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ORIGINAL PAPER

Clinical and epidemiological characteristics of thyroid hemiagenesis: ultrasound screening in patients with thyroid disease and normal population

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Abstract Thyroid hemiagenesis is a rare form of thyroid dysgenesis, in which one thyroid lobe fails to develop. The true prevalence of this rare abnormality is about 0.05–0.2% in normal population. We aimed to determine prevalence of thyroid hemiagenesis in patients with various thyroid disorders and a normal population in a mild to moderate iodine-deficient area. The clinical and thyroid ultrasonography records of 4,833 patients who presented with various thyroid disorders were reviewed. In addition, ultrasonographic data of two large surveys carried out for the community screening of iodine status of children ($n = 4{,}772$) and thyroid disorders of adult subjects ($n = 2{,}935$) were analyzed. In patients with thyroid disorders, we found 12 cases with thyroid hemiagenesis (0.25%). Thyroid hemiagenesis was due to the agenesis of the left lobe in all cases. The underlying thyroid diseases were Hashimoto's thyroiditis ($n = 4$), euthyroid multinodular goiter ($n = 4$), and toxic adenoma ($n = 1$). Three subjects have no underlying thyroid disease. In ultrasonography screening of normal population, altogether, the absence of the left lobe was detected in only two cases, indicating a true prevalence of thyroid hemiagenesis of 0.025%. None of the reviewed patients had thyroid dysfunction. Our community-based data is in accordance with previous studies in terms of prevalence and male-to-female ratio.

Keywords Thyroid · Hemiagenesis · Prevalence · Ultrasound

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Introduction

Thyroid hemiagenesis is a rare form of thyroid dysgenesis, in which one thyroid lobe fails to develop. Although exact pathogenesis of thyroid hemiagenesis is unknown, some genetic alterations in transcriptional control of thyroid development and in the control of migration of the median thyroid bud during embryogenesis have been questioned [1].

The detection of thyroid hemiagenesis is usually an incidental finding during the evaluation of thyroid disorders. Since thyroid hemiagenesis is a rare entity, many case reports have been published describing the association with other thyroid diseases or congenital defects [2–9]. The increased prevalence of thyroid diseases in association with thyroid hemiagenesis and observed female preponderance have been questioned after surveys, investigating the true prevalence of thyroid hemiagenesis in normal population [10–12]. The true prevalence of thyroid hemiagenesis is reported to be 0.05–0.2% in normal population and intact thyroid lobe is usually normal in the subjects with thyroid hemiagenesis. Thus, the high incidence of thyroid abnormalities and female preponderance reported by previous case reports could be related to referring population which includes patients with thyroid disorders.

The objectives of this study were to determine prevalence of thyroid hemiagenesis in patients with various thyroid disorders and a normal population.

Results

From a database of ultrasound records of 4,833 (843 males and 3,990 females) patients with various thyroid disorders, we identified 12 cases of thyroid hemiagenesis, indicating a prevalence of 0.25%. Information regarding observed thyroid hemiagenesis cases is presented in Table 1 All were unrelated individuals. Three of 12 hemiagenesis cases occurred in male patients. The relative prevalence of thyroid hemiagenesis in our cohort was 3:843 (0.36%) among males and 9:3,990 (0.23%) among females.

All patients have left lobe hemiagenesis. Thyroid hemiagenesis was due to the agenesis of the left lobe in ten cases and hypoplasia of the left lobe in two cases. The isthmus was visualized in 6 of 12 patients (50%). The underlying thyroid diseases were Hashimoto's thyroiditis ($n = 4$), euthyroid multinodulated goiter ($n = 4$), and toxic adenoma ($n = 1$). Three subjects have no underlying thyroid disease.

Two cases of thyroid hemiagenesis were observed among the 4,772 children (in one subject) and 2,935 adult subjects (in one subject), indicating a true prevalence of thyroid hemiagenesis of 0.025% in a normal population of mild to moderately iodine-deficient area. The absence of the left lobe was detected in one female and in one male subject and isthmuses were absent in both cases. The remaining right lobe volumes were 6.9 and 7.1 ml. The echogenicity of the remaining thyroid lobe was normal in both cases with thyroid hemiagenesis as were serum TSH, free T4, and free T3, and tests for thyroid antibodies. None of the two cases with thyroid hemiagenesis had a family history of thyroid disease.

