ULTRASTRUCTURAL CHANGES IN SOMATOTROPHS OF THE ADENOHYPOPHYSIS DURING DEVELOPMENT OF TRANSPLANTATION IMMUNITY

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An important aspect of the problem of overcoming tissue incompatibility during organ and tissue transplantation is the elucidation of complex relations between the lymphoid and neuroendocrine systems responsible for immune homeostasis. Among hormones participating in immune responses, a special place is occupied by thymosin, whose synergist is the somatotrophic hormone (STH) of the pituitary gland. STH regulates maturation and function of thymus cells and determines hyperplasia of the lymphoid tissue [4, 6, 10]. It is accordingly interesting to study ultrastructural changes in somatotrophs during the development of the transplantation immune reaction, and this was the aim of the investigation described below.

EXPERIMENTAL METHOD

Two series of experiments were carried out on 144 animals. In series 1, 54 mice of the inbred BALB/c line underwent skin autografting, and in series 2, 54 mice of the same line underwent transplantation of skin allograft from C57BL mice, differing with respect to the strong H-2 histocompatibility locus. The control consisted of 36 intact BALB/c mice. The adenohypophysis was removed 1, 7, 10, and 14 days after the beginning of the experiment. Material for electron microscopy was prepared by the usual method. Electron micrographs were obtained on the N-600 electron microscope with magnification of 1500 to 25,000. For stereometric analysis of the organelles of the somatotrophs the dot counting method [2] was used, in conjunction with the MK-56 programed electronic microcalculator. The numerical results were subjected to statistical analysis at the Computer Center of the Ministry of Health of the Uzbek SSR, on the "Iskra-1256" microcomputer.

EXPERIMENTAL RESULTS

Five types of somatotrophs, differing in their submicroscopic organization depending on the phase of the secretory function, were distinguished in the adenohypophysis of the intact mice, each phase differing not only in the content and topography of the secretory granules, but also in the relative volume of the organoids, architectonics, and localization, and the spatial correlations between them in the cytoplasm.

After auto- and allografting (Tables 1 and 2) significant changes were found in the relative numbers of different types of somatotrophs and their ultrastructure. For instance, only 24 h after autografting (the alarm phase of the general adaptation syndrome; GAS) the number of cells in the phase of active protein synthesis increased, and by the 7th day it was 2.5 times greater, and was accompanied by a reduction almost by half of the number of adenocytes in the degranulation phase. In the period described, conspicuous features were considerable swelling of the mitochondria in somatotrophs, indistinctness of the matrix,

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TABLE 1. Number of Somatotrophs (in %) in Adenohypophysis in Different Functional Phases, Associated with Skin Auto- and Allografting

Days of experiment	Phase of secretory function				
	relative rest	active protein synthesis	deposition of secretion	release of secretion	restoration of organoids
	Autografting				
1st	5,97	41,79	29,85	10,45	11,94
7th	13,04	47,83	26,09	8,70	4,35
10-th	20,11	19,89	39,91	10,04	9,98
14-th	18,21	36,29	27,32	9,12	9,09
	Allografting				
1-st	12,37	31,96	22,68	23,71	9,28
7-th	14,81	25,93	22,19	33,28	3,70
10-th	24,32	45,05	16,22	7,17	7,21
14-th	11,76	23,53	41,18	17,65	5,88
Normal	18,66	20,03	24,02	16,04	21,33

TABLE 2. Volume Fraction (in %) of Intracellular Structures of Adenohypophyseal Somatotrophs in Different Functional Phases 24 h after Skin Auto- and Allografting (stereometric analysis, M ± m)

