EFFECT OF EXPOSURE TO HIGH-ALTITUDE HYPOXIA ON MORPHOLOGY OF THE PITUITARY-GONADS SYSTEM

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UDC 612.432+612.617].06:612.275].086

KEY WORDS: ultrastructure; pituitary gland; testes; high altitude.

Extremal factors associated with high altitudes act on virtually all the organs and systems of the body [1, 3, 6-8]. Activity of the pituitary — testes system under normal conditions has been studied in fair detail [5, 9, 11, 12, 15, 16]. However, the morphological relations between the components of this system at high altitudes have received very little study and the results obtained have been contradictory. The aim of the present investigation was to study the structural basis for interaction within the above-mentioned system.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred mature male rats kept under high altitude conditions (3200 m) for 2 months. The animals were killed under ether anesthesia by decapitation after staying at a high altitude for 24 h and 3, 7, 15, 30, and 60 days. The testes and pituitary gland were fixed for light microscopy in a 10% solution of neutral formalin and in Bouin's fluid, The sections were prepared by the usual method [4] and stained with hematoxylin and eosin, with picrofuchsine by Van Gieson's method, and with aldehyde-fuchsine by the method of Gomori and Gabe. The cells were subjected to quantitative analysis by means of an ocular grid Material for electron microscopy was fixed in 2.5% glutaraldehyde solution and postfixed in 1% osmic acid solution, and embedded in resins [13]. Ultrathin sections were examined in the JEM-7 electron microscope.

EXPERIMENTAL RESULTS

Keeping the animals at a high altitude for 1-3 days led to the development of structural changes in the pituitary gonadotrophic cells Individual follicle stimulating trophocytes were increased in volume. In the cytoplasm, among secretory granules with a varied degree of electron density, large granules with high electron density appeared. Less frequently than in the control pale amorphous bodies were seen and the tubules of the rough endoplasmic reticulum were unevenly dilated. There were no signs of activation of secretory granule formation in the Golgi complex. The mitochondria were enlarged in volume a little, with some degree of translucency of the matrix and fragmentation of the cristae. Similar changes were observed in the luteotrophocytes, large secretory granules with electron-dense contents being observed mainly around the periphery of the cells. Thus in the early stages of adaptation the process of release of hormone stored in the secretory granules was disturbed in the gonadotrophic cells of the pituitary gland, and at the same time signs of depression of the synthesizing function of the follicle-stimulating cells could be detected. Meanwhile there was a very small reduction in weight of the testes. In the interstitial tissue the majority of cells were medium-sized glandulocytes, either clustered together or lying singly. No significant structural changes could be found on light microscopy At the ultrastructural level, signs of hormonal activity remained in most glandulocytes, namely the abundance of branching tubular structures of the smooth endoplasmic reticulum in the cytoplasm (Fig. 1b), dilatation of tubules of the rough endoplasmic reticulum, an increase in the volume of individual mitochondria with condensation of their matrix, and an increase in the number of nuclear pores and marginal distribution of chromatin. Dilated cisterns of the smooth endoplasmic reticulum were identified in the sustentocytes, the number of vesicles was increased (Fig. 1c), the mitochondria was swollen with partial reduction of the cristae, and solitary small spherical mitochondria with electron-dense matrix were encountered. The

Department of Pathological Anatomy, S. M. Kirov Leningrad Postgraduate Medical Institute. Central Research Laboratory, Khirghiz Medical Institute, Frunze. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 111, No. 4, pp. 432-436, April, 1991. Original article submitted June 22, 1990.

