

Prevalence of autoimmune thyroid disease in chronic rhinitis

William R. Reisacher, MD, FACS, FAAOA

Abstract

A retrospective, controlled study was undertaken to determine the prevalence of autoimmune thyroid disease in 111 adult patients with allergic (77) and nonallergic (34) rhinitis seen in a private ENT/allergy practice in the lower Hudson Valley, New York. The control group consisted of 101 patients with no history of chronic rhinitis. Autoimmune thyroid disease was found in 10.4% of the allergic rhinitis group, 14.7% of the nonallergic rhinitis group, and 9.9% of controls, with a trend toward higher prevalence in the nonallergic rhinitis group compared with controls. No statistically significant association was noted between the 3 groups. The female-to-male ratio in the nonallergic rhinitis group was approximately twice as high as in the control group.

Introduction

As early as the 1960s, clinical observation suggested a higher prevalence of thyroid disease in atopic patients than in the general population.^{1,2} Most of the recent work in this area has focused specifically on the relationship between autoimmune thyroid disease (AITD) and allergic rhinitis (AR).³ Amino et al reported that 42% of patients with Graves disease had allergies, compared with 32.6% of the control population.⁴ Increased levels of immunoglobulin E and interleukin 13, characteristic of Th2 cell-mediated AR, have been found in patients with Graves disease.⁵ Nakamura et al reported a familial, springtime occurrence of silent thyroiditis in only those family members who were allergic to Japanese cedar pollen.⁶

Considering the data linking these two entities, it is reasonable to expect that AITD would be more prevalent in the allergic population than in the nonallergic population. However, a study by Krouse and Krouse found the same prevalence of thyroid disease in allergic patients with positive results on skin testing and in controls with no history of chronic rhinitis (NR).⁷ The investigators made no distinction between AITD and non-AITD, and they did not include in the analysis patients with chronic rhinitis of a nonallergic nature.⁷

This study is the first to investigate the association between AITD and chronic rhinitis by comparing the prevalence of AITD in three groups:

- Patients with a history of chronic rhinitis who tested positive for inhalant allergies on skin-prick testing (SPT) or in vitro testing (AR group);
- Patients with chronic rhinitis who tested negative for inhalant allergies (NAR group); and
- Control patients (NR group).

Patients and methods

A retrospective study was conducted of all patients aged 18 years and older who attended a community-based, private general otolaryngology and otolaryngic allergy practice from October to December 2005. An institutional review board was not available at this study location, but no data were used in the analysis that could be used to identify any individual patient. No procedures were performed unless they were part of the patient's routine care.

Information extracted from patients' charts included laboratory data and/or clinical data for AITD, nasal symptoms (congestion, rhinorrhea, sneezing, postnasal drip, facial pressure, diminished sense of taste/smell), physical findings on anterior rhinoscopy or nasal endoscopy (pale mucosa, mucosal edema, thickened mucus, polyps), and any results of allergy testing.

Patients who reported 2 or more nasal symptoms persisting for at least 3 months during the preceding

From Rockland Ear, Nose and Throat Associates, PC, West Nyack, New York.
Dr. Reisacher is now with the Department of Otorhinolaryngology, Weill Medical College of Cornell University, New York City.
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Corresponding author: William R. Reisacher, MD, Weill Medical College of Cornell University, Department of Otorhinolaryngology, 1305 York Ave., 5th Floor, New York, NY 10021. Phone: (646) 962-2093; fax: (646) 962-0030; e-mail: wir2011@med.cornell.edu

year and who had one positive finding or more on nasal physical examination were included in the chronic rhinitis group. Only those who had undergone allergy testing (the vast majority) were included in the study. On the basis of allergy-testing results, patients were placed in either the AR or the NAR group.

For the purpose of this study, only immunoglobulin E-mediated inhalant allergies were used to differentiate these two groups. An SPT (with Multi-Test II [Lincoln Diagnostics, Inc., Decatur, Ill.]) for 30 allergens (dust, trees, grass, weeds, mold, and epidermals) was used, along with histamine as a positive control and 50% glycerin as a negative control. Any positive result (wheal greater than 3 mm) placed that patient in the AR group. Patients who could not undergo SPT had in vitro testing (with ImmunoCAP [Phadia AB, Uppsala, Sweden]) for the same antigens. Any positive results (class 1 or higher) placed the patient in the AR group. Patients who did not have a history of chronic nasal problems were placed in the NR group.

