

Clinical features of spontaneous hypothyroidism in one physician's practice in Jamaica

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Objective: To describe the clinical characteristics of patients with spontaneous hypothyroidism, the frequency of chronic autoimmune thyroiditis, and the thyroid autoantibody most often associated with this condition in a referral population in Jamaica.

Methods: A retrospective study of all cases referred to the author's endocrinology practice from 1995 to 2005 with a diagnosis of spontaneous hypothyroidism was undertaken. The clinical history, examination findings, biochemical test results, thyroid autoimmune antibodies, and imaging data were reviewed.

Results: Spontaneous primary hypothyroidism was correctly diagnosed in 53 subjects. Fifty of the patients were females and three were males. Mean age was 43.3 years (range 12–82 years); 24.4% of the patients had a family member with thyroid disease; 27.1% presented because of a goiter; and 54.2% because of symptoms suggestive of hypothyroidism. The thyroid was palpable in 56.3% and thyroid ultrasound was consistent with Hashimoto's thyroiditis on 64% of occasions. Only 8% of the patients had the atrophic variant of hypothyroidism. Antithyroid peroxidase and antithyroglobulin antibody were positive in 75.8% and 37.5% of patients, respectively. Chronic autoimmune thyroiditis was confirmed in 78.8% of cases.

Conclusion: In these cases in Jamaica, spontaneous hypothyroidism was predominantly a female disorder. Chronic autoimmune thyroiditis was the commonest cause, and antithyroid peroxidase antibody was the thyroid antibody most likely to be positive in this population.

Keywords: spontaneous hypothyroidism, Jamaican, thyroid autoantibodies, L-thyroxine, autoimmune thyroiditis, Hashimoto's thyroiditis

Introduction

Hypothyroidism is an insidious condition associated with significant morbidity. Its symptoms and signs may be nonspecific and subtle which may result in the diagnosis being missed. It may present as subclinical hypothyroidism, as overt hypothyroidism, or as myxoedema. All three presentations may result in cardiovascular abnormalities, including impairment of endothelial function, normal or depressed systolic function, left ventricular diastolic dysfunction at rest, and/or systolic and diastolic dysfunction on effort, and this may lead to poor physical exercise. There may also be increased diastolic blood pressure due to increased systemic vascular resistance and increased central arterial stiffness. In addition, there may be an abnormal lipid profile. Treatment with levo-thyroxine (L-thyroxine) in both subclinical and overt hypothyroidism results in regression of cardiovascular and lipid abnormalities.¹ Hypothyroidism is thus a disease that should not be ignored.

The prevalence of spontaneous hypothyroidism in iodine-replete communities is in the range of 1%–2%.² Although the prevalence of unsuspected overt hypothyroidism

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is low, community screening for hypothyroidism in healthy adults has revealed evidence of significant thyroid disease. In the Whickham survey, 8% of women and 3% of men were found to have subclinical disease.³ In the Colorado screening survey, where 9% of the population had an elevated thyrotropin (TSH), 74% had TSH values between 5.1 and 10 mU/L.⁴

In iodine-sufficient areas, the causes of hypothyroidism (other than destructive treatment for hyperthyroidism) are either an autoimmune disease (atrophic autoimmune thyroiditis) or goiterous autoimmune thyroiditis (Hashimoto's disease [HD]).

Hashimoto described the histology of the thyroid gland in individuals with goiter and hypothyroidism in 1912.⁵ The association of thyroglobulin antibodies (anti-TG) with HD or chronic lymphocytic thyroiditis was documented in 1956. Since then, other antibodies, such as the microsomal fraction of the thyroid that are actually directed against thyroid peroxidase (anti-TPO), to thyroxine (T4), triiodothyronine (T3) and the TSH receptor, have been described in this disorder. The thyroiditis often progresses to permanent hypothyroidism. In patients with clinically evident disease, circulating levels of anti-TPO are seen in 90% or more of patients.⁶ Anti-TG is less frequently positive, being present in 20%–50% of patients. HD is one disorder in the spectrum of autoimmune thyroiditis that includes Grave's disease, the etiology of which is a complex interaction between genetic, environmental, and endogenous factors. For instance, the major histocompatibility complex antigens HLA-B8 and HLA-DR5 are closely associated with this disease. However, these antigens are not seen in certain races.⁷

Jamaica has a predominantly black population of African ancestry. The country has been iodinating salt for some time now.⁸ There are no studies that have evaluated the commonest causes of spontaneous hypothyroidism in Jamaicans or defined the clinical characteristics of patients with this disorder. It is expected that HD would be the commonest cause of primary hypothyroidism in the Jamaican population. It is unknown which thyroid autoantibody is best for defining the disorder in this community.

