To a Problem of a Neuroleptic Cardiomyopathy: Brief Review of a Literature and of Own Researches

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Abstract: *Introduction:* Neuroleptic cardiomyopathy (NCMP) belongs to secondary specific metabolic dilated cardiomyopathies. It is caused by side cardiotoxic effect of antipsychotic drugs. Many aspects of epidemiology, pathogenesis, morphology, clinical picture and diagnostics of NCMP still remain insufficiently explored.

Results: NCMP passes through 3 stages in its development: 1) a latent one, 2) a full-scale one, and 3) a terminal one. Each stage has clinical features, electrocardiograph signs and certain morphology.

Lethal termination in a latent and in a full-scale stage either takes place because of intercurrent diseases or it is a sudden cardiac death of arrythmogenic genesis. In the terminal stage, the direct cause of death is, as a rule, a progressive congestive chronic cardiac failure.

On the macroscopic level, NCMP is characterized by a moderate cardiomegaly; by a noticeable dilatation of heart ventricles; by absence of evident coronary atherosclerosis.

On the microscopic level, all structural components of myocardium (microvasculature, intercellular matrix, cardiomyocytes) are deeply damaged. These pathologic changes are a physical basis of a contractile myocardial dysfunction.

Conclusion: On the basis of the summarizing of the data, which were received in a series of studies, we singled out and proved clinical and morphological criteria of diagnostics of NCMP.

Taking the described clinical and morphologic peculiarities of NCMP into account, it is advisable and quite logic to single-out this pathology into an independent nosologic unit.

Keywords: Neuroleptics, Cardiotoxicity, Clinical picture, Diagnostics, Morphology, Neuroleptic cardiomyopathy, Nosological independence.

INTRODUCTION

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

This disease belongs to secondary specific metabolic dilated cardiomyopathies [5, 6, 7] and is characterized by a diffuse myocardial involvement, by a drastic reduction of its contractile function and, as consequence, by a progressive congestive chronic cardiac failure (CCF) [2, 5, 6, 8-10].

Many aspects of epidemiology, pathogenesis, morphology, clinical picture and diagnostics of NCMP still remain insufficiently explored.

The goal of the real review is the short generalization of the results of the own researches of this problem.

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RESULTS

According to our autopsy findings, among dead patients who had schizophrenia and whose obligatory therapy component had been the intake of antipsychotic drugs, the number of persons having NCMP is considerable and statistically significantly higher (11.4%) than in the total autopsy material of the psychiatric prosectorium on the whole (2.0%) [8].

NCMP passes through 3 stages in its development: 1) a latent one, clinically fully compensated one, 2) a full-scale one, when cardiac disorders are clearly detected, but without evident signs of CCF, and 3) a terminal one, when the clinical picture of CCF comes to the foreground [9, 11-13].

Lethal termination in a latent and in a full-scale stage either takes place because of intercurrent diseases or it is a sudden cardiac death (SCD) of arrythmogenic genesis [5, 11, 13]. The latter, according to our data, is observed in 44.2% patients who died of NCMP [14, 15]. In the terminal stage, the direct cause of death is, as a rule, a progressive CCF [5, 11, 13].

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The disease develops slowly and at first hardly noticeably. In the latent stage it does not practically manifest itself.

In this period the patients' complaints are indefinite or fully absent. Patients most often complain about fatigability and dyspnea on significant exertion. In this regard one has to take certain difficulties of detection of mentally sick patients' complaints into account, on the one hand because of their abnormal behavior and absence of due critical approach to their own state, and on the other hand because of the quite often certain drug-induced loadedness.

Physical findings in the latent stage of NCMP are not numerous and not specific too. As a rule, tachycardia is observed, which is a practically constant phenomenon accompanying intake of neuroleptics [1]. Reduction of heart tones is determined by auscultation. Heart borders are usually little changed. As for arterial pressure (AP), hypotonia and normotonia considerably prevail; an insignificant arterial hypertension (AH) is observed only in approximately one third of cases [5, 11].

In this period the following pathologic signs are most often present on an electrocardiogram (ECG): 1) diffuse muscular changes; 2) various types of asequence, in particular, left bundle-branch block; 3) axis deviation to the left; 4) overload of venous heart; 5) left ventricular hypertrophy [5, 6, 8-10, 16].

In the full-scale stage the clinical picture of NCMP manifests itself clearly enough, but signs of a terminal CCF are absent or little noticeable. Patients' complaints are more definite: weakness, fatigability, heartbeats, dyspnea on significant exertion, sometimes intermittent pains in the heart area. Dullness of heart tones, some expansion of heart borders, tachycardia, intermittent tachypnea are physically detected. In this period a stably normal AP and a labile one with a tendency to a moderate AH are equally often observed [5, 11].

