ORGAN SPECIFICITY OF THYROID TUMORS

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Tests using an organ-specific antithyroid phytoprecipitin have shown that antigen simplification of thyroid tumors starts at the benign tumor stage. During malignant change the thyroglobulin content falls or completely disappears.

When a malignant tumor develops in the thyroid gland, the content of organ-specific antigen (thyroglobulin) falls [1, 2, 5, 9], and in some cases it disappears completely [5, 7, 8]. Very little information is available on the thyroglobulin content in benign tumors, despite their interest for the comparative study of the antigenic composition of benign and malignant tumors.

The variability of the properties of the heterologous [1, 2, 6, 9] and autologous [5, 7] antisera used to investigate thyroglobulin, their interaction with different components of the thyroid extract, and the presence of irrelevant antibodies make it difficult to compare results obtained by different workers.

The object of the present investigation was to study the thyroglobulin content in benign and malignant human thyroid tumors by means of an organ-specific antithyroid phytoprecipitin, discovered by myself [4] and comparing favorably with antisera in its monospecificity toward thyroglobulin, the stability of its properties, and the simplicity of its preparation.

EXPERIMENTAL METHOD

Tumors were obtained immediately after operation from the surgical department of the Institute of Experimental Endocrinology and Hormone Chemistry, and the results of their histological examination were obtained from the Department of Pathological Anatomy of the Institute. Morphologically normal thyroid glands from persons dying from injury were used as controls. The homogenized gland tissue was extracted for 24 h at 4° with 0.85% NaCl in a proportion of 1:2, and then centrifuged. The phytoprecipitin was prepared as described previously [4], purified from ballast proteins, and lyophilized. All investigations were carried out with the same batch of reagent. In view of the strict monospecificity of the phytoprecipitin against thyroglobulin, the antigen content was estimated from its titer, i.e., from the maximal dilution of thyroid extract which was still precipitated by the organ-specific reagent. The gel-precipitation reaction and immunoelectrophoresis were carried out in the modifications adopted in G. I. Abelev's laboratory [3]. Electrophoresis was carried out for 2 h and for subsequent development, antithyroid phytoprecipitin, rabbit thyroid antiserum (obtained by immunization of rabbits with extracts of human thyroid gland followed by absorption with human serum), and rabbit antiserum precipitating human protein (issued by the Research Institute of Forensic Medicine) were used. The numerical results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

The thyroglobulin content was determined in 29 normal thyroid glands, in 29 benign thyroid tumors (7 papillary cystadenomas, 9 microfollicular and 13 tubular adenomas), and in 6 malignant thyroid tumors.

The thyroglobulin titer in normal thyroid glands ranged between 1:64 and 1:128 (mean titer 1:106± 5.7). In 5 malignant tumors (follicular adenocarcinoma, polymorphocellular carcinoma, tubular adenoma with signs of malignant degeneration, papillary carcinoma, metastasis of carcinoma in a lymph gland) loss of the organ-specific antigen was found, and in one tumor (initial stage of papillary carcinoma with the presence of follicles) the thyroglobulin titer was 1:16. In all malignant tumors the thyroglobulin titer was considerably reduced (papillary cystadenoma 1:8±2.2, microfollicular adenoma 1:18±2.9, tubular adenoma

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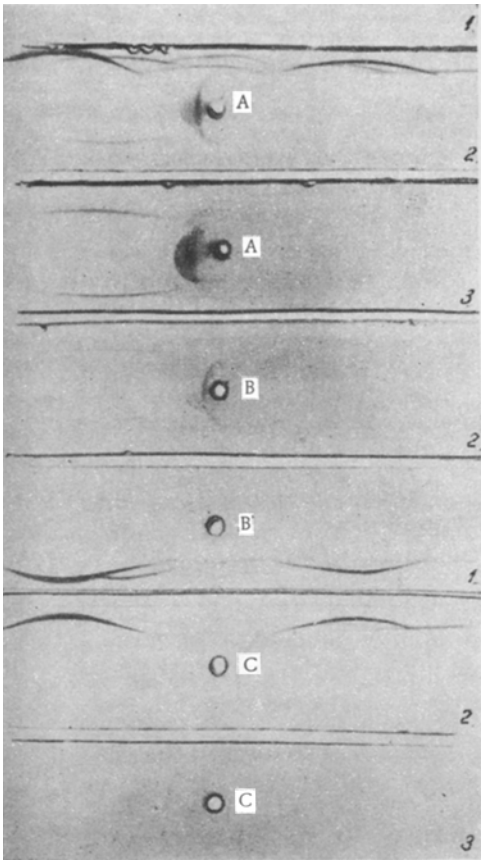

Fig. 1. Immunoelectrophoresis of extracts from normal thyroid tissue and thyroid tumors. 1) Rabbit antiserum precipitating human protein; 2) antithyroid phytoprecipitin; 3) antithyroid rabbit antiserum; A) extract from normal thyroid tissue; B) extract from thyroid adenoma; C) extract from thyroid carcinoma.

1:9±3.4). In 4 adenomas of tubular structure complete loss of antigen was found. Fluctuations in the thyroglobulin titer in the benign tumors (from 0 to 1:32) reflect the relationship between the content of organ-specific antigen and the histological structure of the tumor tissue.

A considerable quantitative difference was found in the thyroglobulin titer in normal and adenomatous parts of the thyroid gland of the same patient: the thyroglobulin titers were 1:128 and 1:2 respectively. After equalization of the antigen content relative to the titer, a reaction of identity was obtained. This shows that the same antigen is present in normal thyroid tissue and in the adenoma, but in different quantitative proportions. Evidently antigenic simplication begins with a gradual decrease in the content of organ-specific antigen at the benign tumor stage.

The results of immunoelectrophoresis are shown in Fig. 1. With rabbit antiserum precipitating human protein, extracts from normal thyroid tissue, from adenoma, and from malignant thyroid tumor tissue formed equally clear precipitation lines in the region of albumins and α^-, β^-, and γ-globulins. With antithyroid phytoprecipitin and thyroid antiserum, extract of normal thyroid tissue formed one precipitation line in the serum α-globulin zone. The same line, but much weaker, was formed by extract of adenomatous tissue. Extract from carcinoma tissue did not react with the organ-specific reagents. Evidently the antigenic simplification during development of a malignant thyroid tumor effects the organ-specific antigen but not the complex of species-specific antigens.

Malignant degeneration thus depresses the synthesis of thyroglobulin, the organ-specific antigen and source of the thyroid hormones. A comparative study of the quantitative thyroglobulin content in the malignant tumor and its precursor, the benign adenoma, shows that antigenic simplification starts at the benign tumor stage. During malignant degeneration the thyroglobulin content falls progressively or disappears completely. Loss of organ-specific antigens in some benign tumors may thus have prognostic importance.

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