

Research paper

Chronic autoimmune thyroid disease in children and adolescents in the years 1999-2004 in Lower Silesia, Poland

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ABSTRACT

The aim of the study was to analyze data related to chronic autoimmune thyroid disease at diagnosis and at follow-up of children and adolescents in Lower Silesia in the years 1999-2004. Age, gender, incidence of thyroid disease in the family, clinical presentation, hormonal findings, levels of thyroid antibodies, results of ultrasonography, and fine needle aspiration biopsy (FNAB) were recorded. 100 children, 10 boys and 90 girls, were included in the analysis. The mean age at diagnosis was 12.3 ± 2.3 years and at last examination 14.9 ± 1.9 years. At diagnosis, increased levels of TSH without overt hypothyroidism was observed in 26 children. In 11 children hyperthyroidism was detected whereas 63 children were euthyroid. An increased level of thyroid peroxidase antibodies was observed in 65% of the children. Ultrasonography was characteristic for Hashimoto's thyroiditis in all patients. Fine needle biopsy was performed when there were diagnostic difficulties (35% children). Thus, in all the children the diagnosis of Hashimoto's thyroiditis was ascertained either by high antibody titer or FNAB. Associated diseases were observed in 33% of the children. Thyroid disease in the family was present in 25% of the children. There was a gradual decline in the number of new cases presented from 1999 to 2004. The reason for this decline remains speculative.

Key words: Hashimoto's thyroiditis, Autoimmune thyroid disease, Iodine prophylaxis

INTRODUCTION

In the past, the most frequent cause of thyroid

disease in children and adolescents was iodine deficiency. To date, in developed countries, thyroid autoimmunity, either lymphocytic thyroiditis or Grave's disease, constitute the most frequently encountered thyroid pathology. Chronic thyroiditis, also called chronic lymphocytic or autoimmune thyroiditis, was first reported by Hashimoto in 1912¹ and it may be clinically manifested as enlargement or atrophy of the thyroid gland.² The term Hashimoto's

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thyroiditis is still used for the goitrous form of the disease. In about 90% of patients with Hashimoto's thyroiditis, high levels of antibodies against thyroid peroxidase (anti-TPO) and thyroglobuline (ATg) are detected. Antibodies blocking or stimulating the TSH receptor have been found in about 10% of the cases (usually in the atrophic form of the disease). Factors which predispose to the development of chronic lymphocytic thyroiditis are genetic and environmental³. Among the environmental factors are high iodine consumption, viral infections and drugs. Many authors have observed an increase in the incidence of autoimmune diseases of the thyroid after introduction of iodine prophylaxis in endemic regions.⁴⁻⁷ Most likely, environmental factors trigger an autoimmune process in subjects with a genetic predisposition.⁸⁻¹⁰ In Poland, obligatory iodine prophylaxis was introduced in 1997. In subjects over 18 years a relative increase of the cytologic diagnosis of chronic lymphocytic thyroiditis has subsequently been observed.¹¹ Contrary to these data, Zimmerman et al¹² did not detect induction of thyroid autoimmunity in iodine deficient children in Northern Morocco 1 year after the introduction of iodized salt. It is well known that Hashimoto's thyroiditis is associated not only with other autoimmune diseases, like diabetes type 1, Addison's disease, myasthenia gravis, vitiligo, celiac disease, but also with genetic disorders like trisomy 21 or Turner's syndrome.

The aim of our study was to retrospectively analyze the mode of presentation and the follow-up of autoimmune thyroiditis in children and adolescents diagnosed in Lower Silesia in the years 1999-2004.

SUBJECTS AND METHODS

The study group included 100 children, 10 boys and 90 girls, who presented at the endocrine out patient department of the endocrine clinic of the University of Medicine Hospital in the years 1999-2004, and originated from Lower Silesia. The age at presentation was 12.3 ± 2.3 years and at last examination 14.9 ± 1.9 years. The following data were recorded: physical examination data, serum values of TSH, FT4, FT3, antithyroid antibodies (anti-TPO), as well as results of thyroid ultrasonography and fine needle aspiration biopsy (FNAB). TSH, FT3, FT4

and anti-TPO were determined by immunofluorescence. Normal values were: TSH; 0.4 to $4 \mu\text{U/ml}$, FT4; 0.8-1.9 ng/dl, FT3; 1.5-4.1 pg/ml; anti-TPO 0-35 IU/ml. Ultrasonography was performed by using a high frequency 715MH3 linear RA transducer.