Discussion

Most observed cases of thyroid hemiagenesis have been found only incidentally after patients have been examined for thyroid conditions since the absence of one thyroid lobe usually does not cause clinical symptoms by itself [2–9]. There has been only one survey to establish its prevalence among patients with thyroid disorders [2]. Since thyroid hemiagenesis is very rare entity, many case reports have been published describing the association with other thyroid diseases or congenital defects, mostly cardiac [2–9]. The associated diseases in the intact thyroid lobe include benign adenoma, multinodular goiter, hyperthyroidism, chronic thyroiditis, Graves' disease, and rarely carcinoma.

Data related to the true prevalence of thyroid hemiagenesis are also limited. Since the scarce amount of data about true prevalence of thyroid hemiagenesis is present and thyroid disorders are common in females, many people draw the erroneous conclusion that concomitant thyroid diseases are common and thyroid hemiagenesis is more frequently found in female than in male patients. More recently, however, studies investigating the true prevalence of thyroid hemiagenesis, like ours, have claimed that the incidence of associated thyroid diseases and female preponderance might have been overestimated. So far, three studies have been published evaluating the true prevalence of thyroid hemiagenesis in the normal population [10–12]. Maiorana et al. [11] reported a prevalence of 0.05% in 24,032 unselected 11- to 14-year-old schoolchildren from southeastern Sicily. In this study, the female-to-male ratio was 1:1.4. Thyroid hemiagenesis was always due to the absence (11 cases) or severe hypoplasia (one case) of the left lobe. Intact lobe thyroid volume was within the normal

Table 1 Clinical, biochemical, and thyroid ultrasound measurements in cases with thyroid hemiagenesis

Patient	Sex	Age (years)	Right lobe volume (ml)	Isthmus	Serum TSH (mIU/ml)	Thyroid antibodies	Associated thyroid disorder	Current treatment
1	F	73	5.9	Absent	2.9	Negative	Toxic adenoma	L-thyroxine replacement
2	F	81	61.8	Absent	2.3	Negative	Euthyroid multinodular goiter	None
3	F	53	6.1	Absent	2.1	Positive	Hashimoto's thyroiditis	L-thyroxine replacement
4	M	20	8.2	Absent	0.6	Positive	Hashimoto's thyroiditis	L-thyroxine replacement
5	F	45	9.7	Present	2.9	Negative	Euthyroid multinodular goiter	None
6	F	44	7.5	Present	2.3	Positive	Hashimoto's thyroiditis	None
7	F	22	9.2	Absent	0.7	Negative	None	
8	F	73	7.8	Present	1.0	Negative	None	
9	F	62	12.0	Present	1.4	Positive	Hashimoto's thyroiditis	L-thyroxine replacement
10	M	66	13.7	Present	1.9	Negative	Euthyroid multinodular goiter	None
11	F	22	9.2	Present	0.7	Negative	None	
12	M	30	9.2	Absent	0.9	Negative	Euthyroid multinodular goiter	None

total thyroid volume range normalized to age in 4 of 12 cases, enlarged in 3, and significantly reduced in 5. Thyroid function was within the normal range. However, children with thyroid hemiagenesis had an average serum TSH significantly higher than controls. They suggested that compensatory hypertrophy of the intact thyroid lobe occurs in most, but not all, cases and is due to thyroid tissue overstimulation by TSH. In a systematic ultrasound study of the thyroid gland volume in 2,845 normal Belgian school children, Shabana et al. [10] found absence of the left lobe in six children (prevalence of 0.2%) with a slight female preponderance (ratio of 2:1). No compensatory increase in intact thyroid lobe volume is noted. There was no association with other thyroid malformations or dysfunction. In a study by Korpal-Szczyrska and Kosiak [12], ultrasound examination of the thyroid gland was performed in 4,004 unselected 7–15-year-old schoolchildren from the seaside zone of northern Poland. Two cases (prevalence of 0.05%) of thyroid hemiagenesis were found, both being absence of the left lobe in two girls. Thyroid volumes, adjusted to body surface area, were within normal range; serum thyrotropin, free thyroxine, and free triiodothyronine were within normal limits. Contradictory results between these studies in respect to compensatory change in intact thyroid lobe might be explained by the fact that iodine status of two areas is different.

