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ORIGINAL ARTICLE

Correlation and presentation of thyroid functional status with thyroid autoantibodies in long-term follow-up of autoimmune thyroiditis: A study of 116 cases

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Background/Purpose: The most common diagnostic finding of autoimmune thyroid disease (AITD) is the presence of antithyroid antibodies. While autoimmune thyroiditis (AT) is a common AITD, aspiration cytology is one of the important diagnostic tools of AT.
Methods: We evaluated 116 AT patients with ultrasound-guided aspiration cytology and then analyzed the correlation between thyroid hormone status and thyroid autoantibodies. This was a retrospective analysis with prospective collection of data with a mean follow-up period of 68.8 ± 37.8 months. The patients were classified as either euthyroid, hypothyroid, or hyperthyroid (HT). Of the 116 patients, 22 were hypothyroid, 37 were euthyroid, and 57 were HT.
Results: During the follow-up period, 95.5% of the hypothyroid group remained hypothyroid and only one patient improved to euthyroid. In the euthyroid group, 16.2% progressed to hypothyroid and 83.8% remained euthyroid. In the HT group, 8.7% progressed to hypothyroid, 70.2% progressed to euthyroid, and 21.1% remained HT. Most patients with a high titer of thyroglobulin antibody (TgAb) will progress to hypothyroid, and patients with a high titer of thyroid stimulating hormone (TSH) receptor antibody (TRAb) will remain HT. Strong correlations

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between thyroid functional status and positive number of thyroid autoantibodies were seen in this study. Patients with all the three antibodies positive had a high prevalence of hyperthyroidism.

Conclusion: In our study, most patients were HT; this may be because of the early diagnosis and treatment of AT in our clinic. Although antithyroperoxidase antibody (TPOAb) is a hallmark antibody of HT, it cannot predict the initial presentation and clinical outcome.

Introduction

Autoimmune thyroiditis (AT), alternatively known as chronic lymphocytic thyroiditis or Hashimoto's thyroiditis, is an autoimmune disorder characterized by an inflammatory infiltration of lymphocytes that replaces the thyroid parenchyma.[1,2] These processes may lead to thyroid cell damage, cell destruction, and subsequently to impaired thyroid hormone production and clinical thyroid dysfunction.[2] This thyroid dysfunction may progress to a euthyroid, hyperthyroid (HT) and then hypothyroid state, which will be the end of AT, based on the cell destruction characteristics and immune-mediated loss of follicular cells.[2,3] At the time of diagnosis, the thyroid function test shows variations—mostly euthyroid or hypothyroid, and rarely HT.[4] Hypothyroidism is thought to be a permanent sequel of AT.[5] A multicenter study showed that 35.3% of euthyroid patients may become hypothyroid within a mean follow-up period of 5 years.[6] However, there is no information about the clinical outcome of initial hyperthyroidism in AT patients.

In our study, the most common autoantibodies encountered include circulating autoantibodies to thyroglobulin (TgAb), antithyroperoxidase antibody (TPOAb), and thyroid stimulating hormone-R (TSH-R) antibody-thyroid binding inhibitory immunoglobulin (TRAb).[7] These autoantibodies are the hallmarks of AT.[8] They are considered to be able to induce HT or hypothyroid states, depending on their activity.[9] Controversy exists as to whether these autoantibodies play an important role in the pathogenesis, or occur merely as an epiphenomenon of thyroid tissue destruction.[3]

The aims of the present study were to assess and confirm the correlation of these autoantibody titers and the long-term clinical process of AT.

Patients and methods

Study population

A total of 116 patients were diagnosed with AT on the basis of fine-needle aspiration cytology (FNAC) criteria using ultrasound guidance and then follow up in the endocrinology department of Chang Gung Memorial Hospital (CGMH) in both Keelung and Taipei from January 1999 to December 2010. This study adheres to the Declaration of Helsinki and was approved by the Ethics Committee of the institutional Review Board at Chang Gung Memorial Hospital. In this study, we excluded the post-thyroidectomy patients, those who undergo radioactive iodide therapy, those with autoimmune diseases such as pernicious anemia, systemic lupus erythematous (SLE), rheumatoid arthritis (RA), type 1 diabetes mellitus, or any evidence of co-existent pregnancy. We also excluded Graves' disease (GD) patients using the typical cytology findings. Graves' cytology is characterized by follicular hyperplasia, which is present in small- to medium-sized monolayer sheets, and a patchy (multifocal) lymphocytic infiltration, with background smears that contain scanty, diffusely distributed, and weakly stained colloid.[10–12]

Thyroid ultrasound and FNAC

A real-time scanner with a 10-MHz ASU-36WL-10 annular-array transducer (ALOKA, Tokyo, Japan) was used for ultrasound (US) measurements. A longitudinal and transverse view of the thyroid was detected.

FNAC was performed with 23–25 gauge needles, connected to a 10-mL disposable syringe and from a non-nodule area (Fig. 1). The aspirated sample was expressed on frosted-end glass slides, air-dried, and stained using the Romanowsky-based method described by Riu.[13,14] All US and cytological results were interpreted by two attending physicians from the endocrinology division at CGMH.

Definition of AT by FNAC

AT is characterized by the predominance of lymphoid cells, and these lymphoid cells chiefly consist of lymphocytes and centroblasts[15] (Fig. 2A and B). Various abundant plasma cells are noted (Fig. 2C and D). Colloid is scantly or entirely absent.[15] Normal thyroid tissue is replaced by a disseminated oxyphilic change (Hürthle cells) of follicular cells or degenerative follicular cells[15](Fig. 2E,F), and cell debris is often seen.

After the patients were diagnosed with AT by US-guided aspiration cytology, we retrospectively reviewed their thyroid function status when they were first diagnosed with thyroid disorders, according to their hospital files. The patients were then recalled and the thyroid hormone status was followed up prospectively. All patients agreed to participate in the observational study and have been followed up in our endocrine clinic until now. During the follow-up period, we completed all of the thyroid autoantibody analyses (TPOAb, TgAb, and TRAb). The thyroid function status (FT4 and TSH) of all participants was measured every 3–6 months until the end of the study. Clinical details on sex, age at onset, total time of illness, and follow-up duration in our endocrine clinic were also collected.

The 116 patients were divided into three groups, based on thyroid function: euthyroid (both FT4 and TSH levels