We had previously documented the limited usefulness of anti-TPO and anti-TG in the diagnosis of Grave's disease in Jamaicans.⁹ The purpose of this study was to define the clinical characteristics of Jamaican patients with spontaneous hypothyroidism, to evaluate the frequency of chronic autoimmune thyroiditis in these patients, and to determine which antibody was most associated with this disorder in Jamaicans.

Patients and methods

This was a retrospective study of patients who were referred in 1995–2005 to the author's single-physician practice that offers endocrine consultations. Inclusion criteria included a referral diagnosis of spontaneous hypothyroidism and not secondary to thyroid or neck surgery, radioiodine therapy, or radiation to head or neck. Primary hypothyroidism was diagnosed if there was elevated TSH with normal or decreased free thyroxine (FT4) or free thyroxine index (FT4I), or if there was only elevated TSH. Overt hypothyroidism was defined as a decreased FT4I or FT4 with elevated TSH, and subclinical hypothyroidism as normal FT4I or FT4 with elevated TSH. Spontaneous hypothyroidism was defined as hypothyroidism occurring in the absence of surgery to the neck or thyroid gland, absence of radiation to the neck or the gland, and absence of radioiodine therapy or treatment with amiodarone. Data obtained from patient charts included age, sex, family history of thyroid disease, initial clinical presentation, clinical features of the thyroid gland itself, functional thyroid status defined by thyroid function tests [TFTs], thyroid ultrasonographic features, and thyroid autoantibodies. The thyroid autoantibodies evaluated were anti-TG and anti-TPO. TFTs and titers of the thyroid autoantibodies were expressed as percentages of the norms because the values were obtained from different laboratories with different normal values and ranges. The dosage of L-thyroxine needed to attain euthyroidism was also evaluated. Euthyroidism was defined as normal FT4 or FT4I and normal TSH.

Results

During the study period, 1278 patients were referred to this practice. Eighty-eight patients had been referred with a diagnosis of presumed spontaneous hypothyroidism. However, 35 were excluded from the study for a range of reasons, including two who had thyrotoxicosis, four who had received radioiodine therapy, five who had had thyroid surgery, 19 who had secondary rather than primary hypothyroidism, two with a history of hypothyroidism not confirmed by TFTs, and three who had normal TFTs after being taken off L-thyroxine. Spontaneous primary hypothyroidism was seen in 4.15% of the patients in this referral practice (Table 1).

Our study population consisted of 53 patients, including 50 females and three males of mean age 43.3 (range 12–82) years. Family history was known in 45 of these patients, and was positive for goiter, hypothyroidism, or hyperthyroidism in 24.4% of cases; 72.7% of the affected family members were first-degree relatives. The reason for presenting to a family physician for evaluation was known in 48 patients and was because of a

Table 1 Thyroid status and exclusion criteria

	(n)
Total number referred	1278
Total number referred with diagnosis of primary hypothyroidism	88
Total number with actual diagnoses:	
– thyrotoxicosis	2
– radioiodine therapy	4
– thyroid surgery	5
– secondary hypothyroidism	19
– euthyroidism	3
– not confirmed	3

Notes: Prevalence of spontaneous primary hypothyroidism in this endocrine practice was 4.15%.

goiter in 27.1% (n = 13), and because of experiencing symptoms suggestive of hypothyroidism in 54.2% (n = 26). Abnormal TFTs were an incidental finding in 16.7% of patients.

Results of thyroid palpation were known in 48 subjects. The thyroid was palpable in 56.3% and, of 25 patients who had undergone thyroid ultrasonography, features were consistent with HD in 64% of cases. Nodularity was seen in 20%, and a smaller than normal gland in 8% of patients. Chronic atrophic thyroiditis was therefore seen in 8% of cases. Thyroid ultrasonography was normal in 8% of patients.

The types of hypothyroidism, and overt versus subclinical hypothyroidism were known in 48 patients. Overt hypothyroidism was noted in 54.8% of cases. The median FT4I or FT4 was 53.3% (range 8.62%–95.73%) of normal.

