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IMMUNOHISTOCHEMICAL CHARACTERISTICS OF CARDIOMYOCYTES IN CHRONIC ISCHEMIC HEART DISEASE

Botirov Doniyor Abdusaidovich,
Shukurova Yulduz Utkurovna
Samarkand State Medical University, Alfraganus University
E-mail: Doniyor.batirov2017@yandex.ru
Phone: +998 (88) 925-00-36

Abstract
In the immunohistochemical study of myocardium in chronic ischemic heart disease (CIHD), the following main markers were used: Desmin, SA sarcomeric actin, and the myogenic regulatory factor MyoD1 (myogenin). The desmin marker applied in this study represents the protein structures of the intermediate filaments forming the framework of myocardial myocytes, determining muscle contractility, and is expressed in both skeletal and cardiac muscles. This intermediate filament protein is mainly localized in the cytoplasm of cardiomyocytes, exhibiting an intense golden-yellow staining pattern and uniform expression in healthy muscle fibers. Cytoplasmic staining appears as homogeneous yellow coloration, which is characteristic of intact muscular components.

Keywords: immunohistochemical examination, desmin, myogenin, myocardium.

Introduction

Relevance of the problem

Ischemic heart disease (IHD) ranks first among all diseases worldwide. Out of the global population of approximately 4.1 billion, a significant proportion suffers from various nosological forms of chronic ischemic heart disease. This underscores the persistence of the problem and the diversity of the proposed diagnostic and therapeutic recommendations. For instance, in the United States and Europe, about 18.3 million deaths annually are attributed to myocardial infarction, while in the Russian Federation and CIS countries, this figure averages 10.8 million, with the highest incidence recorded in 2022. Globally, the total number of deaths caused by CIHD was approximately 45.4 million.

Although both foreign and domestic researchers have extensively investigated the morphological and clinical aspects of CIHD, the diversity and evolution of its etiological factors continue to influence myocardial morphology. The indirect causes of IHD — varying by population, lifestyle, and environmental exposure — necessitate studying specific myocardial morphological alterations and identifying the precise substrates indicating early injury within cardiac substructures.

For example: In the U.S. and Europe, obesity is a major contributing factor to CIHD development. In China and Japan, despite higher levels of physical activity, chronic emotional stress leads to coronary insufficiency and myocardial ischemia. In Siberia and the Far East, deficiency of vascular-strengthening substances (such as Vitamin C) contributes to interstitial

edema and dystrophic changes in the myocardium, associated with acute metabolic disturbances.

Material and Methods

The research material consisted of 132 autopsy cases from the Republican Center for Pathological Anatomy, where death resulted from acute myocardial infarction on the background of chronic ischemic heart disease. Of these, 85 were male and 47 were female.

Tissue samples from the myocardium were prepared for morphological examination. Sections were stained with hematoxylin and eosin (H&E) and microscopically evaluated to assess structural alterations.

Objective

To investigate the morphological characteristics of the myocardium in chronic ischemic heart disease (CIHD).

Discussion and Results

In the present study of chronic ischemic heart disease, a weakly positive desmin immunoreactivity was identified in 73.8% of the examined cases. From a clinicomorphological perspective, this finding indicates excessive proliferation of fibrous structures within the myocardial stroma, blockage of conduction pathways, and disruption of intercellular connectivity among bundles of cardiomyocytes. Within the cytoplasm of cardiomyocytes, the desmin marker exhibited a faint golden coloration in the perinuclear regions, forming homogeneous protein substrates with low-level immunoreactivity. This pattern confirms a marked reduction in the synthesis of intermediate filaments during the course of chronic hypoxic processes in cardiomyocytes. In the control group, this indicator demonstrated strong positive expression in 83.16% of samples, which reflects normal synthesis of intermediate filaments within intact myocardial cells. Thus, during chronic myocardial ischemia, the synthesis of intracellular intermediate filaments decreases sharply, depending on the duration and age-related progression of the disease. According to the WHO classification, the highest reduction rate of desmin expression was observed in individuals aged 45–59 years. In contrast, 71.16% of patients aged 18–44 years demonstrated strong positive immunoreactivity, indicating that, due to ongoing morphological adaptation processes, intracellular synthesis of intermediate filaments remains sufficient at younger ages. Among the 45–59-year-old group, 26.2% of cases showed a negative desmin reaction, whereas in the 60–74-year-old group, 55.61% exhibited weakly positive, and 44.39% demonstrated negative immunoreactivity. These results collectively illustrate the progressive decline in cytoskeletal protein synthesis in cardiomyocytes correlated with advancing age and the severity of chronic ischemia.

