4	37.0 ± 8.5 1.3.4	23.9 ± 7.4 1.3.4	13.6 ± 6.0 1.3.4
VII	263.2 ± 73.1	1.64 ± 0.15	63.4 ± 9.32	72.3 ± 8.9 1.2	19.6 ±7.92	39.7 ± 9.82	28.5 ± 9.02
VIII	316.4 ± 83.72	1.72 ± 0.21	80.0 ± 10.1 1.2	83.4 ± 9.4 1.2	17.0 ± 9.52	45.1 ± 12.62	35.2 ± 12.12

Table 1: *Microscopic changes of the myocardium at NCMP and in the process of APT.*

Note: *1-4 - statistically significant differences between the groups.*

However, certain features peculiar to NCMP, in particular, dyscirculatory disorders and the development of myofibrosis, myocardium acquires after 10 years of taking antipsychotic drugs. In the next decade, thanks to adaptive processes, the pumping function of the heart is not significantly disturbed - the NCMP is in a latent preclinical stage. Only after a 20-year period of APT myocardial changes go so far as to develop myocardial dysfunction, and the disease goes first to the expanded stage, and then to the terminal, accompanied by the progression of congestive heart failure.

A similar conclusion is given by the analysis of the study data, carried out taking into account the stage flow of the NCMP.

For example, changes in the vast majority of indicators in groups II and V differ statistically significantly. So, with the duration of APT less than 10 years NCMP does not develop. At the same time, these differences are insignificant between groups II and VI, which indicates the appearance of the disease in its latent stage in the period from 10 to 20 years of taking antipsychotic drugs.

There are no statistically significant differences between groups III and IV, on the one hand, and groups VII and VIII, on the other. In other words, in the manifest course of NCMP (deployed and terminal stage of the disease), the duration of APT is 20 years or more.

The obtained results fully confirm the preliminary conclusions made earlier with the use of correlation analysis of myocardial microstructure parameters at different stages of NCMP and at different periods of APT.

Conclusion

The comparative morphometric study of myocardium in NCMP as a whole, and at various stages of the disease, on the one hand, and in different periods of APT, on the other one, showed that the development of severe iatrogenic complications in consequence of the side cardiotoxic effects of antapsychotic drugs, begins gradually after 10 years of psychotropic treatment. The disease in this period is in a latent stage.

Clinical manifestations of NCMP occur much later (after 20 years of taking antipsychotics) thanks to the compensatory-adaptive processes occurring during this period in the myocardium.

The results of the study are of great practical importance. In particular, the detected long enough period preceding the beginning of clinical manifestation of NCMP allows to diagnose this gradually developing iatrogenic cardiac pathology in a timely manner and to start the necessary medical and preventive measures in time.

Bibliography

1. Volkov VP. "Cardiotoxicity of phenothiazine neuroleptics (review of literature)". *Psichiat Psychopharmacother* 12.2 (2010): 41-45.
2. Volkov VP. "Phenothiazine dilated cardiomyopathy: some aspects of clinic and morphology". *Clinical Medicine* 87.8 (2009): 13-16.
3. Buckley NA and Sanders P. "Cardiovascular adverse effects of antipsychotic drugs". *Drug Safety* 23.3 (2000): 215-228.
4. Coulter DM., *et al*. "Antipsychotic drugs and heart muscle disorder in international pharmacovigilance: data mining study". *British Medical Journal* 322.7296 (2001): 1207-1209.
5. Volkov VP. "Clinical characteristic of an antipsychotic cardiomyopathy". In: VP Volkov (ed.) Actual problems of therapeutic clinic: collective scientific monograph. Novosibirsk: SibAC Publication (2013): 94-116.
6. Volkov VP. "Morphometric aspects of a morphogenesis of an antipsychotic cardiomyopathy". *Ros Journal of Cardiology* 3 (2012): 68-73.
7. Makhoul M., *et al*. "Dilated cardiomyopathy: an unusual complication of clozapine therapy". *Nature Clinical Practice Cardiovascular Medicine* 5.9 (2008): 566-570.
8. Tanner MA and Culling W. "Clozapine associated dilated cardiomyopathy". *Postgraduate Medical Journal* 79.933 (2003): 412-413.
9. De Berardis D., *et al*. "Update on the adverse effects of clozapine: focus on myocarditis". *Current Drug Safety* 7.1 (2012): 55-62.
10. Volkov V. "Cardiotoxicity of neuroleptics: etudes of studies of the problem". Beau Bassin, LAP Lambert Academic Publication (2018).
11. Volkov VP. "Quantitative pathomorphology of specific dilated cardiomyopathies". Tver, Triada Publication (2016).
12. Avtandilov GG. "Medical morphometry: management". Moscow, Medicine Publication (1990).
13. Avtandilov GG. "Fundamentals of quantitative pathological anatomy". Moscow, Medicine Publication (2002).
14. Gutsol AA and Kondratyev BYu. "Practical morphometry of organs and tissues". Tomsk, Tomsk Univer Publication (1988).
15. Nepomnyashchih LM. "Morphogenesis of the most important general pathological processes in the heart". Novosibirsk, Nauka Publication (1991).

Volume 2 Issue 6 September 2019