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Mini Review Article

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The Role of Cardiomyocyte Apoptosis in the Pathogenesis of Neuroleptic Cardiomyopathy

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Summary

In the presented mini-review of the literature the role of cardiomyocyte apoptosis in the pathogenesis of neuroleptic cardiomyopathy is considered. Despite the insufficient development of the issue and the scarcity of literature data, various ways of negative influence on the heart of the side effect of cardiotoxic antipsychotic drugs leading to a decrease in myocardial mass due to the death of cardiomyocytes by apoptosis are convincingly shown, which initiates the process of heart remodeling with the subsequent development of myocardial dysfunction and progression of heart failure.

Keywords: Antipsychotics, Neuroleptic Cardiomyopathy, Apoptosis of Cardiomyocytes

One of the most dangerous complications of antipsychotic therapy (APT) is neuroleptic cardiomyopathy (NCMP) developing due to the side cardiotoxic action of antipsychotic (neuroleptic) medications (AP) [1-4].

Along with the fact that the etiology of the disease is quite clearly defined, its pathogenesis remains not fully studied. Literary data, though not very numerous and often indirect, give some food for certain seasonings concerning pathogenesis of NCMP.

In general, it seems that the adverse side effect of AP on the myocardium, whether it is a direct cardiotoxic effect or mediated metabolic effect, is diverse and multifaceted, affecting various aspects of the morphology and physiology of the heart. Therefore, the pathogenesis of NCMP is a difficult and complex process, many elements of which are closely linked.

At certain stages, they often occur in parallel, potentiating each other and increasing the overall pathological effect, or make up the links of a vicious circle. The final result of the considered pathogenetic chain is the development of such a formidable complication of APT as NCMP.

One of the important elements of the pathogenesis of NCMP is a decrease in the number of cardiomyocytes (CMC). It is well known that the main determinant of myocardial dysfunction and heart failure (HF) in most pathological cardiac processes, including idiopathic dilated cardiomyopathy (DCMP), may be the loss of CMC (Figure 1), which is one of the main triggers of cardiac remodeling [5-13]. Thus, according to the data of C. A. Beltrami with co-authors (1995), in the terminal stage of DCMP with the manifestation of decompensate chronic HF, the number of CMC in the muscle of left ventricle is reduced by 28% [8].

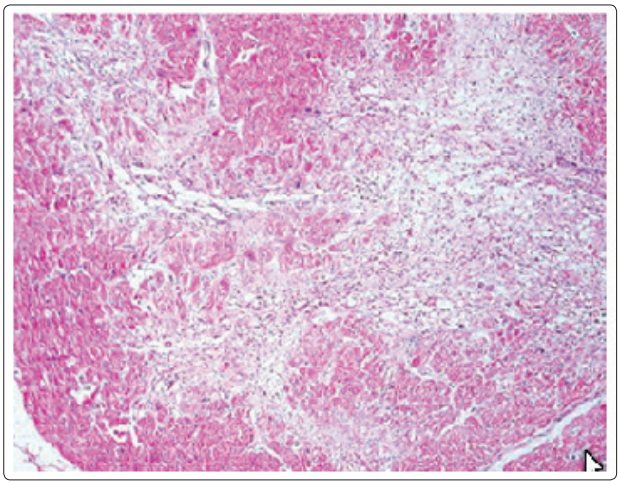

Figure 1: DCMP, end-stage: decrease of number of CMC (hematoxylin and eosin, X40) [14].

And in this progressive decline CMC makes a significant contribution to the process of apoptosis [5, 6, 12, 15-18]. For example, it was found that apoptosis in cardiomyocytes is significantly increased in end-stage CH, myocardial ischemia, and in idiopathic DCMP and ischemic cardiomyopathy [5,12,16,19,20]. The concept of the essential role of apoptosis in the pato- and morphogenesis of DCMP is confirmed by the results of experimental studies [21, 22].

Thus, the CMC apoptosis in idiopathic DCMP is the predominant mechanism of mass loss of myocardium [21-23], leading to the development of mycardial dysfunction and increase circulatory failure [6].

In principle, nothing prevents a similar mechanism from taking place under the NCMP. Indeed, in the literature there is, although very scarce, information about the direct negative impact of AP on the process of apoptosis. For example, the experiment revealed an increase in apoptosis under the influence of chlorpromazine and haloperidol [24,25].

More information can be found regarding the indirect participation of AP in initiation and increase of CMC apoptosis by means of one of the components of the cardiotoxic side effect of these drugs, such as mitochondrial dysfunction (MDF). It is known that MDF and closely related oxidative stress cause increased apoptosis of CMC with all the ensuing negative consequences for the heart. Thus, a number of authors report structural damage to mitochondria and MDF caused by exposure to both typical and atypical AP [5, 26-30].

At least three pathophysiological pathways of MDF development have been established, the triggering factor of which is hypoxia, inflammation and metabolic disorders [31, 32]. These processes are associated, among other things, with the reception of AP. All these collisions are analyzed in detail in my monographs [31, 32].

Thus, the use of AP due to their wide range of side effects affecting a variety of physiological and pathological processes occurring in the heart, leads, although in different ways, to a single ultimate goal – the development of MDF in CMC, which starts the process of apoptosis of the latter, contributing to the reduction of myocardial contractility and the manifestation of chronic HF [31-33]. Such consequences of CMC apoptosis, which plays an important pathogenetic role, are typical for NCMP.

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