A single thyroid lobe is usually sufficient to maintain euthyroidism albeit with significantly higher than usual TSH and FT₃ levels


SUMMARY

BACKGROUND
Thyroid hemiagenesis (THA) is a rare congenital abnormality in which one thyroid lobe fails to develop. Its incidence is uncertain because the absence of one thyroid lobe does not usually cause clinical symptoms and thus often goes unrecognized. THA is usually detected incidentally during an evaluation of other thyroid disorders, and its management remains a matter of debate. It is more frequently found in women than in men, and it is more common in the left thyroid lobe. This is a study of 40 patients with THA that provides the first extensive hormonal and ultrasound analysis of the disorder.

SUBJECTS AND METHODS
This study was designed to prospectively study all patients with THA seen from January 2002 through December 2008 in the Ultrasound Unit of the Department of Endocrinology, Metabolism and Internal Medicine at the University of Medical Sciences, Poznan, Poland. The 40 study patients were referred for thyroid ultrasonography, during which THA was discovered by serendipity during screening ultrasonography in 17 patients and for nonthyroidal disorders, thyroid-related symptoms, or thyroid asymmetry in the others. It was found by self-examination in 1 patient, on physical examination in 22, and as a consequence of mild symptoms of hypothyroidism or hyperthyroidism in 1 patient.

A control group of 80 persons was matched for age and sex to the study patients by randomly selecting participants from 2159 people in a cross-sectional population-based thyroid screening program that was also performed by the authors. After ultrasonography, THA was confirmed by thyroid scintigraphy. All the subjects live in the same region of Poland, which is classified by the World Health Organization as a mildly iodine-deficient area.

RESULTS
The 40 study patients ranged in age from 12 through 79 years, and the prevalence of women was 7:1. Of the 40 patients, 35 (88%) had THA in the left thyroid lobe; 2 patients had a large pyramidal lobe, and the isthmus was absent in all 5 patients with right-sided THA. The most common finding was isolated agenesis of the left thyroid lobe in 28 patients (70%), and the remaining patients had agenesis of the left thyroid lobe and isthmus. THA was often associated with several thyroid disorders, including Graves’ disease, nodular variant Graves’ disease, nonautoimmune hypothyroidism, nontoxic nodular goiter, simple goiter, or toxic nodular goiter.

Thyroid Hormone Status and Ultrasound Findings in Patients versus Controls (Figure 1)
The most frequent thyroid disorders were thyroid nodules and autoimmune thyroid disease. Most patients (26) were euthyroid (65%), 10 had hypothyroidism (25%), and the remaining 4 had...
Thyroid hemiagenesis is a perplexing problem. What we know with reasonable certainty is that THA is a rare congenital abnormality in which one thyroid lobe—usually the left—fails to develop. Almost everything else is controversial. Although its prevalence is uncertain, 5 ultrasound screening studies, 3 of which involved children, which comprised a total of 41,895 patients, found an average prevalence of 0.06%, with a range of 0.16 to 0.05 (1-5). The prevalence range is wide because the absence of one thyroid lobe usually does not cause clinical symptoms, and most of the studies are case studies or small reports that find myriad thyroid abnormalities ranging from thyroid cancer to autoimmune thyroid disease, and most report thyroid dysfunction (6-11). Still, such small studies are always subject to selection bias, which is particularly true in a literature based on case studies.

The study by Ruchala et al. is unique in that it is the largest study of patients with this disorder, and it has a control group that was randomly selected from large cohort that had previous screening ultrasonography, 80 of which were matched for age and sex with the study population. Patients with THA, while usually clinically euthyroid, were found to have significantly

**Comparison of Hormonal, Morphologic, and Immunologic Profiles in Two Age Groups (Figure 2)**

The Patients were divided into two age groups, one (≤25 yr) and the other (>25 yr) (Figure 2). There were significant differences in thyroid volume, presence of heterogeneous decreased echogenicity on ultrasonography, and the incidence of antithyroperoxidase antibodies (TPOAb) were increased. There also was a significant positive correlation between thyroid volume and age at diagnosis (P = 0.009). Of the 40 patients with THA with absent TPOAb, 18 were selected for hormone analysis to exclude the influence of autoimmune disturbances on these tests; there was no significant correlation between thyroid volume and age. There also no significant differences in thyrotropin (TSH), free thyroxine (FT₄), and free triiodothyronine (FT₃) or incidence of focal lesions (Figure 2).

**Antithyroperoxidase Antibodies in 40 Patients and 80 Controls (Figure 4)**

Immunologic assessment revealed a significantly increased prevalence of elevated thyroid autoantibodies (TRAb, TPOAb, and TgAb) in comparison with the control group (Figure 4).

**CONCLUSION**

A single thyroid lobe was usually sufficient to maintain euthyroidism, with significantly higher than usual TSH and FT₃ levels among the study subjects.

**Figure 3.** This figure shows the ultrasound-guided fine-needle aspiration biopsy findings and ultrasonography characteristics of thyroid lesions. *P<0.005 comparing the two groups. The data for this figure were derived from Table 2 of Ruchala et al.