The terminal stage of NCMP course is characterized by addition of known manifestations of an increasing congestive CCF to the already named symptoms, among these manifestations are: dyspnea at rest or on minor exertion, orthopnea, enlargement of liver, peripheral and cavitary edemas, sometimes anasarca etc. By percussion one detects that heart borders are moderately - or less often, more significantly - expanded, what is confirmed by an X-ray examination. Heart tones are dull, tachycardia is almost always present, and arrhythmia is often present. A moderate AH is observed in a little more than one-fourth of patients, the AP of 13.6% other patients constantly exceeds 150/100 mm Hg [5, 11].

On an ECG, in the full-scale and terminal stages of NCMP the following phenomena are the most alarming ones: 1) asequence; 2) prolongation of the QT interval recalculated on Bazett's formula - the corrected QT interval (QTc); 3) overload of venous heart [5, 6, 8-10, 16]. A special attention must be paid to the monitoring of parameters of the QTc interval as a highly informative factor in the case of cardiac decompensation [17].

On the macroscopic level (organ one), NCMP is characterized by a moderate cardiomegaly; by a noticeable almost uniform dilatation of heart ventricles with a some predominance of dilatation of the left one; by absence of evident coronary atherosclerosis, especially in persons older than 45 years.

When microscopic examination of myocardium (tissular and cellular levels) is conducted, an evident myofibrosis and small-focal (substitutive) cardiosclerosis, a chronic interstitial edema, at first hypertrophic and then dystrophic-degenerative and atrophic changes of cardiomyocytes are detected.

At early stages microcirculation violations are detected. Damages of an intercellular matrix (an interstitial edema and a myofibrosis) develop then. Dystrophic-degenerative and atrophic changes of cardiomyocytes come to the foreground in a terminal stage.

DISCUSSION

The high frequency of NCMP in patients with schizophrenia is evidence that just the wide use of neuroleptics in medical practice is the cause of development of the given cardiac pathology in these patients.

It is seen from our researches clinical diagnostics of NCMP is difficult, because its symptomatology has no specific traits [18].

On the basis of the summarizing of the data, which were received in a series of studies [2, 6, 8, 10], we singled out and proved clinical criteria of diagnostics of NCMP [5, 18, 19]. The diagnostic scheme is imagined in the approximately following way.

Large Criteria (absolute ones)

- Treatment with neuroleptics;
- Absence of another cardiac pathology.

Minor Criteria (relative ones)

- Cardiac complaints (even minimal ones);
- Enlargement of heart size (detection by percussion and by an X-ray examination);
- Physical findings (tachycardia, arrhythmia, dullness of heart tones);
- Changes of an ECG, especially an increase of the QTc interval, rhythm disturbance and asequence;
- Presence of a congestive CCF when other causes of its development are absent;
- Patient's SCD (important for postmortal diagnostics).

It is important to emphasize that each of the above-named signs - if taken separately, without connection with others - is not specific for NCMP. But taken together, these criteria can become a reliable basis for clinical verification of the disease. The main factor, which makes us think of NCMP, is a long intake of antipsychotic drugs.

There is reason to believe that the both large signs and at least two minor ones must be present for diagnostics of NCMP. But further research and accumulation of practical experience are nevertheless required in this direction. In particular, the 2nd large criterion can become ineffective after conduction of research on comorbidity of NCMP and other heart diseases, in particular, ischemic cardiomyopathy, especially in persons older than 45 years.

But already in this stage, the proposed criteria of NCMP diagnostics and approximate diagnostic scheme can, from our point of view, become useful for early detection of this serious complication of neuroleptic therapy for the purpose of its timely corrective treatment.

Postmortal diagnostics of NCMP cause certain difficulties, too. They are mainly connected with insufficient development of morphologic criteria allowing a pathologist to diagnose NCMP [20].

Results of own NCMP morphology study, what we conducted on various levels of research, elucidate the pathologicoanatomic picture of this pathology full enough.

In the course of NCMP morphogenesis all structural components of myocardium (microvasculature, intercellular matrix, cardiomyocytes) are deeply damaged, what sharply reduces its contractile reserves. And detected pathologic changes of cardiac muscle microstructure reflect deep tissular changes of dystrophic-degenerative, sclerotic and - to a lesser degree - compensatory-adaptive character, which develop in the myocardium in the process of NCMP morphogenesis. All above-named pathologic changes are objective, reliable morphologic signs and a physical basis of a myocardial dysfunction [21, 22], which ultimately leads to advance of a fatal CCF.

Each of these signs in it self - if taken separately - is not specific for NCMP. But taken together, the above-named morphologic changes form a sufficiently reliable basis for pathologicoanatomic diagnostics of this disease [12, 19, 20].

Thus, NCMP possesses all signs of the concept "illness" that is has own epidemiology, etiology, pathogenesis, clinic and morphology.

CONCLUSION

Taking the described clinical and morphologic peculiarities of NCMP into account, it is advisable and quite logic to single-out this pathology into an independent nosologic unit. According to the ICD-10 it can be placed under the code I42.7 "Cardiomyopathy, caused by effect of drugs and other external factors", with an additional code which reflects the external cause of the disease (class of antipsychotic drugs) – Y49.3-Y49.5 [5, 16].

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