Context & Objective: Primary overt autoimmune hypothyroidism is often divided into primary idiopathic hypothyroidism with thyroid atrophy (Ord's disease) and hypothyroidism with goitre (Hashimoto's disease). Aim of present study was to characterize the 2 subtypes of disease.

Design, Setting & Patients: Population-based study identifying newly diagnosed patients with overt autoimmune hypothyroidism. The authors identified prospectively all patients with incident overt autoimmune hypothyroidism in a Danish population cohort. A total of 247 patients were invited to join a comprehensive program including thyroid ultrasonography (US) and measurements of thyroid autoantibodies. Of the 144 patients investigated (58% of all invited), 139 were compared with 556 sex-, age-, and region-matched controls from the cohort.

Results: Patients had lower median (11.6 ml vs. 13.5 ml; P = 0.001) and a more dispersed distribution of thyroid volumes compared with controls (P <0.001). Log thyroid volume (TV) showed a Gaussian distribution in both males and females with no bimodal pattern. Nearly all patients had measurable thyroid autoantibodies, but with increasing thyroid volume (quartile I, II, III, and IV), the levels of circulating antibodies were higher (median TPO-Ab: 1.540, 3.122, 4.686, and 7.058 U/mL; median Tg-Ab: 72, 143, 119, and 1.195 U/mL), and TV correlated negatively with echogenicity (r = -0.21; P = 0.011). Patients with the smallest TVs were biochemically more hypothyroid at diagnosis (median serum T4: 21, 46, 45, and 37 nmol/L; median serum TSH: 81, 41, 45, and 56 mU/L). No difference between groups was observed in prevalence of TSH receptor autoantibody or duration of symptoms before hypothyroidism was diagnosed.

Conclusions: In primary autoimmune hypothyroidism, TV follows a normal distribution. Cases with glandular atrophy and goiter are only extremes within this distribution and do not represent separate disorders. However, patients with low versus high thyroid volume still differ with respect to several characteristics.

COMMENT

In this article, the authors rightly refer to "Ord’s" disease for the atrophic form of chronic autoimmune thyroid disease (AITD) associated with hypothyroidism, based on the 1890’s description of myxoe-dematous cases by the Clinical Society of London. In Belgium, we tend to name this AITD variant Bastenie’s disease, since it was Paul Bastenie who first described the lymphocytic thyroid infiltration in patients with primary hypothyroidism and absence of goiter (Thesis, 1933).

Irrespective of the name given to this medical condition, hypothyroidism due to AITD is observed in patients with glandular hypertrophy (Hashimoto’s disease) or hypotrophy. A long standing discussion opposes two views, namely that
these two variants represent either the same disease or two distinct diseases. For instance, it was hypothesized that the hypertrophic variant was due to growth stimulating autoantibodies and, conversely, the hypotrophic variant due to growth blocking autoantibodies (both theories have remained unproven, however). It was also suggested that the hypotrophic variant could represent end-stage Hashimoto’s disease, a theory contradicted by the fact that this form of hypothyroidism is commonly observed in Western Europe, even at initial stages of AITD, when thyroid autoantibodies are already present but the thyroid still functions normally (or is only mildly impaired, leading to preclinical hypothyroidism). Another clinical notion is that thyroid antibodies are not always detectable in serum during the initial stages of primary hypothyroidism, as they may become apparent only after several years of evolution. In these circumstances, it has been hypothesized that thyroid antibodies may not circulate, but be present within the gland (representing the organ-specific form of thyroid autoimmunity), where they progressively induce glandular destruction by ADCC (antibody-dependent cell-mediated cytotoxicity).

Our colleagues have established a register linked to diagnostic laboratory databases, where they record every thyroid function test requested by hospitals and general practitioners in 2 regions of Denmark. During the period 1997-2000, the register identified 685 individuals with incident overt hypothyroidism, 578 of whom were related to AITD. Among this cohort, 247 patients were invited to participate (144 patients, i.e., 58% of them, did eventually participate) into a research program that included thyroid ultrasonography and measurements of TPO-Ab & Tg-Ab. Each study case was matched with 4 controls.

Thyroid volume (TV) showed a unimodal Gaussian distribution in AITD patients and controls. There were 2 main differences, namely that mean TV was smaller in patients (11.6 ml) compared to controls (13.5 ml; P=0.001) and also that the Gaussian distribution, although unimodal, was much wider in patients with AITD. My own scrutiny of the results presented in the article indicates that in AITD patients TV was normal (8-20 ml) in 47%, while glandular hypotrophy (1-8 ml) observed in 34% and 18% glandular hypertrophy (21-80 ml) in 18% of the patients. When TV distribution was subdivided into quartiles, it was apparent that glandular hypotrophy was associated with more severe hypothyroidism at diagnosis. However, an inverse picture was found for thyroid antibodies, since TPO-Ab and Tg-Ab titers were significantly higher in patients with a normal/enlarged thyroid gland.

This study confirms that Bastenie’s atrophic form of autoimmune thyroiditis and Hashimoto’s disease do not represent separate disorders but a unique condition (AITD) leading to hypothyroidism. It remains, however, unclear why the same basic immunological attack leads to different phenotypic presentations in patients with AITD. (Daniel Glinoer, M.D.; Ph.D.)
A  
Autoimmune hypothyroidism (n = 139)

B  
Control subjects (n = 556)