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Case Report

Autoimmune thyroiditis in adolescents: Two different presentations

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ABSTRACT

Autoimmune thyroiditis is one of the most common causes of acquired hypothyroidism in children and adolescents. Both genetic susceptibility and environmental factors play a role in etiopathogenesis. We report two cases of autoimmune thyroiditis here with varied presentation. Both of them had different clinical features of hypothyroidism at presentation. On investigation, both of them had elevated thyroid-stimulating hormone (TSH), low T4 and elevated anti-Thyroid peroxidase (TPO) antibodies. Case 1 also had elevated anti-TG antibody level. Based on these findings, diagnosis of autoimmune thyroiditis was made and started on levothyroxine tablet, for which both of them showed both clinical and biochemical improvements.

Keywords: Autoimmune thyroiditis, TSH, T4, Anti-TPO and anti-TG antibody, Levothyroxine

INTRODUCTION

Autoimmune thyroiditis, also known as chronic lymphocytic thyroiditis or Hashimoto's thyroiditis, is the most common aetiology of thyroid disease in children and adolescents.[1-3] Both goitrous (Hashimoto's thyroiditis [HT]) and a non-goitrous (atrophic thyroiditis/primary myxoedema) variant of autoimmune thyroiditis have been distinguished.[2] The prevalence of autoimmune thyroiditis in childhood is an estimated 1–2% with female predominance with male-to-female ratio of 4:1–8:1 depending on the geographical region.[1,3-5] The aetiology of autoimmune thyroiditis is complex and multifactorial. The development of autoimmune thyroiditis depends on an immune defect in an individual with genetic susceptibility (80%) in conjunction with environmental factors (20%).[2,3] Approximately 50% of cases have a family history of autoimmune thyroid disease.[1] Several syndromes are associated with an increased risk for developing autoimmune hypothyroidism, including Down syndrome and Turner syndrome.[1,6] Thyroiditis is defined as evidence of 'intrathyroidal lymphocytic infiltration' with or without follicular damage.[5] The natural history is not completely known in paediatric population, it is variable, with remission, recurrence as well as the evolution to permanent hypothyroidism.[3,4] Euthyroidism is the most common initial pattern (about 52% of patients), followed by overt hypothyroidism (22.2%), subclinical hypothyroidism (19.2%) and hyperthyroidism (6.5%).[6]

CASE REPORTS

Case 1

A 14-year-old female, 1st born child to non-consanguineously married couple, was admitted with a history suggestive of urinary tract infection (UTI) later on probing mother gave

history of recent gain of weight since the past 6 months associated with poor scholastic performance and not interested in other household works. There was a history of not attaining menarche. However, she did not have a family history of delayed puberty or thyroid disorders. She had uneventful antenatal, birth history and normal psychomotor development. She was going to 9th standard with average scholastic performance previously. Now, her IQ is 78. They were taking iodised salt and there was no excessive use of cabbage or cauliflower at home. Provisional diagnosis of acquired hypothyroidism with superadded UTI was made.

On examination, her HR – 64/min, BP – 112/70 mmHg and other vitals were within normal limits.

Her weight was 42 kg (25th-50th percentile) height was 141.5 cm (3rd-10th centile) with BMI of 21.13 (between 50th and overweight) which accounts to CA=WA>HA [Table 1].

On physical examination, she had pallor, dull looking face and dry skin. Sensory motor rythm (SMR) stage was 2 which implies delayed puberty. Systemic examination was normal. There was no enlargement of the thyroid gland.

Investigation was done accordingly which showed T4-0.64 and TSH-160 suggestive hypothyroidism [Table 2]. There was deranged lipid profile, her blood sugar and BP were within normal limits [Table 3]. Ultrasonography (USG) neck was normal. Because of late age of onset, autoimmune thyroiditis was suspected and workup done which showed elevated both anti-TPO (>1000 IU/ml) and TG antibodies (>500 IU/ml) [Table 4]. Radionuclide thyroid scan and uptake study were normal. USG pelvis showed a normal size uterus (6 × 1.5 × 2.6 cm) and ovary. Diagnosis of autoimmune thyroiditis was made. The child was started on levothyroxine 2 mcg/kg/day. Urine culture showed growth of *Escherichia coli* accordingly treated with IV antibiotics. Lifestyle modifications, exercise and diet advice were given. The child showed improvement. Now, she is doing well and on follow-up.

Table 1: Anthropometric parameters of Case 1.

Parameters	Observed	Inference
Weight	42 kg	25th–50th percentile
Height	141.5 cm	3rd–10th percentile
BMI	21.13	Between 50th and overweight
Waist circumference	72 cm	Between 50th and 75th percentile
Equation	CA=WA>HA	Endocrine cause

Table 2: Thyroid function test result of Cases 1 and 2.

