Patients with a primary diagnosis of autoimmune thyroid disease are at significantly increased risk for additional autoimmune diseases


SUMMARY

BACKGROUND

Autoimmune thyroid diseases are common, manifested most commonly as autoimmune thyroiditis (AITD) or Hashimoto's thyroiditis and Graves' disease. The prevalence of spontaneous hypothyroidism is as high as 2% in iodine-replete areas such as the United States and Europe. In addition, autoimmune thyroid diseases are associated with a variety of other disorders such as type 1 diabetes mellitus, Addison's disease, systemic lupus erythematosus, and pernicious anemia, and also appear as a family trait that tends to be associated with many other autoimmune disorders. The object of this cross-sectional multicenter study was to systematically quantify the prevalence of coexisting autoimmune disorders.

METHODS

Data were obtained from a protocol in the national U.K. collection of DNA for studies of genetic susceptibility to autoimmune thyroid diseases, including prospective and systematic collection of clinical data regarding the coexistence of other common autoimmune disorders in index cases and their parents. Patients were recruited from February 2002 through July 2007. The diagnosis of autoimmune disorders was based on patient recall, with confirmation in the index case through verification of current medical records and medications by recruiting physicians. Records confirming the evidence of coexisting autoimmune diseases were considered positive. All subjects completed a structured questionnaire seeking a personal and parental history of common autoimmune disorders, as well as a history of hyperthyroidism or hypothyroidism among parents.

RESULTS

The Prevalence of Coexisting Autoimmune Diseases in Men and Women (Figures 1 and 2)

The study cohort comprised 3286 individuals, 2791 (85%) of whom were white subjects with Graves' disease, 2317 women (83%) and 474 men (17%), and 495 white subjects with Hashimoto's thyroiditis (15%), 427 women (86%) and 68 men (14%) who were recruited from specialist referral thyroid clinics in the United Kingdom. Approximately 90% of the eligible patients participated in the study. The mean age at the time of diagnosis was 43 years for the index cases of Graves' disease, and 42.5 years for Hashimoto's thyroiditis (P = not significant [NS]). The mean age at the time of recruitment in the study was not different in the index cases of Graves' disease (47.3 years) or Hashimoto's thyroiditis (47.5 years, P = NS) (Figures 1 and 2). There also were no significant differences in age at the time of diagnosis or recruitment to the study in patients with Graves' disease or Hashimoto's thyroiditis with no coexisting autoimmune disease or for those with an additional autoimmune disorder (Figures 1 and 2).

**Figure 1.** This figure shows the prevalence of coexisting autoimmune diseases in the index cases of women with Graves' disease. Age1 = age at the time of diagnosis of Graves' disease or Hashimoto's thyroiditis; Age2 = age at recruitment to the study; celiac = celiac disease; IBD = inflammatory bowel disease; MG = myasthenia gravis; MS = multiple sclerosis; PA = pernicious anemia; RA = rheumatoid arthritis; SLE = systemic lupus erythematosus. This figure is drawn from data in Table 2A in Boelaert et al.

**Figure 2.** This figure shows the prevalence of coexisting autoimmune diseases in the index cases of men with Graves' disease. (See Figure 1 for definitions of the abbreviations.) This figure is drawn from data in Table 2B in Boelaert et al.
The Prevalence of Coexisting Autoimmune Diseases in the Index Cases with Graves’ disease or Hashimoto’s Thyroiditis (Figures 3 to 6)

Almost 10% of the 2791 subjects with Graves’ disease and 14% of the 495 with Hashimoto’s thyroiditis had another autoimmune disorder (P = 0.005). The most common autoimmune disease associated with the index cases of Graves’ disease or Hashimoto’s thyroiditis was rheumatoid arthritis (Figures 1 and 2). Those with Hashimoto’s thyroiditis had a 10-fold higher risk for Addison’s disease (<0.001) and a 3-fold higher risk for pernicious anemia (P = 0.004), as compared with index cases of Graves’ disease (Figures 1 and 2). Comparing index cases of Graves’ disease, there were significantly higher prevalence rates of type 1 diabetes mellitus (P = 0.011) and myasthenia gravis (P = 0.001) in men as compared with women; however, Addison’s disease, celiac disease, and multiple sclerosis were exclusively associated with the index cases of Graves’ disease in women. There were no significant differences in the prevalence rates of other autoimmune disorders in men and women with index cases of Hashimoto’s thyroiditis (Figures 4 to 6). Comparing male and female patients, there were no significant differences in age at either diagnosis or recruitment. When comparing age at diagnosis of Graves’ disease between index cases with different autoimmune diseases (Figure 1 to 6), there were significant differences in age at diagnosis between men and women with index cases of Hashimoto’s thyroiditis (Figures 4 to 6).

Figure 3. This figure shows the prevalence of coexisting autoimmune diseases in the index cases of women with Hashimoto’s thyroiditis disease. (See Figure 1 for definitions of abbreviations.) This figure is drawn from data in Table 2B in Boelaert et al.

Figure 4. This figure shows the prevalence of coexisting autoimmune diseases in the index cases of men with Hashimoto’s thyroiditis disease. (See Figure 1 for definitions of the abbreviations.) This figure is drawn from data in Table 2B in Boelaert et al.

Figure 5. This figure shows the relative risk for a diagnosis of other autoimmune diseases in women with index cases of Graves’ disease or Hashimoto’s thyroiditis. (See Figure 1 for definitions of the abbreviations.) This figure is drawn from data in Table 4A in Boelaert et al.

Figure 6. This figure shows the relative risk for a diagnosis of other autoimmune diseases in women with index cases of Graves’ disease or Hashimoto’s thyroiditis. (See Figure 1 for definitions of the abbreviations.) This figure is drawn from data in Table 4B in Boelaert et al.
Rheumatoid arthritis was the most common autoimmune disorder, found in over 3% of patients with Graves’ disease and over 4% of patients with Hashimoto’s thyroiditis. The authors provide the caveat that screening for other autoimmune diagnoses might be indicated if patients with autoimmune thyroid disease present with new or nonspecific symptoms.

Several years ago, Allen et al. (1) studied autoimmune thyroiditis in a homogeneous founder white population, the Old Order Amish of Lancaster County in Pennsylvania, and found that circulating antinuclear antibodies were relatively common in the Amish, with a prevalence of almost 23%, and the prevalence of autoimmune hypothyroidism was nearly 10%. The authors found suggestive evidence of linkage of autoimmune thyroid disease confined to a locus on chromosome 5q11.2–q14.3 that was previously reported to be linked toAITD–hypothyroidism in a Japanese study. The authors suggested that this gene is likely to contribute to the susceptibility to autoimmune thyroiditis in the Amish. Other studies (2) have found subclinical autoimmune thyroid disorders in patients with systemic sclerosis, type 1 diabetes mellitus, celiac disease (3-6), and other diseases (3-9).

The study by Boelaert et al. is a significant contribution that provides important new information on this problem.

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References