Phase	Experimental conditions	Secretory granules	Nucleus	Mitochondria	RER	Golgi complex	Other organelles
Relative rest	Intact	19,28±4,08	34,04±5,61	4,76±1,27	17,62±3,91	2,78±0,66	20,79±4,12
	Autografting	15,20±5,09	29,15±6,39	14,03±4,88	9,75±4,20	4,41±1,39	30,09±2,71
	Allografting	14,65±4,85	21,49±5,46	8,71±4,89	15,31±4,89	9,61±4,01	27,35±2,39
Active protein synthesis	Intact	19,12±5,03	31,45±6,01	4,44±2,33	20,40±4,83	2,26±0,22	20,79±4,12
	Autografting	18,77±3,68	20,92±3,72	9,72±2,49	16,46±3,31	7,60±4,67	26,47±1,89
	Allografting	26,47±7,52	32,77±7,87	6,89±4,31	14,99±5,91	0,64±0,54	18,29±1,64
Deposition of secretion	Intact	25,77±1,27	30,01±1,23	5,95±1,43	8,83±1,41	2,93±1,45	26,48±4,31
	Autografting	28,73±4,87	23,67±5,39	4,19±1,48	13,35±3,65	1,44±0,90	28,61±2,03
	Allografting	37,51±6,45	17,44±4,92	7,74±3,91	8,82±4,05	4,06±2,56	22,41±2,28
Release of secretion	Intact	17,31±1,11	46,73±6,84	4,31±1,19	9,09±1,16	0,42±0,37	21,98±2,87
	Autografting	15,20±5,09	29,16±6,40	14,04±4,84	9,75±4,21	4,42±1,94	27,36±1,93
	Allografting	11,11±5,60	45,24±8,87	5,55±4,08	11,11±5,60	0,75±0,08	26,10±2,33
Restoration of organoids	Intact	16,90±1,90	48,39±1,49	4,30±2,03	16,13±2,03	0,22±0,01	14,03±1,96
	Autografting	20,46±5,38	30,67±6,19	10,84±4,44	22,65±5,75	3,69±2,69	11,58±1,06
	Allografting	13,80±6,61	26,05±7,63	5,08±4,21	33,49±8,69	6,43±5,48	15,12±1,07

Legend. Differences compared with control significant at the 95% level ($p < 0.05$).

lysis of the cristae, and marked hypertrophy and hyperplasia of the Golgi complex and rough endoplasmic reticulum (RER). From the 10 th day after autografting (the adaptation phase of the GAS) the number of cells in the phase of active protein synthesis fell sharply, and was accompanied by a marked increase in the number of somatotrophs in the phase of deposition of secretion. By the 14th day, the phase of exhaustion of the GAS, the opposite picture was observed, the decrease in the number of somatotrophs in the phase of deposition being due not to degranulation, the degree of which remained low, but to crinophagy, giving rise to intracellular utilization of excess hormone.

A different dynamics was observed after allografting (Tables 1 and 2). For instance, 24 h after the operation (inductive phase of immunogenesis) the number of somatotrophs both in the phase of active protein synthesis and in the degranulation phase was increased (by 1.5 times), accompanied by a decrease in the number of cells in the phase of deposition of secretion. Considerable differences also were noted in the volume fraction of organelles in the same phases of the secretory cycle (Table 2). On the 7th day (the period preceding the rejection crisis) the number of somatotrophs in the phase of active protein synthesis was reduced and their number in the phase of degranulation more than doubled. The secretory granules in the latter, in cells in the degranulation phase, were reduced in volume, and variable in size and electron density. The nucleus and RER were reduced in volume and the

