Coexisting Hurthle Cell Neoplasm and Thyroid Hormone Resistance

Guzin Fidan Yaylali[1], Mehmet Sercan Erturk[1], Fulya Akin[1] ,Sibel Guldiken[2] ,Nagihan Yalcin[3]
Hakan Gurkan[4], Akin Ozden[5]

[1]Pamukkale University, Faculty of Medicine, Department of Endocrinology and Metabolism, Denizli, 20070, Turkey
[2]Trakya University, Faculty of Medicine, Department of Endocrinology and Metabolism,Edirne,22030,Turkey
[3]Pamukkale University, Faculty of Medicine, Department of Pathology, Denizli, 20070, Turkey
[4]Trakya University, Faculty of Medicine, Department of Medical Biology, Edirne,22030, Turkey
[5]Pamukkale University, Faculty of Medicine, Department of Surgery, Denizli, 20070, Turkey

Introduction

Resistance to thyroid hormone (RTH) is an inherited syndrome characterized by reduced responsiveness of target tissues to thyroid hormone(TH). It is characterized by high serum concentrations of free T4(Ft4) and usually free T3(Ft3) accompanied by normal or slightly high serum TSH concentrations. The hallmark of RTH is the paucity of symptoms
and signs of thyroid dysfunction despite the presence of high serum T4 and T3 concentrations. Among all clinical findings, goiter is the most common followed by hyperactivity and tachycardia.Diagnosis of RTH depends on characteristic elevations in TH and exclusion of other causes of hyperthyroxinemia When RTH is suspected, the diagnosis should be confirmed by direct sequencing of the TR- β gene to identify mutations. In approximately 85 percent of cases, RTH is due to mutations in the TR beta gene. Hurthle cell neoplasm(HCN) accounts for only about 3-10% of all differentiated thyroid cancers. To our knowledge; there isn't any case reporting coexistence of HCN and RTH; so whe want to present this case.

Case report

A 38 year-old man presented with palpable goiter, tachycardia, nervousness, dysphagia and dyspnea. He had been treated with diagnosis of toxic multinodular goiter. He had no exposure to irradiation or family history of thyroid cancer. He had no ophthalmopathy. Thyroid function tests demonstrated a normal serum TSH of 1.21 uIU/ml but elevated fT3 of 6.00 pg\ml and fT4 of 2.44 ng\dl. Thyroglobulin (Tg) and thyroid peroxidase (TPO) antibodies were normal range and Tg level is elevated. He had normal α-subunit and partially suppressed TSH level by administration of incremental doses of L-T3 ,and positive TSH response to thyrotropin releasing hormone stimulation. Genetical testing was ordered to confirm diagnosis. His thyroid ultrasound showed hypoechoic nodule measuring 24* 18* 34 mm. FNAB of the nodule was compatible with folliculer neoplasm. Histopathological examination after total thyroidectomy revealed HCN with a focus of 20 mm in the long diameter at the nodule location, showing capsular invasion. Radioiodine ablation(RA) was planned.Waiting for RA, he was treated with 300 mcq L-T4 and his TSH did not suppress, which will be also an important problem during the treatment and follow-up of HCN. The suppression of TSH could be difficult when HCN coexists with RTH. Increasing the dose of L-T4 can result in thyrotoxicosis without TSH suppression

Discussion

Resistance to thyroid hormone (RTH) is an inherited syndrome characterized by reduced responsiveness of target tissues to thyroid hormone(TH). It is characterized by high serum concentrations of free T4(Ft4) and usually free T3(Ft3) accompanied by normal or slightly high serum TSH concentrations. It is important to consider mutations in the TSH receptor (*TSHR*) during differential diagnosis
Thyroid cancer account for more then %90 of all endocrine malignancies,most of which are differentiated thyroid carcinomas(1). Hurthle cell neoplasm(HCN) accounts for only about 3-10% of all differentiated thyroid cancers. The exact role of RTH in carcinogenesis is still unknown.

TSH acts as a growth factor due to the high levels and an increased bioactivity of TSH as described in RTH (2). In animal models, spontaneous development of thyroid follicular carcinoma has been described in mice homozygous for a target mutation in the *Trβ* gene (3). The metastatic thyroid cancer exhibited both anaplastic and follicular patterns (4). Molecular analyses in these mice revealed the activation of the cyclin 1–cyclin-dependent kinase-4–transcription factor E2F1 pathway, known to be associated with thyroid tumour cell proliferation (3). In addition, mutation of a single allele of the *TRβ* gene is also sufficient for follicular thyroid carcinoma to develop in mice treated with propylthiouracil, in which TSH levels increase even more (3). Recently, Franco *et al*. (4) have found that the TSH signalling pathway may predispose thyroid cells to BRAF-induced transformation in mice with a thyroid-specific knocking of oncogenic *Braf* (LSL-BrafV600E/TPO-Cre). However, thyroid cancer is still an uncommon occurrence in patients with genetically confirmed RTH.In our case Tr*β* gene mutation is found and hurthle cell neoplasm was diagnosed after total thyroidectomy. The suppression of TSH could be difficult when differentiated thyroid carcinomas coexists with RTH(5). Increasing the dose of L-T4 can result in thyrotoxicosis without TSH suppression

Conclusions:

In conclusion, this is the first case of reporting coexistance of HCN and RTH; management is more challenging.

References

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