MORPHOLOGY AND PATHOMORPHOLOGY

Morphofunctional Characteristic of Mast Cells in BALB/c and C57Bl/6 Mice during Cold Exposure

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 138, No. 8, pp. 207-209, August, 2004
Original article submitted February 20, 2004

Mast cells of the mesentery and subcutaneous tissue in BALB/c and C57Bl/6 mice were studied after single and repeated cold exposure (-20°C, 3 min). Immediate adaptive reactions of mast cells in BALB/c and C57Bl/6 mice did not differ after single cold exposure and were manifested in increased degranulation. Repeated cold exposure of BALB/c mice was followed by an adaptive reaction, which included an increase in the count of mast cells in subcutaneous tissue and normalization of the degranulation index. In C57Bl/6 mice the count of mast cells in subcutaneous tissue decreased, while the degranulation index remained high. These changes reflect the disadaptive response of mast cells to repeated cold exposure.

Key Words: *cold exposure; adaptation; mast cells; BALB/c and C57Bl/6 mice*

An impressive body of evidence illustrates morphological heterogeneity, polyfunctionality, and involvement of mast cells (MC) into the pathological process [2,3]. MC are present practically in all organs and tissues. Perivascular MC closely contact with sympathetic and parasympathetic endings of the autonomic nervous system [12]. Mediators of MC released under the influence of exogenous and endogenous factors modulate the microcirculatory system, blood flow rate, permeability of capillaries, and functional state of microenvironmental cells (lymphocytes, histiocytes, fibroblasts, and endotheliocytes). The development and progression of adaptive reactions and pathological changes in tissues depend on functional activity of MC [11].

Little is known about morphofunctional changes in MC of laboratory animals during adaptation to stress [10]. Various stress factors induce similar reaction of MC, which includes changes in the count and degranulation of cells.

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During immediate and long-term adaptation to physiological hypoxia, degranulation of lung MC in Sprague—Dawley rats highly sensitive to hypoxia is more pronounced than in Wistar rats resistant to hypoxia. In Wistar rats long-term adaptation to hypoxia is accompanied by an increase in the count of MC in the lungs. Analysis of autopsy specimens showed that the count of MC in the lungs increases in high-mountain inhabitants [13].

Our previous studies revealed interstrain morphofunctional differences in localization of MC populations under normal and stress conditions.

Here we studied MC of the mesentery and subcutaneous tissue in BALB/c and C57Bl/6 mice after single and repeated cold exposure.

MATERIALS AND METHODS

Experiments were performed on 60 male BALB/c and C57Bl/6 mice weighing 18-20 g. The animals differed in psychophysiological and immune indexes. The experimental and control groups included 10 animals of each strain [5,15]. Treated mice were exposed to single

0007-4888/04/1382-0182

or repeated cooling at -20°C for 3 min. Cold exposure was followed by a decrease in rectal temperature by 1°C, but did not cause muscle tremor. The animals were examined on days 1 and 10 after cold exposure, which corresponded to the phase of immediate adaptation and transition to long-term adaptation [7]. The mice were euthanized by hexenal overdose 1 day after single exposure or last session of repeated exposure. Subcutaneous tissue was taken from the anterior abdominal wall and mesentery. Film preparations of subcutaneous tissue and mesentery were fixed with 10% neutral formalin and stained with 0.1% toluidine blue (pH 2.0) [14]. MC were counted in the field of view at a magnification of 400. We analyzed 10 fields of view in each preparation. Functional activity of MC was estimated by the degree of degranulation. The index of degranulation was calculated [6]. The results were analyzed by Student's *t* test.

RESULTS

The population of MC in the mesentery and subcutaneous tissue of intact animals was presented by an equal number of dark and light cells. The count of dark cells slightly exceeded that of light cells. Oversaturated and exhausted cells were rarely seen. The count of MC in subcutaneous tissue of C57Bl/6 mice was much higher compared to BALB/c mice (Table 1). No interstrain differences were revealed in the degranulation index for MC of subcutaneous tissue and mesentery.