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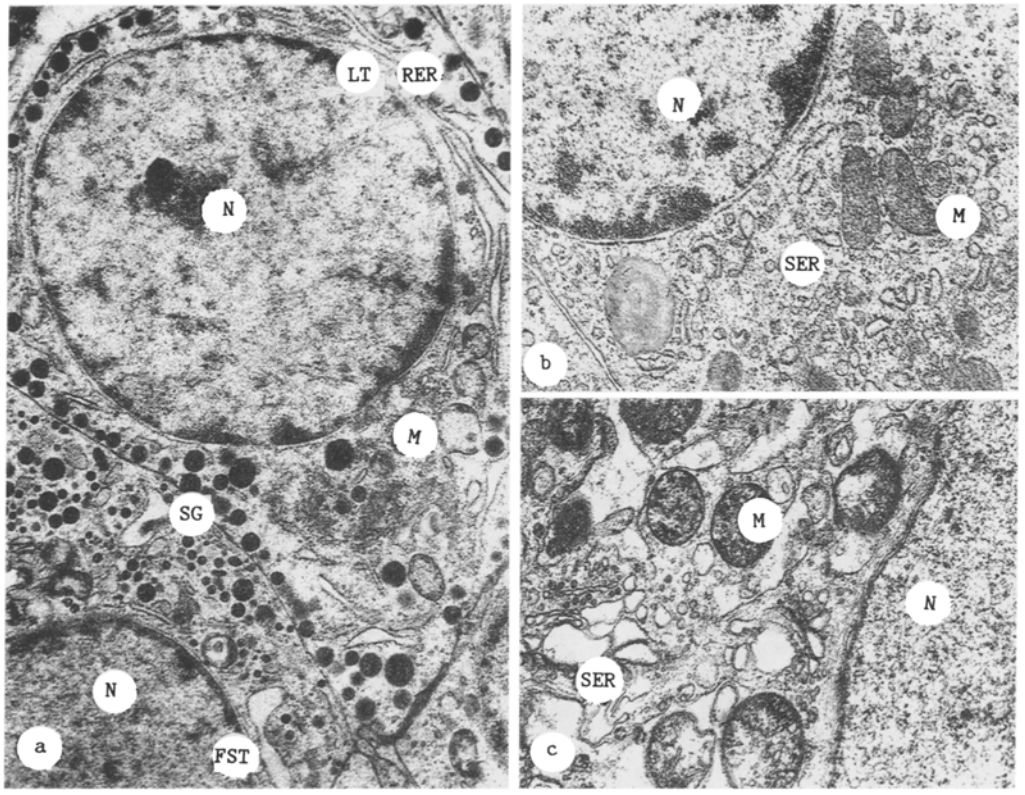

Fig. 1. Ultrastructural changes in pituitary gonadotropic cells and hormone-producing cells of testes on 3rd day after exposure to high altitudes: a) ultrastructure of follicle-stimulating (FST) and luteinizing (LT) trophocytes: N) nucleus, M) mitochondria, SG) secretory granules, RER) rough endoplasmic reticulum. 14,000×; b) increase in volume with condensation of mitochondrial matrix, abundance of structures of endoplasmic reticulum in a glandulocyte: M) mitochondria, SER) smooth endoplasmic reticulum: N) nucleus. 18,000×; c) Dilatation of cisterns of smooth endoplasmic reticulum and swelling of mitochondria in sustentocyte: M) mitochondria, N) nucleus, ER) dilated cisterns of endoplasmic reticulum. 27,000×.

number of ribosomes and the glycogen content were reduced a little, but the number of lipid drops was increased. These changes were found in the sustentocytes of individual seminlferous tubules with evidence of desquamation of the spermatogenic epithelium. All these findings were evidence of reduction of active transport of materisls into the cell and disturbance of the barrier function.

Short-term adaptation of the animals to high altitudes (7th and 15th days) led to an increase in volume of the majority of pituitary gonadotrophic cells. Greatly dilated tubules of the endoplasmic reticulum, and mitochondria of ovoid or rod shape, with a moderately electron-dense matrix, were identified in the translucent matrix of the cytoplasm. Sometimes mitochondria with a translucent matrix and reduction of the cristae were found. Among the dilated structures of the Golgi complex small and medium sized secretory granules were noted. Amorphous light bodies were observed more frequently in the follicle-stimulating trophocytes. Dilated tubules of the rough endoplasmic reticulum, ribosomes, and polysomes predominated in the luteotrophocytes, and secretory granules accumulated along the inner border of the cytolemma. In this series of experiments signs of both activation of the synthesizing function of the gonadotrophic cells and increased release of hormone into the blood stream were observed.

