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A VERIFIED CASE OF THE PRESENCE OF ACTIVE BROWN ADIPOSE TISSUE IN AN INDIGENOUS INHABITANT OF THE ARCTIC REGION OF YAKUTIA

A case of verification of active brown adipose tissue in a 40-year-old patient, a professional hunter resident of the Arctic ulus of Yakutia, is described. Real brown adipose tissue was found in samples of adipose tissue from the paranephral fiber. Adipose tissue samples showed high immunoreactivity to the activity marker of this tissue - mitochondrial protein UCP1.

Keywords: brown adipose tissue, cold, histology, immunohistochemistry, UCP1.

Introduction. Yakutia is one of the largest regions of the Russian Federation with a predominance of extremely low temperatures throughout the year. More than 40% of the territory of our republic is located beyond the Arctic Circle and belongs to the Arctic zone.

The extreme conditions of the Arctic have an impact on the adaptive potential, affect the functional state of the human body and its working capacity, the level of health and the duration of active life.

The exploration and development of the Arctic is one of the priorities of Russia's state policy. The life support and economic potential of the country are essentially determined by the health of the population. Research aimed at ensuring the health of the Arctic population is becoming especially relevant in modern conditions.

The first description of brown adipose tissue dates back to 1551, when Gessner described this tissue in a book on anatomy as "nec pinguitudo nec caro", which means "neither fat nor flesh" [1]. However, as a thermogenic organ necessary for mammalian thermoregulation, it was recognized only less than half a century ago [2]. During the second half of the XX century and the beginning of the XXI, it was believed that it is present only in newborns and disappears after a year [2,3]. Although some indirect data had previously led several authors to assume its presence [1,4-9], and only with the advent of positron emission tomography with 18-fluorodeoxyglucose (PET-FDG), a functional imaging method evaluating areas of increased metabolic activity, began to be used more often in the observation of certain types of cancer, brown adipose tissue was It was found in at least one subgroup of the adult human population [2,10-14]. This discovery aroused great interest among researchers in this field and the hypothesis that the presence or absence of brown adipose tissue may be the cause of such common metabolic diseases as obesity and type 2 diabetes, as well as probably a potential therapeutic target, since excess energy is spent through non-contractile thermogenesis.

However, despite the presence of many indirect signs of activation of brown adipose tissue in adult residents of regions with extremely cold climates, up to now the fact has not been confirmed by histomorphological verification of brown adipose tissue.

In this article we describe a case of a verified fact of the presence of metabolically active brown adipose tissue in an indigenous inhabitant of the Arctic ulus of Yakutia.

Material and methods of research. Histological studies were carried out on the basis of the pathoanatomical Department of t Republican Hospital № 1 of the National Medical Center and the Faculty of Human and Animal Anatomy of the Polytechnic University del Marche (Ancona, Italy). The work was carried out within the framework of international cooperation between the Yakutsk Scientific Center for Complex Medical Problems (Yakutsk) and the Polytechnic University of del Marche (Ancona, Italy).

The patient received samples of adipose tissue from paranephral tissue taken from the area surrounding the renal artery after nephrectomy for urolithiasis.

Patient R., male, 40 years old, height 168 cm, slim build, was born and lives in Srednekolymsky ulus (Arctic zone of Yakutia), professional hunter-cadre officer, nationality Evenk. He spent a significant part of his working time outdoors and was exposed to significant exposure to cold.

Ethics Committee. The study was approved by the local Committee on Biomedical Ethics of the Yakut Scientific Center of Complex Medical Problems(Protocol No. 46 of May 24, 2018).

Histology. The collected samples were fixed by immersion in 4% paraformaldehyde in 0.1 M phosphate buffer (FB), pH 7.4. After thorough washing in FB, the samples were dehydrated in a graduated series of ethanol, purified in xylene and waxed. Serial paraffin sections with a thickness of 3-4 microns were obtained from each sample. The samples were stained with hematoxylin and eosin to assess morphology. All studies were carried

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out on a Nikon Eclipse 800 light microscope (Nikon, Tokyo, Japan).

