REACTION OF THE THYROID TISSUES TO STIMULATION IN VARIOUS STATES OF THE HORMONAL BALANCE AND IN RADIATION SICKNESS

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UDC 615.753-099-031:611,441]-06:617-001.28-07:616.441-008.6

The reaction of the tissues of various organs to coal tar has been studied by many investigators [1-3, 6, 9]. However, the reaction of the thyroid to injection of coal tar has never been studied.

In the present investigation the reaction of the thyroid gland tissues to coal tar was examined in order to determine the character of the course of the tissue processes in a chronic inflammatory process in the presence of changes in the hormonal balance and general state of the organism.

EXPERIMENTAL METHOD

Four series of experiments were carried out on sexually immature (2-3 months) and adult (1.5-2 years) male rabbits. A drop of coal tar was injected into one lobe of the thyroid of the animals in the experiments of series I. In series II, in an analogous experiment, the opposite lobe of the thyroid was removed. In the next two series of experiments similar procedures were carried out against the background of radiation sickness produced by whole-body x-ray irradiation (500 R for the sexually immature and 800 R for the adult animals) three days before the experiment. The doses indicated above in the present experimental conditions caused death of 50% of the irradiated animals.

The acute stage of the radiation sickness was the first 15-20 days, and recovery took place 35-40 days after irradiation (verified by the blood picture).

Material for histological investigation was taken 1-90 days after injection of the tar into the organ, fixed in Carnoy's and Maximow's fluids, and embedded in paraffin wax. Preparations were stained with Mayer's hematoxylin and counterstained with eosin and with azan by Heidenhain's method. Histochemical reactions were carried out with suitable controls for DNA by Feulgen's method, for RNA by Brachet's method, for neutral mucopolysaccharides by McManus's method, and for acid mucopolysaccharides by Hale's method.

EXPERIMENTAL RESULTS

The reaction of the thyroid gland tissues to stimulation showed a number of common features in all the series of the experiments. Separation of the injected drop of tar into small (20-100 μ) and large (150-500 μ) droplets was observed, and these were surrounded by inflammatory changes which varied in intensity. In the region of the large tar droplets the adjacent tissues were necrotic and infiltrated by leukocytes. Around the small droplets no marked necrotic changes could be found. The tissues next to them showed inflammatory proliferation. Meanwhile, the character and intensity of the destructive and proliferative processes varied from one series of experiments to another.

In the animals of series I, the thyroid gland tissues were stimulated around the large tar droplets and the zone of necrosis. During the first day of the experiment the interfollicular epithelial islets showed activation followed by proliferation. The follicles reacted differently to inflammation. The small follicles lost their colloid, collapsed, and on the 3rd day of the experiment were indistinguishable from the interfollicular islets. The larger follicles lost their colloid, became enlarged, and some of the cells of their walls proliferated, forming bands which invaded the inflammatory connective tissue. Finally, the largest follicles died and were absorbed. A similar reaction of the folliclular epithelium was observed by the author during cultivation of the thyroid gland by F. M. Lazarenko's method [7]. It may be concluded from this that the epithelium of the different types of follicles varies in the degree of its ability to differentiate, thus determining its reaction to inflammation. Characteristically the functional

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Department of Histology and Embryology, Tyumen Medical Institute (Presented by Active Member of the Academy of Medical Sciences of the USSR S. R. Mardashev). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 63, No. 4, pp. 109-112, April, 1967. Original article submitted November 9, 1965.

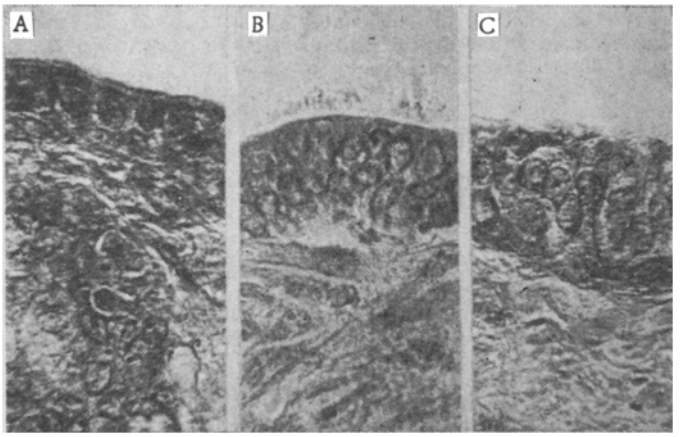

Fig. 1. Varieties of epithelium in the walls of the cysts. A) Simple, B) stratified ciliated epithelium, C) transitional epithelium. Objective 90x, ocular 10x. Here and in Figs. 2 and 3, staining with Mayer's hematoxylin and eosin.

activity of the epithelium of the small and large follicles was different, as demonstrated previously by the author using the method of autoradiography with radioactive iodine [8].

The intensity of the reaction of the thyroid epithelium varied with the distance from the focus of irritation. The region next to the barrier of leukocytes and necrotic tissue was the zone of the most marked inflammatory changes. Next followed a zone of irritated tissues with an intensive process of formation of new microfollicles. Finally, a zone free from inflammatory changes could be distinguished.