TFT	Case 1	Case 2	Ref. range
T3	4.8	11.6	81–178 ng/dl
T4	0.64	1.93	4.5–12.5 mcg/dl
TSH	160.0	100.0	0.4–4.2 micro IU/mL

Case 2

A 10-year, 2-month-old male, 3rd born child to non-consanguineous married couple, admitted with the complaints of not gaining height as compared to his siblings and peer group noted for 2 years. Since the past 3 months, the child was lethargic with decreased activity, had lost interest in reading and writing associated with loss of appetite but he was gaining weight. There was also a history of generalised swelling of body, constipation and cold intolerance since the past 2 months. He did not have a family history of similar complaints. The child had normal psychomotor development before this, was going to the 5th standard with average scholastic performance. Now, his IQ is 75. They were taking iodised salt and there was no excessive use of cabbage or cauliflower at home. Based on the above history, provisional diagnosis of pathological short stature secondary to hypothyroidism was made.

On examination, HR – 70/min, BP – 104/68 mmHg and other vitals were within normal limits. His weight was 30 kg (25th-50th percentile) and height was 120cm (<3rd percentile) with body mass index (BMI) of 20.83 (obese) which accounts to CA>WA>HA. Child had Midparental Height (MPH) OF 157.75+8 cm, projected height of 153 cm and Waist to hip ratio of 0.97 (obese). Waist-to-hip ratio was 0.97 (obese) [Table 5].

He had pallor, coarse face with depressed nasal bridge, dry and cold skin and non-pitting oedema (myxoedema). SMR stage was 2 which was appropriate for age. Systemic examination was normal. There was no enlargement of the gland.

Investigation was done accordingly which showed T4-1.93 and TSH-100 suggestive hypothyroidism [Table 2]. There was

Table 3: Lipid profile, haemoglobin and blood sugar levels of Cases 1 and 2.

Lipid profile	Case 1	Case 2	Ref. range
Total cholesterol	319.5	300	<200 mg/dl
Triglyceride	397.9	346	<150 mg/dl
HDL	16.9	15.8	>60 mg/dl
VLDL	79.5	95.9	<30 mg/dl
LDL	223.02	218.5	<130 mg/dl
Haemoglobin	9.9 g % (>12)	10 g % (>11.5)	
Fasting blood glucose	86 mg/dl	98 mg/dl	

Table 4: Thyroid autoantibody levels of Cases 1 and 2.

Antibody level	Case 1	Case 2	Ref. range
Anti-TPO antibody	>1000 IU/ml	500 IU/ml	<50.00 IU/ml
Anti-TG antibody	>500 IU/ml	100 IU/ml	<60.00 IU/ml

Table 5: Anthropometric parameters of Case 2.

	Observed	Inference
Weight	30 kg	25th–50th percentile
Height	120 cm	Less than 3rd percentile
BMI	20.83	Obese
Equation	CA>WA>HA	Endocrine cause
Waist circumference	62 cm	50th–75th percentile
Waist-to-hip ratio	0.97	Obese

deranged lipid profile, his blood sugar and BP were within normal limits [Table 3]. USG neck was normal. Because of late age of onset, autoimmune thyroiditis was suspected and workup done which showed elevated anti-TPO (>500 IU/ml), however, anti-TG antibodies were within normal limits [Table 4]. Diagnosis of autoimmune thyroiditis was made. The child was started on levothyroxine 2 mcg/kg/day. Lifestyle modifications, exercise and diet advice were given. The child showed improvement. Now, he is doing well and on follow-up.

DISCUSSION

Autoimmune thyroid diseases constitute both HT and Graves' disease. Both are characterised by infiltration of the thyroid by T and B lymphocytes that react against thyroid antigens and thereby producing thyroid autoantibodies. The autoantibodies are directed against thyroid peroxidase (anti-TPO), thyroglobulin (anti-TG) and thyroid-stimulating hormone receptors (TRABs).[4] Two types of autoimmune thyroiditis are causes of persistent hypothyroidism: Hashimoto's disease (goitrous form) and atrophic thyroiditis (non-goitrous form).[5]

Several studies have shown that autoimmune thyroid disease has definite genetic propensity for thyroid autoimmunity and they run in families.[7] Direct cytotoxicity by CD8 T cells is believed to be the main mechanism of hypothyroidism *in vivo*.[5] The autoimmune injury of the gland is responsible for clinical and biochemical alterations. The natural history of the disease is as follows: (1) Toxic, transient and self-limited thyroiditis; (2) euthyroid goitre and (3) hypothyroidism with/without goitre.[4] There is no fixed duration for each stage. Conversion of Hashimoto's thyroiditis into Grave's disease has been observed in at least 3–4% of children and adolescents.[8,9]

The high incidence of autoimmune thyroid diseases in females suggests the participation of X chromosome genes or even an influence by the absence of chromosome Y.[3,4,10] There is also increased risk for other autoimmune diseases, most commonly diabetes, alopecia, vitiligo and celiac disease.[11-13] In the present case, one was female and the other one was male, the patient did not meet criteria for other associated autoimmune comorbidities.