Immunohistochemistry. Immunoreactivity on the mitochondrial protein UCP1 was studied as minima. The slices were incubated in 3% H2O2 solution (in dH2O; 5 min) to block endogenous peroxidase, then washed in phosphate buffered saline solution (PBS) and incubated in 2% blocking solution (in PBS; 20 min).

Histochemical reactions were performed using a set of Vectastain ABC (Vector Laboratories) and SigmaFast 3,3'-diaminobenzidine (Sigma-Aldrich) as a substrate. Further, the sections were stained with hematoxylin, dehydrated and installed in Eukitt (Fluka, Deisenhofen, Germany). To assess the specificity of antibodies in each case, negative control data were obtained by excluding the primary antibody.

Morphometry. Sections stained with UCP1 were used to count adipocytes (~5000 adipocytes in each sample). The number of adipocytes was calculated using the Lucia Image software (version 4.82, Nikon Instruments, Florence, Italy). The results are presented as a percentage of UCP1-immunoreactive multilocular adipocytes from the total number of counted adipocytes.

Results and discussion. The material presents fragments of paranephral fiber taken from the area surrounding the renal artery. Among white adipocytes with a univacuolic structure and an eccentric nucleus, there are extensive fields of smaller cells with a multivacuolic structure, a central location of the nucleus and pronounced vascularization – brown adipocytes (Fig. 1).

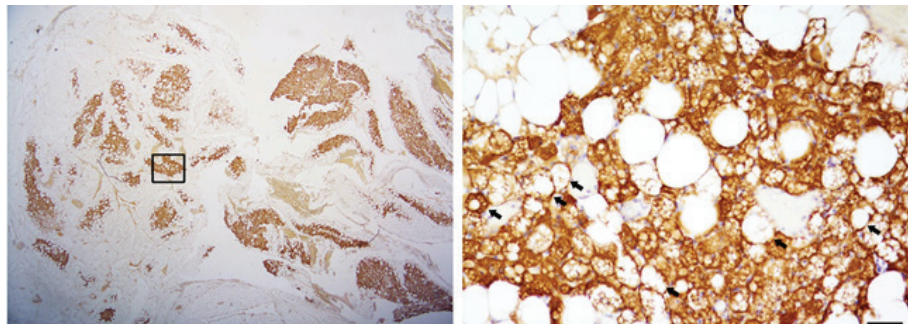
Microscopic examination shows characteristic of brown adipose tissue, compared with white adipose tissue, a typical histological picture of brown adipose tissue was revealed.

Immunohistochemical examination on UCP 1 showed that the percentage of multilocular and paucilocular adipocytes was 54.9% (Fig. 1). All UCP1-positive multilocular adipocytes of this patient were particularly intensely immunoreactive compared to those examined in biopsies obtained during necropsy.

However, the presence of abundant single-ocular immunoreactive UCP1 cells in all the studied visceral deposits confirms the idea that the visceral adipose tissue of adult men is endowed with the ability to transdifferentiate adipocytes. In particular, the almost exclusive presence of monoclonal immunoreactive UCP1 cells in the perirenal fat of the studied especially supports such plasticity. Typical climatic conditions of the Arctic can explain the high content of multilocular adipocytes in the examined.

In conclusion, it should be noted that this report is the first evidence of the presence of brown adipose tissue confirmed by the UCP1 marker in adults living in the Arctic region. It should be noted that a significant abundance of multilocular cells, their population expressing UCP1, and more intense immunoreactivity in persons exposed to cold support cold-induced browning of visceral fat in adults, which may later become the basis for specific therapy of obesity and related metabolic disorders.

a b



Immunohistochemical analysis (UCP1) of the adrenal fat of a patient who underwent nephrectomy for urolithiasis. Magnification, left figure 600 microns and right figure 40 microns

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