Subclinical hypothyroidism was seen in 16 (38.1%) of the patients. There were three who had only an elevated TSH available for analysis and were not included in the category of subclinical hypothyroidism. The prevalence of subclinical hypothyroidism in this practice was 1.25%. Of the total with elevated TSH, the median value was elevated to 615% of the norm (range 109.7%–28236%).

Anti-TPO was performed in 33 of the patients and anti-TG in 32. The former was positive on 75.8% of occasions (n = 25) whereas the latter was positive on only 37.5% of occasions (n = 12). Anti-TG was negative on 41.7% of occasions in those with a positive anti-TPO. Of those with a positive anti-TG, anti-TPO was negative in only one case (8.3%). The anti-TPO titer was elevated by more than 1000% of the norm in 80% of patients (n = 22) and the anti-TG titer in six of 12 subjects (50%).

The average dose of L-thyroxine needed to attain euthyroidism in this population was known in 50.9% of the patients (n = 27) and in 50% (n = 8) of those with subclinical hypothyroidism. The L-thyroxine dose needed

was 1.47 (range 0.88–2.20) µg/kg in the former group and 0.99 µg/kg (range 0.88–1.41) in the latter group (Table 2).

Discussion

The clinical characteristics of Jamaican patients with spontaneous hypothyroidism referred to an endocrinology practice are described. The patients were more likely to be female than male. Other studies have noted the preponderance of females with this disorder. The disease was predominantly seen in middle-aged patients in our study, as reported by others.³ The family history of thyroid disease seen in our patients is also consistent with previous reports.¹⁰ Tamai et al documented that within a six-month to five-year period, 7.2% of previously euthyroid relatives of patients with Grave's disease developed hyperthyroidism or hypothyroidism. Tomer et al identified that there are multiple genes that predispose

Table 2 Clinical characteristics of identified patients

Gender (Female:Male)	50:3
Median age (years)	43.3
(range in years)	(12–82)
Family history of thyroid disease (n = 11)	24.4%
Causes for presentation (n = 48)	70.0%
Goitre (n = 13)	27.1%
Hypothyroidism (n = 26)	54.2%
Incidental (n = 8)	16.7%
Other (n = 1)	2.1%
Results of thyroid examination (n = 48)	
Palpable (n = 27)	56.3%
Not palpable (n = 21)	43.7%
Results of thyroid ultrasound (n = 25)	
Hashimoto's thyroiditis (n = 16)	64%
Nodular (n = 5)	20%
Smaller than normal (n = 2)	8.0%
Normal (n = 2)	8.0%
Types of hypothyroidism (n = 42)	
Overt hypothyroidism (n = 23)	54.8%
Subclinical hypothyroidism (n = 16)	38.1%
Unknown (n = 3)	7.1%
TSH value	
Median value of the TSH (% of the norm)	615
Positive thyroid autoantibodies	
Anti-TPO (n = 33)	75.8%
Anti-TG (n = 32)	37.5%
Positive anti-TPO and negative anti-TG	41.7%
Positive anti-TG and negative anti-TPO	8.3%
Average L-thyroxine dose	
All patients (n = 27)	1.47 µg/kg
Range	0.88–2.20 µg/kg
Subclinical hypothyroidism (n = 8)	0.99 µg/kg
Range	0.88–1.41 µg/kg

Abbreviations: TSH, thyroid-stimulating hormone; anti-TPO, antibody against thyroperoxidase; anti-TG, antibody against thyroglobulin.

to Grave's disease and hypothyroidism, and that although some are unique to each disease, many are common to both conditions.¹¹ However, the Whickham Survey follow-up study did not document an association between family history of thyroid disease and risk of developing hypothyroidism 20 years later.¹² This suggests that factors other than genetics are important. In fact, the concordance rate for autoimmune hypothyroidism in monozygotic twins is less than 1.¹³ Environmental factors have also been implicated. In this study we did not evaluate any of these environmental factors, such as high iodine intake, selenium deficiency, pollutants such as tobacco smoke, or infectious diseases such as chronic hepatitis C.¹⁴