The most common symptoms of hypothyroidism include easy fatiguability, constipation, cold intolerance and menstrual irregularities. Oligomenorrhoea and/or menometrorrhagia are frequent, due to a poor conversion of oestrogen precursors.[7,14] Children may present with pubertal delay or precocious puberty.[7,13] Other features include dry, cold, yellow and thickened skin, secondary to the accumulation of hydrophilic mucoproteins in the dermis (such as hyaluronic acid) as well as the atrophy of the sweat glands. There will also be a history of obesity and short stature.[5,15,16] The most common physical examination finding is a goitre. Other findings include bradycardia, delayed reflexes and oedema of the face and extremities (myxoedema). Hypothyroidism causes poor linear growth and/or growth failure and, if undiagnosed, may compromise adult height.[3,5] In the present case, it was observed that the clinical manifestations presented by the patient correspond to the most frequently reported in the literature.

The diagnosis of autoimmune thyroiditis is established by clinical characteristics, elevated TSH, detection of serum antibodies against thyroid antigens (mainly thyroid peroxidase and thyroglobulin) as well as the presence of goitre. The serum TSH concentration is elevated in primary hypothyroidism and its determination is an appropriate screening test for thyroid dysfunction.[5] The presence of goitre on examination or elevated TSH levels should prompt the measurement of anti-TPO antibodies. Anti-thyroperoxidase (anti-TPO) antibodies are the most sensitive and best screening test in the diagnosis of autoimmune thyroiditis.[2,5] They are found in approximately 90% of the patients.[5] Antithyroid peroxidase antibody titres correlate well with the number of autoreactive lymphocytes that infiltrate the thyroid.[8] Antibodies to thyroglobulin (anti-TG), the most abundant protein in the thyroid gland, are less sensitive (positive in only 60–80% of patients) and less specific (positive in a greater proportion of healthy controls) than antithyroid peroxidase antibodies.[17] The typical patient with hypothyroidism secondary to autoimmune thyroiditis will have an elevated TSH (>10IU/mL), a low FT4 and positive anti-TPO antibodies.[5]

In the present case, both the cases had elevated TSH, low T4 and elevated anti-TPO antibodies, however, only Case 1 had elevated anti-TG antibodies while the Case 2 had normal anti-TG antibodies.

Thyroid ultrasound is an important laboratory test for the diagnosis and follow-up of cases of autoimmune thyroiditis. An irregular texture in the parenchyma in the scan is suggestive of thyroiditis. The presence of nodules or cysts requires special attention to rule out the possibility of carcinoma.[4] In adults, USG thyroid has been shown to have definite value in the diagnosis of autoimmune thyroiditis. However, the role of USG in the evaluation of autoimmune thyroiditis in paediatric population is not yet

Table 6: Levothyroxine dosing according to age.

Age in years	Levothyroxine dose (mcg/kg/day)
1–3	4–6
3–10	3–5
10–16	2–4
17 and above	1.6

defined.[18] Imaging studies (thyroid ultrasonography and/or thyroid uptake and scan) may be performed if thyroid Ab tests are negative or if a nodule is palpable, but are rarely necessary.[19] Improvements in the measurement of circulating autoantibodies and ultrasonography have obviated the need for biopsy or FNAC in the diagnosis of autoimmune thyroiditis. Both of our cases had normal ultrasound neck findings.

The treatment of acquired hypothyroidism is similar to that of congenital hypothyroidism. Levothyroxine tablets are the treatment of choice administered once daily, 15–30 min before food consumption, avoiding coadministration with calcium, iron, soy products, sucralfate, potassium-binding resins, antacids containing aluminium and bile acids binding resins.[5] Levothyroxine dosing is based on body surface area (100 μg/m^2/d) or on age and weight following the general pattern, as shown in [Table 6].[4,20]

TSH normalisation is the goal of replacement. In our practice, we aim to reach values in the lower part of the normal range (0.5–2 micro IU/mL), FT4 in the upper half of the normal range.[5] Thyroid function tests should be obtained about 6–8 weeks after the initiation or every 6–8 weeks following a change in levothyroxine dose. Once biochemical euthyroidism has been achieved, TSH can be monitored every 4–6 months, up to the attainment of final height.[5] The goals of treatment are to achieve clinical and biochemical euthyroidism and to attain normal linear growth and development throughout childhood and adolescence.[2]

Accordingly, both the cases have been started with levothyroxine tablets 2 mcg/kg/day. Thyroid function tests done after 6 weeks showed improvement.

CONCLUSION

The patient showed improvement in clinical symptoms after the replacement of levothyroxine, along with significant decrease in serum levels of TSH. As thyroid ultrasound was normal showing no calcification or increased vascularity or any nodule, there was no need for biopsy or fine needle aspiration cytology (FNAC) in this case, but follow-up should be continued to carry out further evaluations. These two case scenarios help us to know the clinical presentation of autoimmune thyroiditis in the paediatric population and hence being the most common thyroid disease in this age group.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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