RESULTS

The results are presented as means and standard deviation (SD). All patients had normal growth, (Table 1) weight and puberty. Thyroid disease in the family was ascertained in 25% of the children. Mean age of the children at diagnosis of autoimmune thyroiditis was 12.3 ± 2.3 years. At diagnosis, 26 children (26%) had increased levels of TSH, without overt clinical hypothyroidism, 11% had symptoms of mild hyperthyroidism whereas 63% were euthyroid. In general, the patients were presented with the following signs or symptoms: thyroid enlargement, weakness, tachycardia, decrease or increase of body weight or dry skin. The mean level of TSH in the whole group at diagnosis was $15.18 \pm 41.1 \text{ uIU/ml}$, the mean level of FT4 was $1.78 \text{ ng/dl} \pm 2.84$, the mean level of FT3 was $4.14 \text{ pg/ml} \pm 2.5$. Positive anti-TPO were found in 65% of the cases. The remaining did not have high titer and the diagnosis was made by FNAB. The mean level of antibodies (anti-TPO) was $622.15 \text{ IU/ml} \pm 579.9$. At last examination (aged 14.9 ± 1.9) mean level of TSH was $1.88 \text{ UI/ml} \pm 1.26$, FT4 $1.66 \text{ ng/dl} \pm 1.58$, FT3 $3.63 \text{ pg/ml} \pm 1.43$, anti-TPO $517.41 \text{ IU/ml} \pm 488$. The hormonal data and those of antithyroid antibodies are shown in Tables 2 and 3, separately for the 3 groups (euthyroid, hypothyroid and hyperthyroid). A characteristic ultrasonographic picture was observed in all patients: hypoechogenicity, with increased blood flow. The echo structure in general was heterogeneous. A fine needle biopsy was performed in 35% of children and in all of them the diagnosis of Hash-

Table 1. Certain anthropometric data of patients with chronic lymphocytic thyroiditis

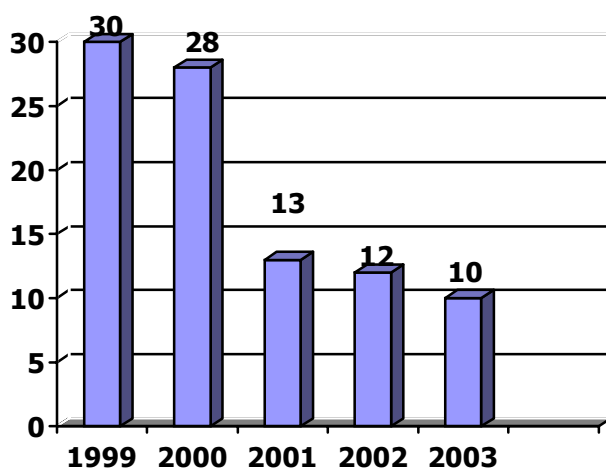
	age (years)	height (cm)	BMI (kg/m ²)
at diagnosis			
n = 100	12.3 ± 2.3	165 ± 9.6	20.5 ± 2.3
at last examination			
n = 100	14.9 ± 1.9	167 ± 9.5	20.3 ± 1.7

Table 2. Hormonal levels and anti-TPO titer at diagnosis (mean $\pm$ SD)

Clinical condition	FT3 pg/ml N 1,5-4,1	FT4 ng/dl N 0,8-1,9	TSH mIU/ml N 0,4-4,0	ATPO uIU/ml N 0-35
Euthyroid n:63	4,1 $\pm$ 1,1	1,7 $\pm$ 0,9	2,41 $\pm$ 1	135 $\pm$ 53
Hyperthyroid n:11	4,9 $\pm$ 1,5	2,9 $\pm$ 1,9	0,25 $\pm$ 0,6	667 $\pm$ 302
Hypothyroid n:26	3,2 $\pm$ 2	0,9 $\pm$ 0,5	35,3 $\pm$ 14,8	834 $\pm$ 352

