http://dx.doi.org/10.35630/2199-885X/2021/11/4.10

IMPACT OF HYPOXIA AND INFECTION ON THE MORPHOLOGY OF THE THYROID GLAND

Received 9 July 2021;
Received in revised form 11 August 2021;
Accepted 16 August 2021

Samira Yaqubova

Department of Pathological Anatomy, Azerbaijan Medical University, Baku, Azerbaijan

syagubova.71@gmail.com

ABSTRACT — The investigation aimed to study the microscopic features of the thyroid gland under the influence of barochamber hypoxia and staphylococcal infection in the experiment.
Materials and methods of the study. During the study 30 healthy adult male white rats weighing 180–200 g were used. Morphological features of the gland were studied by histological methods.
Results of the study. Analysis of the study results shows that morphological changes occurring in the thyroid gland cells are more pronounced in animals of the infectious group than in animals of the hypoxia group. Thus, under the influence of infection, atrophic changes prevail in the gland tissue, and under the influence of hypoxia, hyperplasia, and hypertrophy, proliferation and differentiation of gland cells are observed. This can be considered a structural reconstruction of the gland tissue and its adaptation to new conditions.

KEYWORDS — hypoxia, infection, thyroid gland, morphology, follicle.

INTRODUCTION

Nowadays, it is indisputable that social development creates a new environment with high-stress factors for individuals, as well as for society as a whole. According to Selye, *stress is a non-specific reaction of the body to any strong irritation*. The development of the body's ability to withstand stress and the general adaptation syndrome is the result of stressful influences [1]. On the other hand, stress factors play an exceptional role in the development of many pathologies in the body, including endocrine pathologies [2,3]. Thus, with chronic stress, the endocrine system, especially the thyroid gland, is more involved in the pathological process as a result of a violation of the hormonal balance, as well as intersystem connections. Stress factors such as hypoxia and infection should be particularly noted [4].

Hypoxia and inflammation are closely related pathological processes in the body at the molecular, cellular, and clinical levels, i.e. just as hypoxia can cause inflammation in the body, inflammation also causes hypoxia [5]. Thus, a violation of the body's supply of oxygen and energy leads to the formation of localized areas of hypoxia [6], and hypoxia areas — to the development of inflammatory processes. On the other hand, the inflammatory process often leads to severe hypoxia [7]. In this case, a mosaic (mixed) change in the histoarchitectonics of the thyroid gland is observed [4].

The analysis of the literature data shows that the morphofunctional rearrangement of the thyroid gland under the influence of stress factors, especially hypoxia and infection, is not sufficiently studied. Although there are currently available data on this issue in the literature, these data do not reflect many aspects of thyroid pathology in hypoxia and infection (staphylococcal peritonitis), which does not allow us to assess the role of the gland in many diseases, including endocrine pathology.

The investigation aimed to study the microscopic properties of the thyroid gland under the influence of barochamber hypoxia and staphylococcal infection in the experiment.

MATERIALS AND METHODS

During the study, 30 healthy adult male white rats weighing 180–200 g, divided into 3 groups were used. The control group (group I) did not interfere (n=10), a model of hypoxia was created on animals included in the hypoxia group (group II) (n=10), and a model of staphylococcal infection (peritonitis) was created on animals included in the infection group (group III) (n=10). For this purpose, group II animals were placed in a special pressure chamber, ventilated daily for 2 hours 5 times a week, at atmospheric pressure in the pressure chamber equal to the pressure at an altitude of 2000–3000 m above sea level, with a temperature of 19–20° C. Group III animals were infected with *S. aureus* culture by injecting 1×10^9 microbial cells/kg (per kg) in the volume of 1 ml into the peritoneal cavity. The animal studeies were conducted in compliance with the international ethical guidelines.

RESEARCH RESULTS

In histological preparations prepared from the thyroid gland of animals of the control group, the connective tissue capsule of the gland and the processes extending from the capsule and dividing the glands into separate lobules are visible. The follicles, different in shape and size, which make up the organ parenchyma are covered with a cuboid epithelium and filled with colloids (Fig. 1).