In our study, we observed thyroid hemiagenesis prevalence of 0.25% in an outpatient referral population with thyroid disorders and 0.025% in a normal population. Three of 12 thyroid hemiagenesis cases observed in our referral population with thyroid disorders had normal thyroid function tests and normal morphology in intact thyroid lobe on ultrasonography. Observed two thyroid hemiagenesis cases in our normal population screening also had no thyroid malformations or dysfunction. Our results certainly support previous observations that thyroid hemiagenesis is almost always due to left lobe defect. One reason for observed higher prevalence of hemiagenesis in patients with thyroid disease as compared to a normal population could be related to patient selection. Patients with thyroid hemiagenesis were referred to thyroid clinic after finding of hemiagenesis during routine physical examination or imaging procedures ordered for reasons other than thyroid. The prevalence of hemiagenesis was tenfold greater in the patient population than in the population at large, this could be related to the fact that subjects with hemiagenesis are more prone of developing thyroid diseases. In normal population, the number of cases of thyroid hemiagenesis identified in our study is very small. Since only two cases are noted to have thyroid hemiagenesis in the normal population, it is unwise to emphasize that there is no sex preponderance in the present study.

Our community-based data is in accordance with largest previous community-based study by Maiorana et al. in terms of prevalence. Associated thyroid pathology is not an obligate finding.

Materials and methods

Study design

The study protocol was approved by the Baskent University Ethics Committee for Human Studies. The results of all thyroid ultrasound scans obtained between March 2005 and January 2008 at the Baskent University Thyroid Center, Ankara, Turkey, were retrospectively evaluated. The database included 4,833 (843 males and 3,990 females) patients with suspected thyroid diseases referred for thyroid ultrasound. Details of each patient with thyroid hemiagenesis, historical complaints, and physical examination findings were obtained from the records completed at the time of the initial evaluation of the patient.

We also retrospectively analyzed the results of two community-based large sonographical surveys:

(1) School-age children ($n = 4{,}772$; 2,425 males and 2,347 females), aged 11–14 years, all attending primary school, living in known endemic areas of Turkey, were evaluated by thyroid ultrasound examination during a survey for iodine-deficiency goiter. The survey was carried out between 1997 and 1999.
(2) Adult subjects ($n = 2{,}935$; 1,496 males and 1,439 females), aged 18–65 years, living in Ankara, were evaluated by thyroid ultrasound examination during a survey for thyroid disorders. The survey was carried out in 2002.

Turkey was moderately iodine-deficient area before mandatory iodization (average urinary iodine concentration 25.5 μg/l). Further, in 1999, an obligatory model of iodine prophylaxis was initiated with iodization of household salt. The area is mildly iodine deficient (average urinary iodine concentration 92 μg/l) at the moment.

In patients with thyroid diseases, thyroid ultrasonography was performed by single physician (A.G) using a 10-MHz linear probe (Logiq 5 Pro, GE Medical Systems, WI, USA). In community screening, a 7.5-MHz linear probe (Logiq 200, GE Medical Systems, WI, USA) was used. Volumes of thyroid glands were calculated according to the ellipsoid formula: volume (ml) = depth (cm) × width (cm) × length (cm) × $\pi/6$. If a subject has total absence or severe hypoplasia of one thyroid lobe (<1/10th of the normal thyroid lobe volume), he/she was defined as having thyroid hemiagenesis. Presence or absence of isthmus and any ultrasound abnormality observed during the initial

examination was also reported. Thyroid function was evaluated by measuring thyroid hormones (free T4 and free T3) and thyroid antibodies (antithyroid peroxidase and antithyroglobulin) were measured by commercially available methods.

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