Meanwhile a further decrease in weight of the testes was observed. Destruction of the spermatogenic epithelium was observed in almost half of the seminiferous tubules. The total number of glandulocytes was increased, with a higher proportion of small forms (28.9 compared with 12.4% in the control). Electron-microscopic investigation often revealed cells with irregularly shaped nuclei, with chromatin condensed near the inner edge of the karyolemma, with a large number of small mitochondria with condensed matrix; the number of branched tubular structures of the endoplasmic reticulum, ribosomes, and polysomes was reduced, and small lipid drops were frequently seen. Signs of destruction increased in the sustentocytes, and whereas on the 7th day they were focal, by the 15th day they were much more extensive in character. Tubules with completely degenerated cells were

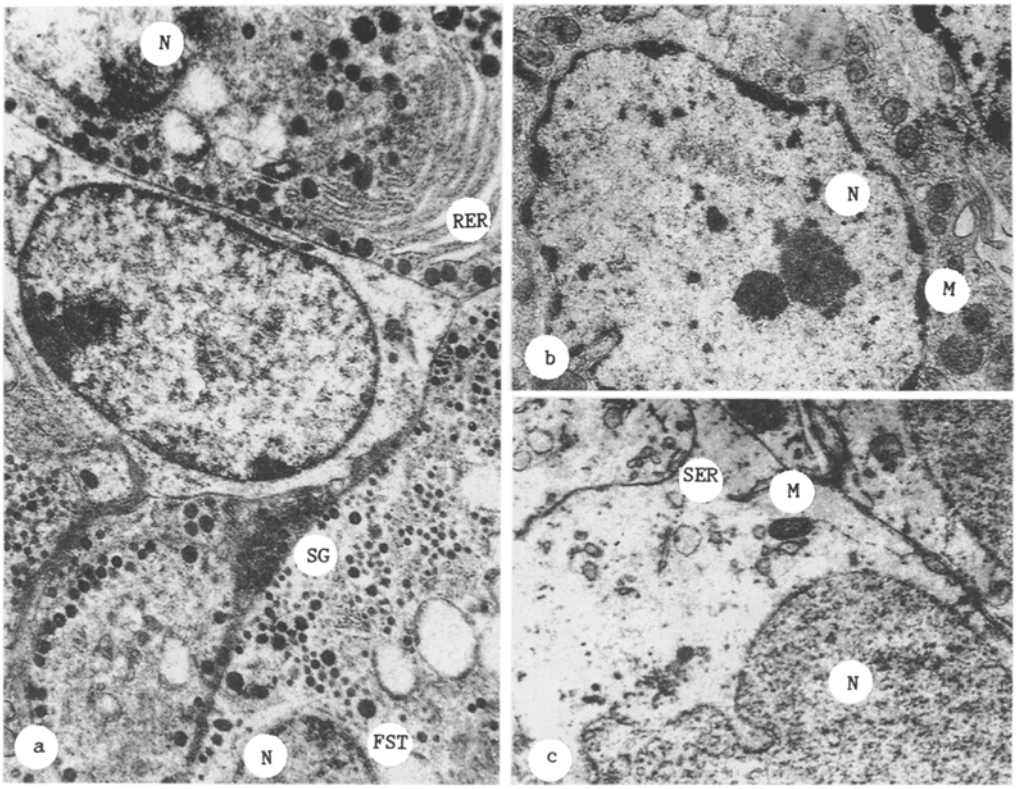

Fig. 2. Ultrastructure of cells of pituitary gland and testes on 30th day of stay at high altitudes. a) Pituitary gonadotrophic cells: FST) follicle-stimulating cell; LT) luteotrophic cell; N) nucleus; SG) secretory granules; RER) rough endoplasmic reticulum. 12,000×; b) Nucleus of glandulocyte with invaginations of karyolemma N) nucleus; M) mitochondria. 11,000×; c) Decrease in content of organelles in sustentocyte: N) nucleus; M) mitochondria; SER) smooth endoplasmic reticulum. 7500×.