Patient data were stored in a spreadsheet format. Statistical analysis was performed using chi-square tests for association between the AR, NAR, and NR groups and the presence of total AITD. Two-tailed *p* values were calculated using commercially available software (GraphPad [GraphPad Software, Inc., La Jolla, Calif.]); *p* ≤ 0.05 was considered statistically significant.

Results

After a review of 613 charts, 111 patients were placed in the chronic rhinitis (both allergic and nonallergic) group and 101 patients were placed in the control (NR) group (see table 1 for demographic characteristics). Patients in the NR group came to the office for a variety of ear, throat, neck, and facial problems. A few had undergone allergy testing (e.g., for Ménière disease), but even if results were positive, they were not placed in the AR group because they did not have chronic rhinitis.

Of the 111 patients with chronic rhinitis, 77 (69.4%) tested positive for inhalant allergies (AR group) and 34 (30.6%) tested negative (NAR group). Overall, rhinitis symptoms were similar between the AR and NAR groups. Female-to-male ratios were approximately even for the AR and NR groups, but patients in the NAR group were twice as likely to be female compared to controls.

Among all 212 patients, 23 (10.8%) had AITD. Of these 23 patients, 14 (60.9%) had hypothyroidism, 4 (17.4%) had hyperthyroidism, and 5 (21.7%) had eu-

Table 1. Patient demographics

Characteristic	NR (n = 101)	AR (n = 77)	NAR (n = 34)	AITD (n = 23)
Mean age (yr)	48.1	41.8	44.9	57.0
Female-to-male ratio	0.91:1	1.03:1	1.82:1	6.67:1

NR = no rhinitis; AR = allergic rhinitis; NAR = nonallergic rhinitis; AITD = autoimmune thyroid disease.

thyroid thyroiditis. AITD was found in 8 (10.4%) of the AR group, 5 (14.7%) of the NAR group, and 10 (9.9%) of the NR group. Overall, the mean age for the AITD group was higher than for the AR, NAR, and NR groups by approximately 10 to 15 years, and the female-to-male ratio was 6.67:1.

Table 2 shows results of tests of association and calculation of odds ratios using chi-square analysis with two-by-two boxes. There was no statistically significant association between the presence of AITD and the presence of AR or NAR in the study population or in the control population.

Discussion

As indicated by available evidence, a relationship clearly exists between AITD and AR, but its nature remains unclear. According to the literature, the relationship extends to atopic conditions beyond AR. Using the Oxford database, which covers 2.5 million people, Goldacre et al found a significant association between asthma and both hypothyroidism and thyrotoxicosis.⁸ Verneuil et al demonstrated that the frequency of thyroid autoantibodies was significantly higher in patients with chronic urticaria (26.7%) than in controls (3.3%).⁹

In the current study, findings of clinical manifestations alone indicate that AITD and AR are independent of one another. However, other studies have suggested that an association may be related to subclinical parameters, such as serum antibodies. Levels of autoan-

Table 2. Chi-square tests of association

Comparison	Chi-square value	Odds ratio	<i>p</i> value
AR to AITD	0.03	0.93	0.87
NAR to AITD	0.62	1.53	0.43
NR to AITD	0.18	0.83	0.67

AR = allergic rhinitis; AITD = autoimmune thyroid disease; NAR = nonallergic rhinitis; NR = no rhinitis.

tibodies (antithyrotropin-receptor antibodies, antithyroid peroxidase antibodies, and antithyroglobulin antibodies) have been found to increase after seasonal exacerbation of AR, but they might serve as a marker of immune system stimulation rather than clinical exacerbation of thyroid disease.¹⁰ Increases in antibodies alone, secondary to atopic or autoimmune reactions, might not be sufficient to produce clinical changes that would be apparent on routine evaluation. All the patients in the Verneuil study who had urticaria with increased thyroid autoantibodies had normal thyroid hormone levels.⁹

Effects of AITD, AR, and NAR. Further investigation is required to clarify any direct effects that AITD and AR might have on one another. Evidence suggests that AITD and AR might also have indirect effects on each other, through activation of other systemic processes. Up-regulation of Th1-inducing cytokines has been found in association with painless thyroiditis, an active phase of Hashimoto thyroiditis; and Th2 up-regulation has been found in Graves disease.^{4,10} Overactivation of the Th2 cytokine pattern is also known to be a dominant feature of AR. Moens et al suggested that a suppressor T-cell defect is responsible for both atopic disease and thyroid autoimmunity.¹¹