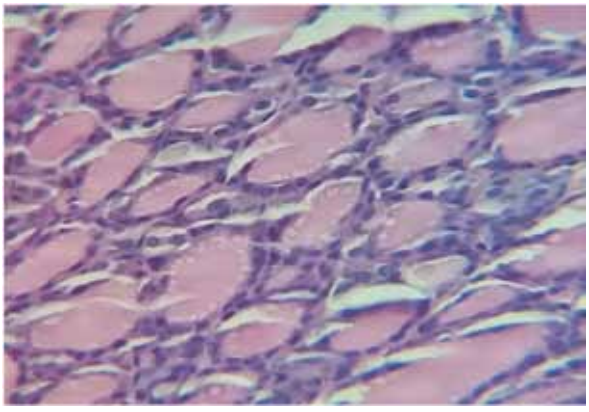

Fig. 1. *A photomicrograph of a the histological section of thyroid gland of the control rat (H&E×200)*

In histological preparations, oval-shaped follicles predominate, but there are also round follicles of small diameter. Microscopically, along with mature follicles, small immature follicles covered with prismatic epithelium from the inside and without a colloid in the cavity are also observed. Usually, the main part of the follicle consists of follicular endocrinocytes or thyrocytes. The cytoplasm of thyrocytes and the rounded nuclei located in the center of the cytoplasm are visually distinguishable.

On the 15th day of the experiment, a microscopic examination of the thyroid gland of animals of the hypoxia group showed that the cytoplasm of thyrocytes is pale, weakly eosinophilic, the nuclei are light, slightly swollen. In the center, there are hyperchromic nuclei and small vacuoles. Signs of hydropic dystrophy can be observed in thyrocytes, especially in the central zone, and the accumulation of fat droplets in some cells, but these changes are local (Fig. 2). In some areas, endothelial cell apoptosis deserves attention. Despite the structure of the thyroid stroma is normal, but weakly destroyed collagen and reticulin fibers, as well as signs of local metachromasia, a small paravasal edema are noticeable. However, under the influence of prolonged hypoxia, it is possible to see the development of fibrosis tissue along the periphery of the gland, as well as an increase in the number of fibroblasts. Thus, due to interstitial fibrosis, the thickening of the capsule of the gland and the narrowing of the follicle lumen is visible.

On the last day of the experiment (day 30), the thyroid gland of animals adapted to prolonged hypoxia acquired a normal structure and size, and the tissues that make up the structure of the gland — the parenchyma and stroma — were reconstructed. Microscopically, the capsule surrounding the gland, the lobules and septa separating them, as well as the border between the central and peripheral zones of the gland is visible. The follicles are located close to each other and have significantly increased in size. The follicular cavity is filled with a thick colloid. The cytoplasm and nuclei of thyrocytes are transparent, *light* in color. The presence of vacuoles in the cytoplasm of the cells of some follicles of the central zone indicates that fatty degeneration is not completely absorbed in these cells, but this vacuolization is very small and local (Fig. 3).

In histological preparations, the proliferation of connective tissue and fibroblasts between the follicles, the development of fibrous tissue in the interstitial space, the thickening of the gland capsule, as well as the proliferation of collagen fibers indicate the complete restoration of the glandular stroma.

The thyroid gland reacts sharply to *S.aureus* cultures injected into the peritoneal cavity. On the 15th day of the experiment, the morphological disorganization of the thyroid gland became more pronounced. The capsule of the gland is thickened, diffusely deformed in some areas, with visible erosive-scaly areas. Adhesion of neutrophilic leukocytes and mononuclear cells, macrophages, and lymphocytes with the formation of exudative inflammatory foci in the inner layer of the capsule is noted. Microscopically, the basement membrane of thyrocytes is also loosened, edematous, and relatively deformed. Most of the thyrocytes undergo dystrophic changes, mainly proteinous degeneration, some of the thyrocytes are degranulated, and some are in a state of necrobiosis and necrosis. Necrotic thyrocytes continue to desquamate into the follicle cavity, and the areas around the follicles, consisting of necrotic tissue rich with neutrophilic leukocytes and lymphocytes are visible (Fig. 4).

Atrophic processes in the parenchyma of the gland have intensified; the lobular structure is partially disturbed. The main part of the gland consists of large or cystic enlarged follicles, which are irregularly replaced by small follicles. Small atrophic follicles contain few colloids and are almost invisible. In large follicles, the vacuolized eosinophilic colloid is observed. The stroma is thickened due to the growth of connective tissue. However, the fibrous framework is deformed, diffuse stromal edema, as

well as perivascular cellular infiltration of the organ, is preserved.

