SHORT COMMUNICATION

Apoptotic changes in the myocardium in the course of experimentally-induced pleurisy

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The secreted proinflammatory interleukins IL-1, IL-6 and TNF in the course of experimentally-induced pleurisy can be the cause of pathological changes in the ultrastructure of cardiac muscle and of apoptosis. The pleurisy was induced in rats by means of carrageenin. The scraps of cardiac muscle obtained during the inflammatory reaction in the pleura were analysed by means of an electron microscope. The scraps were also stained with the TUNEL method in order to find the apoptotic foci. It was proved by the experiment that the inflammatory process affected mitochondria in the cardiomyocytes, enhanced collagen fibre synthesis and contributed to the formation of apoptotic foci in the cardiac muscle.

Key words: pleurisy, ultrastructure of cardiac muscle, apoptosis

INTRODUCTION

The elimination of the damaging factor is the foremost target in the inflammatory process. Hence, the whole array of defence and reparative mechanisms, the humoral and cellular immunological response, are triggered in the course of inflammation. The immunological processes are localised in the affected organ. However, they also induce a systemic response. The inflammatory response is composed of an acute and a chronic phase. The acute phase, which sets in within hours of the damaging factor invading the organism, turns into the chronic phase as it takes its course. The phases of the inflammatory process take place in a prearranged order so that successive activation of the inflammatory mediators is synchronised with a cellular response. Elimination of the inflammatory factor in the affected organ may exert a negative influence on the other systems of an organism as a result of uncontrolled activation of the proteolytic processes [6]. These mechanisms play an essential role in the elimination of the inflammatory factor and in expulsion of the damaged cells. An appropriate quantity of adrenal glicocorticoids is secreted in the course of the inflammatory process. These cooperate closely with cytokines such as IL-6, IL-1 and TNF, which are secreted by macrophages, fibroblasts and mast cells. The released glicocorticoids stimulate limphocytes Th2 and enhance the synthesis of acute phase proteins. In addition, the endogenous glicocorticoids are responsible for hindering phagocytosis and stabilising the lisosomal membranes, which prevent cell damage. Moreover, a significant quantity of proinflammatory cytokines is released within the first hours of inflammatory process. These cytokines are responsible for the induction of platelet aggregation, the activation of macrophages and the enhancement of neutrophil adhesion. Neutrophils secrete proteases such as collagenase and elastase [4]. The enzymes bring on the domination of the destructive processes in the inflammatory focus, which in turn increase the blood concentration of collagen degradation products [3, 6]. Blood coagulation is also activated in the early phase of inflammation. The increased concentration of proinflammatory cytokines (IL-1, TNF) activates the fibroblasts to release IL-6, which stimulates hepato-

cytes to produce, in due course, fibrinogen [1]. An increase in lipoproteins and cholesterol concentration in the blood is also an element in the systemic inflammatory response.

Lipoproteins form complexes with fragments of antigen. This process weakens the inflammatory reaction, which also causes pathological changes in the vascular epithelium [8]. Hence, the increase in the blood concentration of lipids is a preventive reaction of the organism, which is bound to counteract the negative influence of antigens on the organs. Furthermore, lipids participate in the reconstruction of cellular membranes after ablation of the inflammatory focus [5].

The types of change which take place in the inflammatory focus in the lungs have previously been investigated [3]. The succession of destructive and reparative processes has been established as a result of morphological examination of the inflamed tissue and measurement of collagen degradation products in serum. The previous investigations suggest that the inflammatory processes make a significant contribution to the pathogenesis of atherosclerosis in blood vessels, which impairs the circulatory system. Hence, the aim of the study was evaluation of the ultrastructure of the myocardium with special attention to apoptotic foci in the heart muscle during experimentally-induced pleurisy. The study would inevitably reveal whether inflammatory process in a distant organ (the lung) can induce destructive changes in the heart.

MATERIAL AND METHODS

The study was performed on 25 rats of the Buffalo strain aged 16 weeks and weighing 180–200 grams. The experimental pleurisy was induced by means of 1% solution of carrageenin (Sigma Company). The carrageenin solution was injected intrapleurally in a volume of 0.15 ml. The scraps of heart muscle (left ventricle) were taken after 24, 72 and 120 hours, following the onset of the inflammatory reaction. Afterwards, the scraps were routinely prepared for electron microscope analysis and stained with the TUNEL method in order to determine the presumed apoptotic foci.