Table 3. Anti-TPO titer and thyroid hormones (mean $\pm$ SD) at follow-up (aged 14.9 $\pm$ 1.9 years)

Clinical condition at presentation	TSH (μ IU/ml)	FT4 (ng/dl)	FT3 (pg/nl)	anti-TPO (IU/ml)
Hypothyroid	2,7 $\pm$ 1,5	1,2 $\pm$ 0,5	3,3 $\pm$ 2,3	679 $\pm$ 340
Hyperthyroid	1,9 $\pm$ 0,9	1,8 $\pm$ 0,3	3,1 $\pm$ 2,1	452 $\pm$ 353
Euthyroid	2,5 $\pm$ 1,7	1,2 $\pm$ 0,5	2,7 $\pm$ 1,7	120 $\pm$ 34

**Figure.** The number of new cases of chronic autoimmune thyroiditis in the years 1999-2003.

imoto's was made. Malignancy was not detected in any of the cases. Additional diseases were observed in 33 children (33%); these were type 1 diabetes mellitus (14%), PCOS (5%), Turner syndrome (3%) and Down syndrome (3%). Thyroxine therapy was administered in the 26 patients with subclinical hypothyroidism.

DISCUSSION

Environmental and genetic factors are both involved in the etiology of Hashimoto's thyroiditis (HT).^{10,13} In populations in whom iodine prophylaxis was introduced, an increase of autoimmune diseases of the thyroid was noted.³ The obligatory io-

dine prophylaxis consisting in iodination of kitchen salt (30 $\pm$ 10 mg KI/kg salt) was introduced in Poland in 1997 and in the year 2002, Poland was accepted by WHO in the group of countries with sufficient iodine supply. The frequency of goiter has decreased in Poland to below 5% of the population.¹⁴ The studies performed in certain countries, currently with a good iodine supply, have shown an increase of autoimmune thyroiditis in children. In Greece in a study reported in 1999 it was shown that the predominant form of nontoxic goiter was autoimmune thyroiditis. In Poland, Bobeff and al found that in children from the Lodz macroregion the frequency of chronic thyroiditis increased from 3.7% in the years 1992-1996 to 11.2% in the years 1997-2001.¹⁵ Zimmerman and al have reported a transient increase in the prevalence of detectable antithyroid antibodies after introduction of iodized salt¹². In our own study we observed a decrease in the frequency of new cases of chronic lymphocytic thyroiditis from 1999 to May 2004 from 30% in the year 1999 to about 10% in 2003. This could be interpreted as a flare-up of HT shortly after the introduction of obligatory iodine prophylaxis and a tapering off subsequently. Alternatively, the decrease may represent a diversion of the patients to other centers. The majority of children were euthyroid (63%). Subclinical hypothyroidism was ascertained in 26% of the children, and a hyperthyroid state in 11%. It is of interest that the lowest titer of anti-TPO was detected in the euthyroid group and the highest in the hypothyroid. Hashimoto thyroiditis, as expected, was much

more frequent in girls, in agreement with other reports in the literature.^{16,17} In children with high TSH, the introduction of thyroxin therapy led to the normalization of TSH, without changes in anti-TPO titer over the 2 years of follow-up. Coexisting diseases were diagnosed in 33 children (33%), most often diabetes type 1, which is in agreement with the reports in the literature^{13,18-22}. Thyroid diseases in the family were ascertained in 25% of the children. Segni and et¹³ found a positive family history in 36% and Marinovic²⁰ in 23% of examined children.

In summary, in 65% of children with sonographic evidence of thyroiditis, a high titer of thyroperoxidase antibodies was detected. In the remaining 35% with low antibody titer, the diagnosis was ascertained by FNAB. The majority of the children (63%) were euthyroid at presentation (clinically and hormonally), and 11% were mildly hyperthyroid. There was a decline in the number of new cases of HT from 1999 to 2004, which could be incidental. Alternatively, it could be the result of a transient rise in the years 1999-2000 following obligatory salt iodination in Poland in 1997.

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