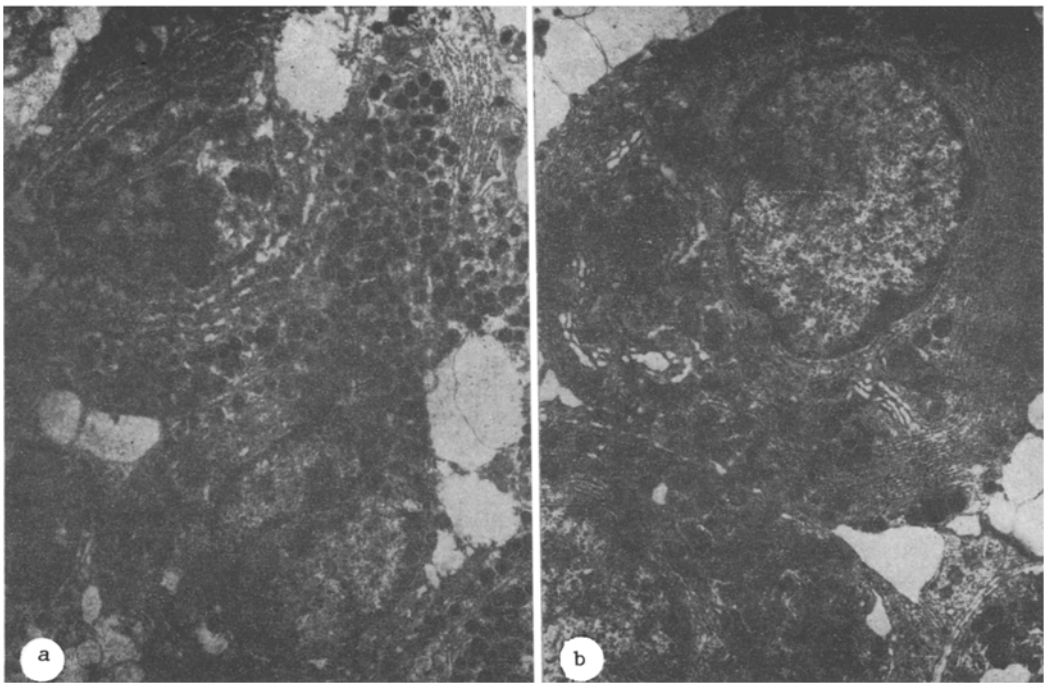

Fig. 1. Ultrastructure of somatotrophs in phase of active protein synthesis: during rejection crisis (a) and after rejection of allogeneic skin graft (b). Magnification: 3500 (a), 6000 (b).

Golgi complex was located in the perinuclear region. During the rejection crisis (10th day) the number of cells in the phase of active protein synthesis in the adenohypophysis was increased by 2.5 times, whereas their number in the degranulation phase was reduced more than fourfold. After rejection (14th day) a tendency was noted for the number of somatotrophs in the phase of deposition of secretory granules to rise, accompanied by a fall in the number of cells in the phase of active protein synthesis. The latter differed in their ultrastructure from those in the period of the rejection crisis (Fig. 1a, b).

Changes differing in character, intensity, and genesis thus develop in the ultrastructure of the somatotrophs after auto- and allografting. After autografting, for instance, during the first 7 days protein synthesis was activated at a time of low STH release into the blood stream, leading to deposition of secretory granules. Similar changes in somatotrophs have been described during responses to stress of varied genesis [5, 7, 8]. Different relations between cells and the volume fraction of the organelles in different phases of the secretion cycle were observed during the development of the transplantation immune response. In the induction phase of immunogenesis (after 24 h of the experiment) an increase in the number of cells both in the phase of active protein synthesis and in the degranulation phase was observed, to reach a peak in the period preceding the rejection crisis; this is evidence of forced discharge of the hormone at a time of intensive secretion formation. In the rejection crisis period the intensity of degranulation fell, and this was accompanied by a sharp increase in the intensity of synthetic processes, leading after rejection to the majority of cells being in the stage of deposition of secretion.

When these data are compared with changes in the ultrastructure of the reticuloendothelial cells of the thymus in the same animals after allografting, synergism in their functional activity may be seen to be exhibited. On the 3rd day after allografting hypertrophy of the Golgi complex and an increase in the quantity of osmiophilic granules in the secretory vesicles and hyperplasia of the ribosomes were observed. Activation of these cells increased in the period before the rejection crisis, and in the rejection period itself [1, 9]. At this same time, lymphoreticular proliferation, blast transformation, and macrophagal and plasma-cell reactions in the lymph nodes, spleen, and thymus, reached their maximum [1, 3].

The results show that an important role in the development of the transplantation immune response is played by the functional state of the somatotrophs, and this must be taken into consideration when problems relating to hormonal correlation of this type of immunity are studied.

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MORPHOLOGICAL AND PHYSIOLOGICAL CHARACTERISTICS OF LYMPH NODES, THYROID GLAND, AND TESTES OF RATS DURING STRESS-INDUCED ADAPTATION AND ACTIVATION

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The study of dependence of the character of response of an organism to the factor acting on it has led to the discovery of general nonspecific adaptive responses (GNAR) such as the training response, developing in response to a weak stimulus, and the activation reaction developing in response to a stimulus of average strength [4, 6]. Unlike stress, which is the nonspecific basis of many pathological processes, these GNAR are physiological and are characterized by increased activity of the defensive systems of the body [4, 6]. An important role in this situation is played by inclusion of lymphoid and endocrine organs in the reactive process. The aim of this investigation was to compare quantitatively the morphological and physiological changes taking place in lymph nodes, the thyroid gland, and testes of rats and to establish correlation between characteristic parameters of the state of these organs during the development of a response of stress and activation.

EXPERIMENTAL METHOD

Responses of stress and activation were induced by subcutaneous injections of adrenalin into 80 noninbred male albino rats weighing 160-170 g, in doses of 125 µg/kg (group 1) and 5 µg/kg (group 2) body weight. The development of the response was signaled by values of blood parameters [5, 7]. The rats were killed by decapitation 2 days after the injections. Lymph nodes, thyroid gland, and testes were fixed in Carnoy's fluid. Paraffin sections 5 µ thick were stained by Brachet's method. Morphometric investigations were carried out with an ocular

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