**Figure 4.** This figure shows the anti-thyroid antibodies in 40 patients and 80 controls. †P < 0.005. ‡P = 0.019. TgAb = thyroglobulin antibodies; TRAb = thyrotropin-receptor antibodies. The data for this figure were derived from Table 4 of Ruchala et al.

**COMMENTARY**

Thyroid hemiagenesis is a perplexing problem. What we know with reasonable certainty is that THA is a rare congenital abnormality in which one thyroid lobe—usually the left—fails to develop. Almost everything else is controversial. Although its prevalence is uncertain, 5 ultrasound screening studies, 3 of which involved children, which comprised a total of 41,895 patients, found an average prevalence of 0.06%, with a range of 0.16 to 0.05 (1-5). The prevalence range is wide because the absence of one thyroid lobe usually does not cause clinical symptoms, and most of the studies are case studies or small reports that find myriad thyroid abnormalities ranging from thyroid cancer to autoimmune thyroid disease, and most report thyroid dysfunction (6-11). Still, such small studies are always subject to selection bias, which is particularly true in a literature based on case studies.

The study by Ruchala et al. is unique in that it is the largest study of patients with this disorder, and it has a control group that was randomly selected from large cohort that had previous screening ultrasonography, 80 of which were matched for age and sex with the study population. Patients with THA, while usually clinically euthyroid, were found to have significantly
higher serum TSH, FT3, and FT4 concentrations as compared with those in controls. Furthermore, there was a higher incidence of functional, morphologic, and autoimmune thyroid disorders in the patients with THA as compared with that in normal subjects with a bilobate thyroid (P<0.05).

The authors conclude that patients with THA should have ongoing follow-up because thyroid pathologies are likely to develop, presumably due to long-lasting TSH overstimulation, and patients with elevated TSH levels should be treated with levothyroxine. In effect, they are suggesting levothyroxine therapy for subclinical hypothyroidism on the basis of the 40 study patients who remained clinically euthyroid during the period under study.

It is a matter of debate whether THA should be considered clinically insignificant, or whether the absence of one lobe regularly predisposes a patient to the development of clinically important thyroid disease that requires therapy. This dilemma is nearly impossible to resolve, considering the long-term clinical outcome of this anomaly has not been fully studied. It is a fact that the diagnosis of THA is usually made by serendipity when some other thyroid disease is being evaluated or is identified during screening ultrasonography, which, along with the paucity of clinically overt cases of thyroid disease, makes it difficult to provide strong recommendations concerning treatment. The detection of THA is almost always discovered incidentally in the course of evaluating patients for other thyroid disorders. It is more frequently found in women than in men (3:1 ratio) and in the left lobe as compared with the right.

We have no clear information concerning the inherent pathogenesis of this condition, or why one lobe or the other is involved. A literature search by Ruchala et al. found that nearly 300 patients with THA have been described in the literature; most of these reports are case studies. Although there were no malignant thyroid lesions in Ruchala et al.’s patients, therapy was instituted on the basis of cytologic examination and ultrasonography. Surgical treatment was recommended to six patients because of a “suspicious sonographic appearance,” nondiagnostic fine-needle aspiration biopsy findings, toxic nodular goiter, and a large goiter volume. In the final analysis, the real question is, does this provide compelling evidence that therapy should be instituted in this group of patients?

A recent study by Gursoy et al. (2) found 12 cases of THA among 4883 patients with various thyroid disorders, along with ultrasonography data from a large community screening survey of 4722 children and of 2935 adults with thyroid disorders. The underlying thyroid diseases that were discovered were Hashimoto’s thyroiditis (n = 4), euthyroid multinodular goiter (n = 4), and toxic adenoma (n = 1). None of the patients had thyroid dysfunction.

In another study by Maiorana et al. (4), thyroid hemiagenesis was studied by neck ultrasonography in almost 25,000 unselected 11 to 14-year-old schoolchildren from southeastern Sicily. Twelve cases of thyroid hemiagenesis were identified, giving a prevalence of 0.05%, which in all 12 cases involved the left thyroid lobe. Yet thyroid volume was within the normal range of total thyroid volume normalized to age, was enlarged in 3, and was significantly reduced in 5. Thyroid-function studies were always within the normal range; however, children with THA had an average serum TSH significantly higher than that of 18 matched controls (2.8±0.6 vs. 1.9±0.5 mU/L, P<0.001). The authors concluded that their study confirms that thyroid hemiagenesis is nearly always due to left-lobe defect and that compensatory hypertrophy of the residual thyroid lobe occurs in most, but not all, cases and is due to thyroid-tissue overstimulation by TSH. They also suggest systematic follow-up of all identified cases of THA.

In conclusion, there is a reasonable consensus that patients with THA should have long-term follow-up with thyroid-function tests, but treatment of subclinical hypothyroidism in this group appears to be no different from that for patients with routine subclinical hypothyroidism that only mandatorily demands therapy when the overt hypothyroidism develops.

— Ernest L. Mazzaferrri, MD, MACP

References