I believe examining the heterogeneous NAR group is important for comparison in evaluating the relationship between AITD and AR. Patients in this group have conditions of varying etiologies, such as vasomotor rhinitis, atrophic rhinitis, rhinitis medicamentosa, nonallergic rhinitis with eosinophilia, chronic rhinosinusitis, metabolic conditions, structural obstruction, and physical or chemical irritation of the nose. Autoimmune disease might also be a cause. Settipane and Lieberman reported the presence of hypothyroidism in 2% of patients with NAR.¹²

NAR might be a confounding variable in examination of AR in the clinical setting. About half of patients presenting with chronic rhinitis do not have AR, and differentiation between NAR and AR is often based on clinical observation alone, without benefit of formal allergy testing.¹³ Symptoms of the two entities overlap extensively, so it is possible that in clinical practice, the diagnosis of "allergies" may be assigned to patients who actually have NAR.

A prevalence of AITD that was almost 50% higher in the NAR group than in the AR group was a surprising finding, although the difference was not statistically significant. In addition, in the AR and NR groups, the female-to-male ratios were approximately even, whereas

in the NAR group, the female-to-male ratio was twice that of the control group. This finding is consistent with data from the 1999 National Rhinitis Classification Task Force Survey of Non-allergic Rhinitis.¹⁴ Reports of an even higher female predominance in AITD are consistent with the 6.67:1 female-to-male ratio found in this study. Reasons for the finding are unknown. Drawing conclusions about any linkage between AITD and NAR is difficult on the basis of current data and requires further investigation.

Limitations of the study. The sample was small, particularly for the hyperthyroid and euthyroid categories. Although in most study patients the diagnosis of AITD was based on laboratory data of thyroid function (thyrotropin, free T₄, or autoantibody levels), in a few the diagnosis was based on the patient's history and knowledge of a previously determined diagnosis. Patients were classified as having AR only if the clinical symptom complex of chronic rhinitis coupled with positive inhalant allergy testing was present. It is possible that patients with rhinitis secondary to food allergy were inaccurately categorized as being nonallergic.

Another problem was placement of patients in either the AR or NAR category, because 34% of patients with chronic rhinitis have both allergic and nonallergic features.¹⁴ Also, patients younger than age 18 were excluded from the study because of their low incidence of AITD, but Lindberg et al studied patients in this age group who had various allergic diseases and found elevated levels of thyroid peroxidase autoantibodies, as well as ultrasound evidence of autoimmune thyroiditis, compared with controls.³

Clinical implications. Results of this study indicate that no additional workup for AITD is necessary based solely on the presence of AR or NAR. It is important, however, to keep in mind the underlying mechanisms of these entities and the associations between them, which might be subclinical. Unexplained or unexpected exacerbations in AR or NAR might warrant further investigation of AITD, and vice versa, as part of the patient's overall management.

This study suggests a linkage between AITD and NAR. These conditions might share immune features or represent coexisting autoimmune disease, and further investigation will proceed in this direction. Studies with larger patient populations and more stringent classification of AITD will also be helpful in determining whether medical and surgical management of chronic rhinitis or AITD will affect the clinical course of the opposite entity.

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Continued from page 520

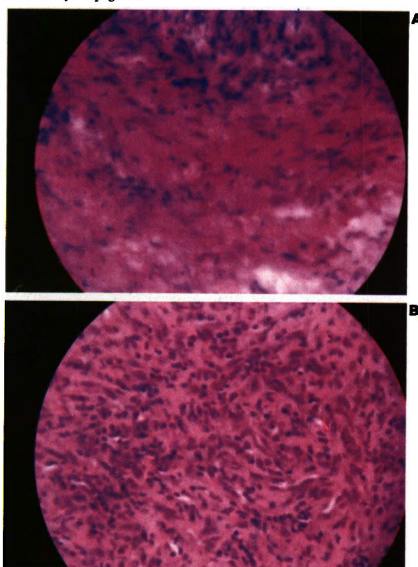


Figure 3. Microphotographs show the metastatic tumor (A) in the sinus and the primary adenocarcinoma (B) of the prostate (H&E, original magnification $\times 40$).

from metastatic tumors. Only with biopsy does the true nature of the tumor become evident, but even then, a specimen may not exhibit any obvious microscopic features that would readily indicate its origin.⁷

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