Expression Levels of the Desmin Marker in Different Age Groups with Chronic Ischemic Heart Disease (in %)

Groups	Total number of cases	Strong positive	Moderate positive	Weak positive	Negative reaction
Control group	12	86,16%	12,12%	1,72%	-
18–44 years	26	71,16%	16,5%	12,34%	-
45–59 years	26	-	-	83,16	16,84%
60–74 years	26	-	-	55,61%	44,39%
75–90 years	26	-	-	40,12%	59,88%
Total	116				

Subsequent immunohistochemical investigations were primarily focused on identifying the MyoD1 (myogenin) protein marker. This protein is mainly expressed in cardiomyocytes during the embryonic stage, indicating their proliferative activity. In applied medical research, MyoD1 is utilized as a diagnostic marker for malignant myogenic tumors and, in the context of ischemic heart disease, it serves as an indicator of mesenchymal cell transformation surrounding necrotic cardiomyocytes, thus reflecting the processes of reparative regeneration. In cases of chronic ischemic heart disease (CIHD), MyoD1 was applied as a marker of prolonged reparative activity in cardiomyocytes, characterizing the ongoing regenerative potential of myocardial tissue. This, in turn, demonstrates the transformation and differentiation of stem cells located within the endocardium and pericardium, and confirms that fibroblasts in fibrotic myocardial regions can partially undergo metaplasia into myocytes. According to Zhao B., Chen S., Liu J. et al. (J Cell Mol Med., 2013; 17(1):123–133), activation of the H9c2 gene leads to a sharp decrease in myogenin concentration within cardiomyocytes, promoting restructuring of cardiomyoblasts and the formation of microfocal cardiomyogenesis zones around areas of myocardial necrosis.It is noteworthy that, in ischemic heart disease, positive MyoD1 reactions should not be interpreted as indicators of neoplastic transformation, but rather as evidence of cardiomyoblast and fibroblast transformation into functional myocytes around zones of myosclerosis. This process, as emphasized by several researchers, may be enhanced by fat-soluble vitamins, which stimulate myocardial regeneration under chronic ischemic conditions. Therefore, in our study, the application of the MyoD1 marker serves as an important criterion for identifying mesenchymal cell metaplasia during the reparative regeneration of the myocardium in chronic ischemic heart disease.

Expression Levels of the MyoD1 Marker in Different Age Groups with Chronic Ischemic Heart Disease (in %)

Groups	Total number of cases	Strong positive	Moderate positive	Weak positive	Negative reaction
Control group	12	-	-	1,01%	98,99
18–44 years	26	-	26,92%	61,54%	-
45–59 years	26	-	30,96%	69,04%	-
60–74 years	26	-	-	16,65%	83,35
75–90 years	26			7,82%	92,18%
Total	116				

In patients aged 60–74 years with chronic ischemic heart disease, a marked decrease in the reparative regeneration of myocardial subunits, particularly cardiomyocytes, was observed. This was manifested by weakly positive and negative MyoD1 immunoreactivity, indicating significant impairment of myocardial regenerative capacity. These findings are directly associated with a reduction in the number of stem cells located within the myocardial stroma, endocardium, and pericardium, as well as with predominance of coarse fibrous structures within the stromal component of the myocardium. Morphologically, these changes reflect a disruption of the morphofunctional integrity of the myocardium, characterized by cardiomyocyte bundles of variable size and blockage of conduction pathways due to replacement by fibrous connective tissue. Clinico-morphologically, this demonstrates that in the 60–74-year-old group, the reparative regenerative index of the myocardium decreases sharply, making symptomatic therapeutic interventions less effective. Similarly, in individuals aged 75–90 years, the predominance of weakly positive and negative MyoD1 reactions confirms a further decline in reparative regenerative activity of myocardial cells under chronic ischemic conditions.

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