The number of light and exhausted cells increased after single cold exposure. The count of MC in mouse subcutaneous tissue and mesentery remained unchanged after single cold exposure (Table 1). The degranulation index in subcutaneous tissue and mesentery significantly increased in mice of both strains.

After repeated cold exposure the count of MC in subcutaneous tissue significantly increased in BALB/c mice, but decreased in C57Bl/6 mice (Table 1). The number of MC in the mesentery of repeatedly treated animals did not differ from the control.

Cooling is followed by cold spasm of small arteries and arterioles in the skin, redistribution and reduction of blood flow in capillaries, decrease in heat emission, changes in tissue metabolism, and increase in heat production [8]. Perivascular MC contacting with nerve endings play a key role in vascular reactions and metabolic changes during cold exposure [2].

The count of MC in the mesentery and subcutaneous tissue of BALB/c and C57Bl/6 mice remained unchanged, while the degranulation index increased during immediate adaptation to cold (Table 1). The immediate adaptive reaction to cold is related to changes in functional activity of MC without variations in cell count.

Degranulation of MC is accompanied by the release of bioactive substances histamine, heparin, proteases, and lipid transmitters (prostaglandins, leukotrienes, and platelet-activating factor). Biolactive substances of MC perform vasoactive functions, affect blood rheology, and modulate the state of autonomic nervous endings and functional activity of microenvironmental cells [4].

BALB/c mice exhibited adaptive reaction to repeated cold exposure, which was manifested in the increased count of MC in subcutaneous tissue. However, the degranulation index in these animals did not differ from the control. In C57Bl/6 mice repeatedly exposed to cold stress the count of MC significantly

TABLE 1. Morphometric Characteristics of MC in Connective Tissue and Degranulation of MC in BALB/c and C57Bl/6 Mice under Normal Conditions and after Single and Repeated Cold Exposure ($M \pm m$)

Group	Subcutaneous tissue		Mesentery	
	BALB/c	C57Bl/6	BALB/c	C57Bl/6
MC count in 1 field of view				
Control	14.5±1.1	21.2±1.4	3.6±0.3	3.7±0.3
Cold exposure (-20°C, 3 min)				
single	17.5±2.2	21.0±3.6	4.2±0.4	3.3±0.5
repeated	26.5±1.5**	15.4±1.7*	3.9±0.3	3.9±0.4
Degranulation index				
Control	2.31±0.04	2.40±0.06	2.21±0.13	2.31±0.05
Cold exposure (-20°C, 3 min)				
single	2.72±0.11*	2.86±0.07**	2.81±0.11**	3.17±0.12**
repeated	2.20±0.03	2.78±0.07*	2.23±0.08	3.02±0.08**

Note. *$p<0.01$ and **$p<0.001$ compared to the control.

decreased in subcutaneous tissue, but remained unchanged in the mesentery. The degranulation index in subcutaneous tissue and mesentery of C57Bl/6 mice remained high. Morphofunctional characteristics of MC suggest the long-term adaptive reaction to repeated cold exposure is not formed in C57Bl/6 mice.

Differences in the reaction of MC to cold exposure are determined by genetic characteristics of the organism that play a role in the stress response and adaptation [9]. Previous studies revealed interstrain differences in the resistance to emotional stress, content of neuropeptides, sensitivity to hypoxia, and type of the immune response in BALB/c and C57Bl/6 mice [1,5,15]. Antigenic stimulation of C57Bl/6 and BALB/c mice induces the immune response that is realized via T helper cells of types 1 and 2, respectively [15].

Morphofunctional changes in the population of MC reflect interstrain differences in the adaptive response to cold exposure.

Immediate adaptive reactions of MC in BALB/c and C57Bl/6 mice did not differ after single cold exposure and were manifested in increased degranulation. Repeated cold exposure was followed by adaptive reaction of MC in BALB/c mice. We observed an increase in the count of MC in subcutaneous tissue and normalization of the degranulation index. In C57Bl/6 mice the count of MC in subcutaneous tissue decreased, while the degranulation index remained high. These changes reflect the disadaptive response of MC to repeated cold exposure.

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