often seen. Dilated cisterns of the smooth endoplasmic reticulum, fused with each other and forming gigantic vacuoles, were present in the translucent matrix of the cytoplasm of the sustentocytes. The number of ribosomes, and the glycogen content in the cells were reduced, but conversely, large lipid drops and secondary lysosomes were more often seen. The number of mitochondria was reduced. All these findings were evidence of continued processes of destruction in the testes, despite the fact that the gonadotrophic cells of the pituitary gland were in a state of high functional activity.

By the 30th day of exposure to high altitudes, the cytoplasm of the gonadotrophic cells characteristically contained many secretory granules of varied electron density, as well as enlargement of these granules (Fig. 2a). Cisterns of the endoplasmic reticulum in the translucent matrix of the cytoplasm remained dilated and the mitochondria were increased in volume, with a translucent matrix Compared with the previous period of observation, secretory granules were found less frequently among elements of the Golgi complex. Thus against the background of a long exposure to high altitudes, signs of functional activity persisted in the pituitary gonadotrophic cells, but compared with the previous time of the investigation, signs of inhibition of release of secretion were noted.

Meanwhile the process of destruction in the testes affected more than half of the seminiferous tubules. Among the glandulocytes there were numerous damaged small cells (34.7%). On electron-microscopic investigation most cells were in an inactive state. In the translucent matrix of the cytoplasm lipid drops were very frequently seen, the number of branched tubular structures of the smooth endoplasmic reticulum was reduced, and the mitochondria mainly had a condensed matrix. The nuclei had become irregular in shape (Fig. 2b) with deep invaginations of the karyolemma, a widened perinuclear space, and a lumpy distribution of chromatin. The Sertoli cells of most seminiferous tubules were distinguished by considerable loss of organelles, reduction of the number of ribosomes, and a reduced glycogen content. The mitochondria had become elongated in shape The cisterns and vacuoles of the endoplasmic reticulum remained enlarged in volume. The nuclei were irregular in shape, with marked invaginations of the karyolemma and a dustlike distribution of the chromatin (Fig 2c).

In animals kept a longer time (60 days) under high altitude conditions, the changes observed were almost the same as at the previous time, but in addition, giant pale bodies with a floccular matrix could be seen in the follicle-stimulating trophocytes. In the glandulocytes and also in the sustentocytes there was a weak tendency toward recovery of the disturbed structures.

Exposure to extremal high altitude factors leads to changes in functional relations between the gonadotrophic cells of the pituitary and testes, as shown in the early stages by some reduction of the synthesizing function of the gonadotrophic cells and the process of hormone release by them, whereas in the testes it was mainly by a disturbance of the barrier function and of active transport in the sustentocytes. With lengthening of the period of adaptation, signs of hormonal activity were increased in the gonadotrophlc cells, processes of destruction increased in severity in the gonadotrophic cells, but despite this fact, destructive processes were more marked in the sustentocytes, which correlated with structural changes in the glandulocytes. Disturbance of correlation in the pituitary — testes system at this moment was evidently due to the strong influence of the direct damaging action of high-altitude hypoxia on the testes [2]. The decrease in number of tubular structures of the endoplasmic reticulum, the decrease in the number of ribosomes, and predominance of small mitochondria with condensed matrix in the Leydig cells led to disturbance of their ability to respond to the stimulating action of pituitary gonadotrophic hormones by activation of the morphological features of secretion. Weakening of the hormone-producing function of the glanulocytes was not compensated by an increase in the number of Leydig cells. This, in turn, aggravated the dyshormony in the pituitary—gonads system, for self-regulation of these glands, in accordance with the negative feedback principle, was disturbed [5, 10, 17, 18], and it was manifested by the end of the 2nd month of adaptation as inhibition of hormone release by the gonadotrophic cells while a high level of synthesis was maintained.

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