Thyroid Stimulating Hormone Resistance Syndrome – A Case Report

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Abstract

Resistance to thyrotropin or thyroid stimulating hormone (RTSH) can be defined as decreased responsiveness to thyroid stimulating hormone (TSH) characterized by high TSH with normal but occasionally low T_4 and T_3 usually in absence of goiter or ectopic thyroid. It can be diagnosed when TSH is >30 mIU/L but free T_4 (FT_4) is within normal limit. Patient usually presents in euthyroid state with abnormally high TSH but may also present with mild to overt hypothyroidism. The precise prevalence is not known, but 20-30% infants may show transient mild RTSH. In adults it is rare.

Here we report a case of RTSH in which a 19 years old young girl presented in euthyroid state with mild goiter.

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Introduction

Resistance to thyroid stimulating hormone (TSH) is a syndrome characterized by a high serum TSH level due to decreased sensitivity of thyroid cells to TSH. It can be diagnosed when TSH level is >30 mIU/L. However thyroid hormone concentration may vary, normal to high depending upon the resistance.[1,2] Patients may present in euthyroid state with or without goiter. Some may present with mild to severe hypothyroidism. Affected individuals usually have normal or hypoplastic thyroid glands, high serum TSH concentrations, and normal or low serum T_4 and T_3 concentrations. In case of hypothyroidism of RTSH, even after treatment with thyroxin, FT_4 remains within normal range but TSH remains very high.

RTSH is inherited as autosomal recessive or dominant genetic disorder.[3] The RTSH is very rare and usually found transiently in children. The precise prevalence is not known, but 20-30% infants may show mild RTSH. In adults it is rare. Here we report a case of RTSH where a 19 years old young girl presented in euthyroid state with mild goiter.

Case

A 19 years old girl came to the deparment of Endocrinology of BIRDEM General Hospital with the complains of swelling in front of the neck (Thyroid) for last 6 months. She was born by normal vaginal delivery and her parents were unrelated. There was no history of developmental delay or growth retardation. She had no signs or symptoms of thyroid dysfunction (hypo or hyper) except thyroid enlargement (WHO Grade 2a). She had menarche at 11 years of age and her menstrual cycle was regular. She was the youngest among 3 children of her parents. There was no history of thyroid disease or any autoimmune disease in her family. She was from a low income family and her intelligence quotient (IQ) was normal.

Her clinical examination revealed pulse rate- 94/min, BP-110/70 mmHg, height -152cm and weight-45 Kg with BMI 19.48. She was clinically euthyroid. Thyroid gland was diffusely enlarged. Both lobes were symmetrical and non-tender. No eye signs or bruit over the thyroid were found.

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Investigations showed Free T_4 (FT_4) 14.6 pmol/L (Normal RR 9.14-23.81) and TSH >100 mIU/ml (Normal RR 0.47-5.01). Anti-thyroid antibody was negative. Ultrasonogram of thyroid gland revealed mild enlargement of both lobes (right Lobe 3.5 cm and left lobe 3.2 cm at its long axis). Thyroid scan (^{99}Tc) showed diffuse mild enlargement of both lobes. As patient was completely euthyroid with only mild diffuse goiter and normal FT_4 but had very high TSH level, the diagnosis was thyroid stimulating hormone resistance syndrome (RTSH). No thyroxin was given and the patient was kept in follow up.

After 7 months she was found clinically euthyroid with similar enlargement of thyroid gland. The FT_4 was 16.2 pmol/L and TSH was >100 mIU/L. Finally she was diagnosed as a case of RTSH at euthyroid state and advised for further follow up without thyroxin suppplementation.

Discussion

TSH resistance syndromes (RTSH) can be broadly defined as reduced or absent end-organ responsiveness to thyrotropin or TSH. The other forms of disorders of thyroid may be reduced sensitivity to thyroid hormone which is a process that impairs the effectiveness of thyroid hormone and ersistent elevation of serum levels of T_4 and T_3 with "inappropriately" nonsuppressed TSH.[1] Affected individual with RTSH has high serum TSH concentrations, and normal or low serum T_4 and T_3 concentrations. They are often identified at birth through neonatal screening for congenital hypothyroidism. When FT_4 is within normal limit but TSH is >30 mIU/L, it indicates TSH resistance. The most important differential diagnosis is TSH secreting tumor of the pituitary, which presents with thyrotoxicosis, high TSH with high T_4 and T_3.

RTSH may be fully compensated (increased TSH but euthyroid), partially compensated (high TSH and mild hypothyroid) and uncompensated (complete lack of TSH receptor function with severe hypothyroidism).[2]

Though the precise prevalence is not known, but 20-30% infants may show mild RTSH which is transient. In adults it is rare. RTSH is inherited in either autosomal recessive or dominant manner.[1,3] Three genetic causes of RTSH have been so far identified. They involve two distinct genes and linkage to a gene locus. The hormone resistance may be due to the following mechanisms: Impaired biologic activity of the hormone, impaired function of hormone receptor, quantitative reduction in receptor without receptor gene defect and post receptor abnormalities.[3-5]

Individuals with fully compensated RTSH are euthyroid and need no treatment. In the absence of other risk factors there is no evidence that persistent elevation of serum TSH levels induces pituitary TSH secreting tumor or thyroid neoplasia. Individuals with partially compensated or uncompensated RTSH should be treated with L-thyroxine, like any other hypothyroid patient. Because these individuals have normal responsiveness to thyroid hormone, the goal is to normalize their serum TSH concentration.

In our case, the patient had fully compensated RTSH and need no thyroxin. Such cases should be monitored every 6-12 months for thyroid functions. In our knowledge, previously no RTSH case was reported from Bangladesh.

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