At the end of the experiment — 30 days later, during the microscopic examination, the glandular parenchyma of the surviving animals (n=2) was characterized by irregularly arranged, atrophied, and deformed, small follicles with a narrow slit-like cavity devoid of colloids. There is an increase in connective tissue fibers between thyrocytes. The weakening of exudative processes leads to the activation of fibroblasts, the accumulation of macrophages and lymphocytes in the capsule and stroma of the thyroid gland, and the formation of new loose connective tissue. However, the collagen fibers that are a morphological feature of fibrillogenesis, local scarring, are mainly formed *de novo*, which is not typical for the intact gland. The follicles undergo acute hypertrophy and hyperplasia (Fig. 5).

DISCUSSION

The adaptation of the body to the effects of some endogenous and exogenous factors, including hypoxia and infection, depends on the intra-systemic restructuring of the structural elements of the thyroid gland [7], the thyroid gland plays an important role in the regulation of processes occurring under the influence of these factors. However, this regulation is complex, so it requires special research [8]. Under the influence of experimental hypoxia, the function of the thyroid gland is weakened, as well as compensatory-adaptive processes, manifested in a decrease in the height of epithelial cells of glandular tissue, changes in the diameter of follicles, changes in the ratio of epithelium and connective tissue, occur [9]. Morpho-functional changes occurring in the follicular cells of the thyroid gland in the early stages of chronic endotoxicosis — a decrease in the number of follicular thyrocytes, the development of vacuole degeneration and desquamation of some cells into the lumen of the follicle, plethora of capillaries and focal diapedesis hemorrhages in the parenchyma of the gland — are accompanied by a restoration of the activity of thyrocytes [10]. At the later stages of the experiment, the proliferation of intact follicular and interfollicular epithelium is observed, the lost parenchyma is replaced by a stroma, glandular tissue undergoes a microfollicular transformation in the form of small foci and remodeling to the macrofollicular type. With the formation of the microfollicular structure of the gland, the processes of stromal proliferation prevail, which can be considered as pathological tissue regeneration under conditions of intoxication [8]. Morphological changes occurring in thyrocytes also lead to a decrease in the concentration of hormones produced on the background of a decrease in the number of functioning thyrocytes, a weakening of the functional activity of the thyroid gland [8, 10].

According to the results of our study, under the influence of chronic hypoxia and infection, marked structural changes occur in the cells of the thyroid gland, which lead to a restructuring of the structure of the gland. But these changes are more prominent in animals of the infection group compared to animals of the hypoxia group. Thus, under the influence of infection, atrophy of both the stroma and the parenchyma of the gland gradually develops, the interaction of small and large follicles in the paren-

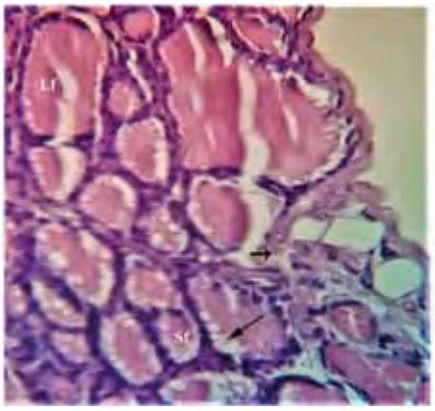

Fig. 2. *Histological section of thyroid gland of the rat showing large (Lf) and small follicles (Sf), fibrosis (thick arrow) and colloid droplets (long arrow). 15th day of the hypoxia model (H&E×200)*

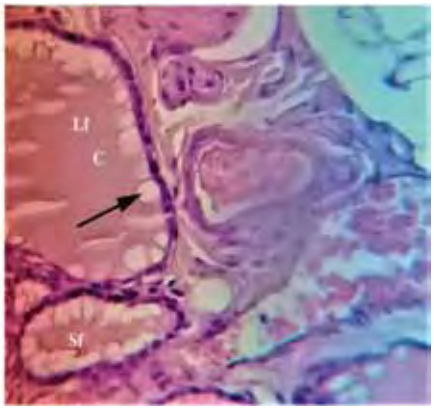

Fig. 3. *Histological section of thyroid gland of the rat showing large (Lf), and small follicles (Sf), colloid (C) and colloid droplets (arrow). 30th day of the hypoxia model (H&E×200)*