By the 20th day of the experiment the inflammatory reaction had disappeared. The proliferating epithelium showed evidence of differentiation with the formation of new follicles. In the newly formed follicles the colloid at first gave a positive Hale's reaction, and later a PAS positive reaction, making it possible to determine the order of synthesis of the acid and neutral mucopolysaccharides in the thyroid in the process of secretion.

In the analogous series of experiments on the irradiated animals the inflammatory reaction was considerably less marked and the zone of inflamed tissues was much narrower than in the preceding series of experiments. The epithelial proliferation was very slight and was observed only on the first days of the experiment. This was directly associated with the dynamics of the changes taking place in the thyroid during radiation sickness.

Control investigations of the state of the thyroid of the irradiated rabbits not receiving injections of coal tar showed that initially the functional activity of the organ was increased for 8-10 days after irradiation. This was followed by a decrease in the functional activity of the gland. This was expressed morphologically by considerable flattening of the epithelium of the follicles, which were filled with colloid and contained no resorption vacuoles. The morphological state of the organ returned to normal on the 35th-40th day after irradiation. The dynamics of the changes in the thyroid after irradiation was found to be similar by other investigators [12].

In the animals in the experiments of series II, undergoing partial thyroidectomy, by the 2nd day the proliferating epithelium at the border between the necrotic and viable tissues had developed into a continuous layer. On the 7th day the tar droplets were completely eliminated by the epithelium, which showed marked polymorphism. In the wall of the same cyst areas of simple (Fig. 1A) stratified ciliated (Fig. 1B), transitional (Fig. 1C), and stratified squamous epithelium (Fig. 2A) could be seen. Areas of inflammatory proliferation of infiltrative type developed from the layers of epithelium (Fig. 2B). The inflammatory reaction in the organ disappeared by the 12th-15th day. However, at later periods intensive proliferation of the thyroid epithelium continued, a manifestation of the compensatory reaction to creation of thyroid insufficiency. In accordance with observations of other authors [4, 11], this could be regarded as a manifestation of regeneration hypertrophy.

Previous investigations of the thyroid epithelium by the method of cultivation in vivo [5, 7, 10] showed that in the implanted tissues no protective layers are formed in a focus of aseptic inflammation around foreign bodies or necrotic tissues. The proliferating epithelium observed in the present investigation suggests that prolonged inflammation caused by coal tar may bring to light the most primitive eliminative properties of the thyroid epithelium.

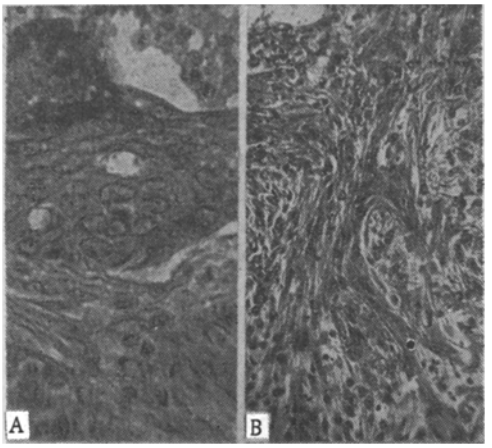

Fig. 2. Forms of growth of the epithelium in the cyst wall. A) Stratified epithelial layer in the cyst wall (objective 90x, ocular 7x), B) downward growth of the epithelium (objective 40x, ocular 7x).

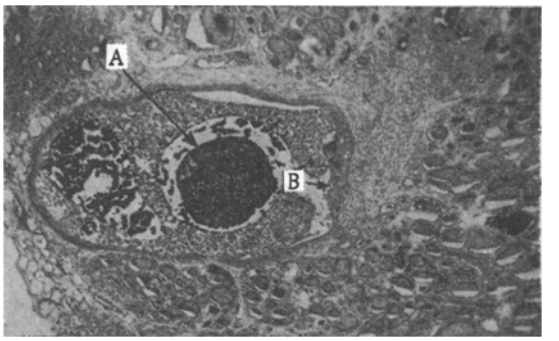

Fig. 3. Elimination of tar droplets. A) Coal tar, B) stratified epithelial layer. Objective 8x, ocular 7x.

In the analogous series of experiments on the irradiated animals, intensive proliferation of the epithelium with the formation of protective layers of epithelium around the tar drop was observed only on the first days (Fig. 3). The proliferation of the epithelium ceased by the 6th or 7th day.

It was concluded from the analysis of these results that the differences in the reaction of the follicular structures in the inflammatory focus demonstrates differences in the degree of differentiation of the epithelium forming them. The profuse proliferation of the thyroid epithelium, especially in the conditions of thyroid insufficiency, indicates the high regenerative power of the thyroid gland. The changes in the inflammatory reaction and proliferation of the thyroid epithelium in the conditions of radiation sickness were the result of depression of the reactive properties of the organism and the inflammatory reaction in the thyroid gland. The intensive proliferation of the thyroid epithelium of the irradiated animals on the first days after irradiation was due to the high functional activity of the thyroid epithelium. The polymorphism of the newly formed layers of epithelium arising in the inflammatory focus indicates the genetic link between the thyroid and the epithelium of the foregut.

The results of these investigations show that the thyroid, like the anterior portion of the digestive tube, is a derivative of the prechordal anlage.

The link disclosed between the intensity of the proliferative processes and the functional state of the organ suggests that the proliferative processes in the thyroid bear a definite relationship to the thyrotropic action of the pituitary.

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