RESULTS

The electron microscope analysis of the cardiac muscle scraps in the course of induced pleurisy demonstrated an increase in mitochondria volume in the 24th hour of the experiment in comparison with the control group (Fig. 1, 2). Besides this, derangement of the internal structure of the mitochodria was observed in the 72nd hour of the induced inflammation in pleurisy (Fig. 3). The further course of the inflam-
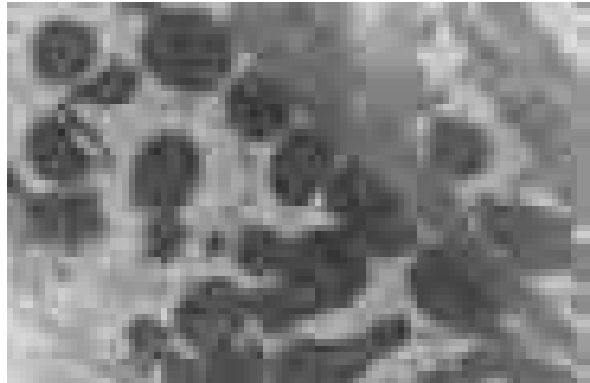

Figure 1. Control group. Cardiomyocytes, mitochondria. Electron microscope, magnified 20 000 times.
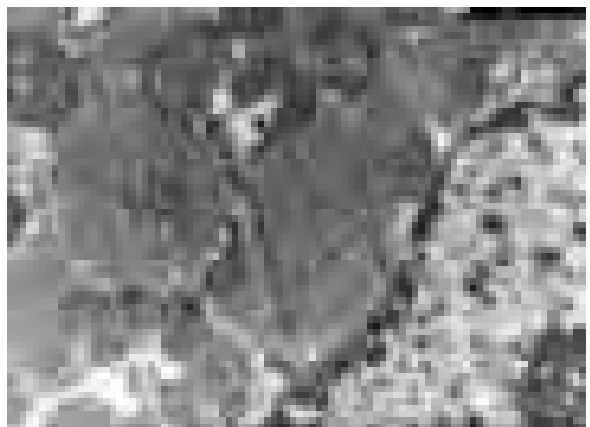

Figure 2. Oedema of mitochondria and cardiomyocytes. 24th hour following the onset of pleurisy. Electron microscope, magnified 20 000 times.

Figure 3. Derangement of the structure of mitochondria in cardiomyocytes. 72nd hour following the onset of pleurisy. Electron microscope, magnified 25 000 times.

matory process (120th hour) was characterised by the enhanced activity of fibroblasts and increased collagen production (Fig. 4).

Figure 4. Activation of fibroblasts, collagen fibres. 120th hour following the onset of pleurisy. Electron microscope, magnified 20 000 times

Analysis of the stained preparations of cardiac muscle showed the apoptotic nuclei in cardiomyocytes in the 120th hour of the inflammatory process (Fig. 5).

DISCUSSION

The changes observed in the ultrastructure of the cardiac muscle are related to damage to the energy centres, namely the mitochondria, which play a significant role in the maintenance of the chronotropic, inotropic and batmotropic activity of the heart muscle. Stimulation of the cardiac fibroblasts and increased synthesis of collagen in the course of the inflammatory process presumably exerts a significant influence on the dynamics of the heart's systole and contributes to the depressed haemodynamic effectiveness of cardiac muscle. With reference 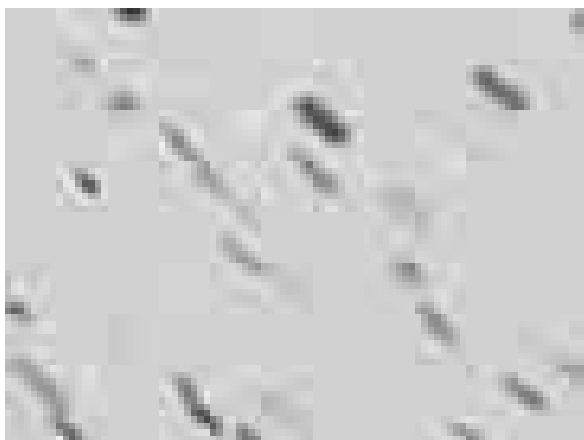to the results obtained, it must be stressed that the inflammatory reaction, which takes place in the distant organ, can exert a negative influence on the function and morphology of cardiac muscle. It is also immensely significant that apoptosis of the cardiomyocytes was observed soon after the onset of inflammatory reaction in pleurisy. The appearance of such conspicuous changes in the morphology of the cardiac muscle in the course of non-bacterial pleurisy shows that the inflammatory foci in the organism may have their negative influence on the function of the distant organs and especially the heart [8]. The secretion of proinflammatory cytokines IL-1, IL-6 and TNF in the early stage of inflammatory reaction is presumably a significant cause of the above-mentioned pathological changes in the heart [2]. With enhanced adhesion of the neutrophils to the vascular endothelium and release of the proteolytic enzymes (elastase and collagenase) IL-1 aggravates the inflammatory reaction and can therefore be a mediating cause of apoptotic changes. Increased collagen synthesis by fibroblasts, which can impair the function of cardiomyocytes, is related to IL-1 and IL-6 activity. The increased production of glicocorticoids, stabilising cellular membranes in inflammatory reaction, can ward off the aforementioned adverse effects of cytokines [7]. The elevated blood concentration of triglycerides and cholesterol observed is connected with the increased secretion of glicocorticoids in the course of the inflammatory process.

CONCLUSIONS

1. Pathological changes in the ultrastructure of the mitochondria of cardiomyocytes were found in the course of experimentally-induced pleurisy.

2. Apoptotic foci in the cardiac muscle were observed in later stages of the inflammatory process.

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Figure 5. Apoptotic nuclei of cardiomyocytes. TUNEL method, magnified 600 times.

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