Immunohistological Findings in Hashimoto's Thyroiditis, Focal Lymphocytic Thyroiditis and Thyroiditis de Quervain

Comparative Study

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Summary. 65 cases of focal lymphocytic thyroiditis and Hashimoto's disease and five cases of thyroiditis de Quervain were studied with immunohistological methods. In both focal lymphocytic thyroiditis and Hashimoto's disease, lymph follicles with active germinal centers were found which contained germinal center cells that stained positively for intracytoplasmic immunoglobulins (heavy and/or light chains). Positively staining germinal center cells made up only a minor portion of overall immunoglobulin-positive cells; most of the positive infiltrating cells were plasmacytes arranged in small groups or clusters among thyroid follicles. Thus the number of immunoglobulin-containing cells differed greatly between focal lymphocytic thyroiditis, where sites of infiltration were represented by lymph follicles, and Hashimoto's disease. In the former, only a few cells outside lymph follicles stained positively for intracytoplasmic immunoglobulins, whereas in the latter numerous cells within areas of coherent infiltration did. Furthermore, in most cases of Hashimoto's disease macrophages and giant cells with positive staining for lysozyme were present in variable numbers, while in focal thyroiditis they were less frequent or absent. Between these two immunohistologically separable groups, i.e. focal lymphocytic thyroiditis and Hashimoto's disease, there were many cases with features of both. Considering the occurrence of such intermediate forms and some immunohistological similarities between Hashimoto's disease and focal lymphocytic thyroiditis (nearly identical ratio of the different immunoglobulin classes and similar distribution of immunoglobulin-positive germinal center cells), it is likely that these lesions represent different activities of a same immunological process.

Thyroiditis de Quervain was characterized immunologically by numerous macrophage clusters and giant cells that both stained positively for lysozyme. Compared with the giant cells seen in Hashimoto's disease (mainly of Langhans type), those of de Quervain's thyroiditis (mainly of foreign body type) were
larger and more numerous. Lymph follicles (with or without active germinal centers) were not observed. Among infiltrating cells, numerous plasmacytes that stained positively for intracytoplasmic immunoglobulins were identified. Their number and the distribution pattern of the different classes of immunoglobulins contained within them was similar to those seen in Hashimoto’s disease.

Key words: Hashimoto’s thyroiditis – Focal thyroiditis – Granulomatous thyroiditis – Immunohistology

The first antigen detected in Hashimoto’s disease was thyroglobulin (Roitt et al. 1956; Doniach and Roitt 1957); subsequently the microsomal fraction of thyroid epithelial cells (Trotter et al. 1957; Roitt and Doniach 1958; Holborow et al. 1959), a second component of colloid (other than thyroglobulin) (Balfour et al. 1961), and the epithelial surface antigen were also identified (Fagraeus and Jonsson 1970). Infiltrating lymphocytes and plasma cells were identified as sites of antibody production against thyroglobulin and microsomal antigen (Mellors et al. 1962; McLachlan et al. 1979). The serum concentrations of antibodies to thyroglobulin or microsomal antigen correlate only roughly with the extent of thyroid infiltrates (Roitt and Doniach 1958; Porter and Fennell 1961). Low titers of antibodies are therefore compatible with both diffuse and focal infiltration in the gland. Thyroid antibodies are present also in other inflammatory or neoplastic thyroid diseases (Stuart and Allan 1958; Blizzard et al. 1959; Cline et al. 1959).

Separation of Hashimoto’s thyroiditis from focal thyroiditis by morphological methods is easy in cases of diffuse or slight focal infiltration, but becomes difficult or impossible when focal infiltrates are pronounced (Woolner et al. 1959). The overlapping of the histological features of Hashimoto’s disease and focal lymphoplasmocytic thyroiditis is obvious; the question arises as to whether these are two distinct entities or only one pathologic process with Hashimoto’s thyroiditis at the one end and focal thyroiditis at the other end of a broad spectrum. The present study was undertaken in order to answer this question.

Material and Methods

Thyroid tissue from 65 patients who had undergone partial or total thyroidectomy for goiter or suspected malignancy was investigated. 60 patients revealed slight to severe lymphoplasmocytic infiltration of the thyroid, and thyroiditis de Quervain was diagnosed in 5 patients. 6 μm thick sections from samples of each case were stained with HE, PAS, and Gomori. In all cases, detection of intracytoplasmic immunoglobulins was performed by a modified application of the method of Sternberger et al. (1970). Preincubation with trypsin was carried out with a solution of 0.01 % MERCK trypsin (art. no 24579) for 1–2 min at room temperature. Dilutions of primary antisera were 1 : 2,400 for kappa, 1 : 2,400 for lambda, 1 : 200 for IgG, 1 : 400 for IgM, 1 : 800 for IgA and 1 : 100 for lysozyme. In each case, a positive reaction control was performed with slides of a lymph node showing features of follicular hyperplasia. Negative controls were performed by replacing the specific antiserum by normal rabbit serum or pure TRIS saline. All antisera used were obtained from DAKO Immunoglobulins Ltd., Copenhagen, Denmark.

Semiquantitative analysis was carried out with a MOP-AMO instrument.

Degree of Infiltration of Thyroid Tissue was assessed by counting infiltrating cells, i.e. lymphocytes, plasma cells, monocytes and macrophages. The smallest units to be counted amounted to at least 10 mononuclear cells. On each slide, a focal point was marked with a pencil. 10 squares measuring