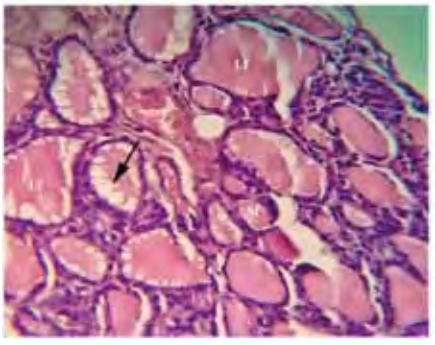

Fig. 4. *Histological section of thyroid gland of the rat showing large (Lf) and small follicles (Sf), and colloid droplets (long arrow). 15th day of the infection model (staphylococcal peritonitis) (H&E×200)*

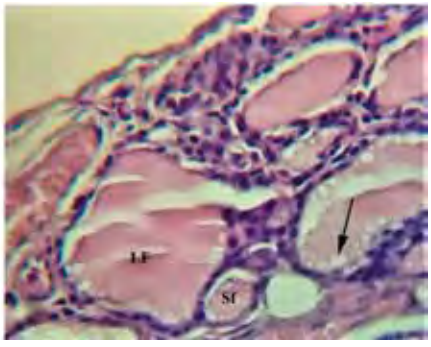

Fig. 5. *Histological section of thyroid gland of the rat showing large (Lf) and small follicle (Sf) and colloid droplets (arrow). 30th day of the infection model (staphylococcal peritonitis) (H&E×200)*

chyma is disrupted, sclerotic processes are observed in the stroma. Long-term effects of hypoxia increase the resistance of glandular tissue to hypoxia and glandular cells adapt to the hypoxic condition, the process of folliculogenesis occurs with an increase in the number of small follicles with proliferative potential and high metabolism in the parenchyma of the gland and focal growth of connective tissue in the stroma.

CONCLUSION

Thus, under the influence of infection, atrophic changes prevail in the gland tissue, and under the influence of hypoxia, hyperplasia, hypertrophy, proliferation, and differentiation of gland cells are observed. This can be considered a structural reconstruction of the gland tissue and its adaptation to new conditions.

REFERENCES

1. **NADOLNIK L.I.** Stress and the thyroid gland // Biomedical Chemistry, – 2010; 56(4): – p. 443–456.
2. **PONCIN, SYLVIE, ET AL.** "Oxidative stress in the thyroid gland: from harmlessness to hazard depending on the iodine content." Endocrinology 149.1 (2008): 424–433.
3. **KALASHNIKOVA S.A.** Morphological characteristics of endocrine organs in chronic endogenous intoxication // Bul. Experimental Biology and Medicine, – 2011; 151(2): – p. 211–214.
4. **ELTZSCHIG, HOLGER K. PETER C.** Hypoxia and inflammation // New England Journal of Medicine – 2011: 364(7): – p. 656–665.
5. **COLGAN SP, CAMPBELL EL, KOMINSKY DJ.** Hypoxia and Mucosal Inflammation // Annu Rev Pathol. – 2016; 11: – p. 77–100. doi:10.1146/annual-pathol-012615-044231. doi: 10.1146/annurev-pathol-012615-044231.
6. **KARHAUSEN J, FURUTA GT, TOMASZEWSKI JE, ET AL.** Epithelial hypoxia-inducible factor-1 is protective in murine experimental colitis // J Clin Invest. – 2004; 114: – p. 1098–106. DOI: 10.1172/JCI21086
7. **PAVLOV AV, ERMAKOVA OV, KORABLEVA TV, RASKOSHA OV.** Morphometric analysis of the follicular structure of the thyroid gland in chronic low-dose γ-irradiation. Morphology 2013. V. 143. No. 2. S.43–46. 40.
8. **POLYAKOVA L., KALASHNIKOVA SA, NOVOCHADOV VV, RAZVALYAEVA AV.** Structural and functional changes in the thyroid gland in chronic endotoxicosis // Volgograd Journal of Medical Scientific Research. 2006. No. 3. p. 18–19.
9. **ALEXANDROVA NV.** Adaptive-compensatory changes in the thyroid gland during experimental hypoxia // Bulletin of NovSU. 2005. No. 32. p.88–91.
10. **MITRYUKOV VV, BAZHENOV EL, KIRYANOV NA, IVANOVA GS.** Structural and functional characteristics of the thyroid gland in the early stages of peritoneal endotoxicosis, Scientific Bulletin Medicine Series. Pharmacy. 2013. No. 4 (147). Issue 21/1, pp. 86–89.