In our study, the diagnosis was suggested by the presence of goiter on only a minority of occasions. The usual presentation is that of goiter being discovered as an incidental finding during clinical examination.¹⁵ Fifty percent of our patients presented with symptoms of hypothyroidism, although this is an unusual finding. In the series by Doniach et al symptoms of hypothyroidism were seen at presentation in only 20% of patients.¹⁶ The thyroid gland usually has a diffuse, very firm, or even hard goiter. Nodules are seen infrequently, unlike the nodular thyroid gland documented in 20% of our patients. However, in a series by Erdogan et al nodularity on ultrasonography was a common finding.¹⁷ The presence of a single nodule should be evaluated for thyroid carcinoma. None of our patients had this. The possibility of thyroid lymphoma, especially in the elderly, should always be borne in mind when an elderly patient has hard, firm nodules, if there has been enlargement of the thyroid gland over time, or when there are symptoms of compression.

As expected, the atrophic variant of HD was detected in only a minority of cases.¹⁷ The reduced echogenicity seen in 64% of our patients is lower than the 77.9% seen in the series by Pederson et al.¹⁸ In that study, they compared the ultrasound findings from multiple ultrasonographers with cytology, anti-TPO titers and/or TSH levels. Of the 452 cases of diffuse reduction in thyroid echogenicity, 352 had Hashimoto's thyroiditis and 47 had Grave's disease, giving reduced echogenicity a positive predictive value for autoimmune thyroiditis of 85%–91% at a 95% confidence interval. In another study, Vitti et al found an abnormal thyroid ultrasound pattern in 96% of cases of atrophic variant of hypothyroidism, with these subjects having both an abnormal thyroid echographic pattern and a diffuse low thyroid volume.¹⁹ Thirty-eight percent of the patients with hypothyroidism had subclinical hypothyroidism and 54.8% had overt hypothyroidism. In the Colorado study, there were more patients with subclinical

than overt hypothyroidism. The difference in our study may be the result of the referral practices of general practitioners, economics, and the health-seeking behavior of patients, rather than reflective of the general population. Variation in prevalence may also reflect the cut-off value for TSH, as well as the age, ethnicity, and gender of the population studied.¹⁰ For instance, blacks in the US who are free of thyroid diseases are noted to have lower TSH values.²⁰

The prevalence of thyroid autoantibodies in the general Jamaican population is 1.5%. It is similar to that seen in other populations.²¹ Thyroid peroxidase antigen, once known as thyroid microsomal antigen, is present on the apical surface of thyroid follicular cells. This is the antigen that appears to be most closely involved in cell-mediated cytotoxicity.²² It is suggested that the presence of this antibody is most closely related to the development of hypothyroidism. In fact, in the NHANES III study, anti-TPO (but not anti-TG) was a predictor of hypothyroidism.²³ The prevalence of anti-TPO in our patients with primary hypothyroidism was 75.8%. This is lower than that reported in patients with hypothyroidism discovered in the study of the general population in the US. Whilst the anti-TPO titer declines with increasing duration of the disease, the difference most likely reflects differences in genetic and environmental influences.^{7,20} Anti-TG was less frequently seen than anti-TPO. This was also the experience in the study by Baker et al who documented that 15 of 65 patients had this antibody.²⁴ It suggests that anti-TPO is sufficient alone as a diagnostic test for chronic autoimmune thyroiditis in our population. However, in one of our patients, anti-TPO was negative and anti-TG was positive. So, while anti-TG may not be a good predictor of hypothyroidism, it remains an important marker of this chronic autoimmune disease.

The average dose of L-thyroxine needed to make patients euthyroid in the present study was higher than the 1.06 ± 0.36 $\mu\text{g/kg}$ per day noted by Checchi et al in an Italian population and by Gordon in an American population.^{25,26} While this higher dose may be related to low patient compliance, drug interference, and malabsorption, Checchi documented that increased dosages were seen where parietal cell antibodies were present. This association were seen where parietal cell antibodies were present even in the absence of gastritis. This observation will require further exploration in the Jamaican population, in which 1.4% of individuals have antibodies against the parietal cell.²¹

Conclusion

The patients with spontaneous hypothyroidism were typically female and middle-aged. There were more cases

of subclinical than overt hypothyroidism, and there were differences in their mode of presentation and in the degree of nodularity of the gland. Thyroid antibody positivity in this population was 78.8%. The most commonly seen antibody was anti-TPO. It is suggested that a population-wide study be performed to evaluate further the clinical features of this disorder in the general population.

Disclosure

The author reports no conflicts of interest in this work.

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