Case report: thyroid hormone resistance followed up with systolic time interval index measurement

Tiroid hormonu direnci olan ve sistolik zaman araliği endeksi ölçümü ile takip edilen bir olgu sunumu

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Abstract

Introductıon: Thyroid hormone resistance (THR) is an end organ hyporesponsiveness in tissues. And systolic time interval index (Preejection period / Left ventricular ejection time) is a useful and alternative way to follow up metabolic and tissue effects of the thyroid hormone.

Case presentation: A 72 year old male patient had been referred to Akdeniz University Endocrinology Division because of high thyroid hormone levels on routine screening. He had elevated thyroid hormone levels accompanied with tachycardia. He had no hand fine tremor. His hypophyseal MRI had normal appearance. His thyroid autoantibody tests were in negative limits. His systolic time interval index was 0,185 (0.29-0.34) before treatment. He was evaluated as thyroid hormone resistance. After one month of methimazole treatment, his systolic time interval index increased up to 0,238. His TSH, free T_4, free T_3 levels were 26.59 μIU/mL (0.35-5.5), 0.89 ng/dL (0.89-1.76) and 3.05 pg/mL (2.3-4.2) respectively following treatment. And he had no longer tachycardia.

Conclusion: Misdiagnosis of THR in clinics are common and it causes treatment failures in patients. And systolic time interval index measurement is also a reliable way to follow-up treatment of hyperthyroxinemia.

Key words: Thyroid hormone resistance, systolic time interval index

Özet

Giriş: Tiroid hormon direnci (THR) dokularda end-organ cevabının azalması ile oluşur. Tiroid hormonunun metabolik ve doku düzeyindeki etkilerini takip etmek için sistolik zaman aralığı indeksi (Preejeksiyon periodu / Sol ventrikül ejeksiyon zamanı) de alternatif bir yöntemdir.

Olgu sunumu: Tiroid hormon düzeylerindeki yükseklik nedeninin araştırılması için 72 yaşındaki erkek hasta ikinci basamaktan Akdeniz Üniversitesi Hastanesi Endokrinoloji Bölümü'ne sevk edilmiş. Hastanın TSH, ST_4 ve ST_3 değerleri normal aralıkların üzerinde idi ve eşlik eden taşikardisi mevcuttu. Fizik muayenede elde tremor bulunmamaktaydı. Hipofiz MRI normal görünümdeydi. Tiroid otoantikor testleri negatif aralıklarda idi. Sistolik Zaman Aralığı İndeksi ölçümü tedavi öncesi 0,185 (0,29-0,34) idi. Hasta tiroid hormon direnci olarak değerlendirildi. Bir aylık metimazol tedavisini takiben Sistolik Zaman Aralığı İndeksi 0,238'e yükseldi. TSH, serbest T_4, serbest T_3 düzeyleri tedavi sonrasında sırasıyla 26.59 μIU/mL (0,35-5,5), 0.89 ng/dL (0,89-1,76) ve 3.05 pg/mL (2.3-4.2) olarak bulundu. Hastanın eşlik eden taşikardisi ise kayboldu.

Sonuç: Klinikte THR tanısı genellikle atlanır ve THR hastalarına sıklıkla yanlış tanı konulup yanlış tedavi verilir. Bununla birlikte Sistolik Zaman Aralığı İndeksi THR tanısını koymada ve tedavi takibinde güvenilir bir yoldur.

Anahtar sözcükler: Tiroid hormon direnci, sistolik zaman aralığı indeksi

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Introduction

Thyroid hormone resistance was first reported by Refetoff in 1967[1]. It is an end organ hyporesponsiveness in tissues. It is a rare syndrome with a variously quoted incidence as 1 in 50.000 or 1 in 40.000 live births[2].

Thyroid hormone effects myosine isoforms' synthesis and increases β receptor number and sensitivity in myocardia. Hyperthyroidism results in a transition to V3 isoform that is fast myosine and hypothyroidism results in a transition to V1 isoform that is slow myosine[3,4]. Thyroid hormone also increase myosine ATP ase activity thus actin-myosine bind becomes stronger[4]. Systolic time interval measurements can show peripheral influence of thyroid hormone. And systolic time interval index (Preejection period (PEP) / Left ventricular ejection time (LVET)) is useful in the follow-up of the tissue effects of the thyroid hormone[4]. PEP / LVET ratio is 0.29-0.34 in males and 0.30-0.35 in females is a reliable normal healthy population value[3]. Systolic time interval index less than 0.28 can differentiate hyperthyroid patients from euthyroid and hypothyroid patients with a sensitivity of 93,1% and with a specifity of 96,8%[3].

In this case we report a male patient with high thyroid hormone levels(TSH, fT_4, fT_3) without a family history of thyroid diseases and without complaints. And we used systolic time interval index to see tissue effects of thyroid hormone and to follow up our treatment.

Case presentation

A 72 year old male patient had been referred to Akdeniz University Endocrinology Division because of high thyroid hormone levels on routine screening. His TSH level was found 9.95 μIU/mL (normal range 0,35-5,5); his free T_3 (fT_3) level was found 5,27 pg/mL (normal range 2.3-4.2); and free T_4 (fT_4) level was found 2.22 ng/dL (normal range 0,89-1,76). His thyroglobuline level was 43,1 U/ml (normal range 0-60), his TPO antibody level was 35,8 U/ml (normal range 0-60) and his thyroid receptor antibody (TRab) test was negative. Decrement in thyroid glands' parenchymal echogenicity, rough parenchym and no nodule were visualized in thyroid ultrasound. Other laboratory findings were LDL: 127 mg/dL (normal range 0-130), fasting glucose level: 93 mg/dL (normal range 70-100).

He had tachycardia but any other symptoms. He did not have a family history of thyroid disease. His blood pressure was 140/80 mm Hg, his pulse was 102 per minute and his respiratory rate was 14 per minute. His body mass index was 24,1 kg/m^2. He had no neck tenderness and his thyroid gland was not palpable. He had no hand fine tremor. Other systemic examinations were normal. His only concomitant chronic illness was primary hypertension. He had been using lisinopril 20 mg-hydrochlorothiazide 25 mg compound antihypertensive drug.

Hypophyseal MRI was scheduled to rule out a TSH-secreting adenoma. But his hypophyseal MRI had normal appearance.

The patient had no symptoms, but only tachycardia. We measured his systolic time interval index (Preejection period (PEP) / Left ventricular ejection time (LVET)) with echocardiography to see tissue effects of thyroid hormone. His systolic time interval index was 0,185 (normal range: 0.29-0.34 in males) before treatment. The patient was considered as clinically hyperthroid according to the thyroid hormone's tissue effect. He had increased TSH, free T_4 and free T_3 levels, although he was clinically hyperthyroid. We considered he had thyroid hormone resistance. We started methimazole two times (2x5) a day. After one month treatment we measured his systolic time interval index with echocardiography again to follow up the peripheral thyrotoxicosis. His systolic time interval index increased up to 0,238. His TSH, free T_4, free T_3 levels were 26.59 μIU/mL, 0.89 ng/dL and 3.05 pg/mL respectively. He had also no longer tachycardia. Methimazole was stopped and planned to follow up his thyroid hormones two weeks later.

Discussion

Misdiagnosis of THR in clinics are common and it causes treatment failures in patients. Nearly one-third of patients was misdiagnosed as primary hyperthyroidism and treated inappropriately[5].

Differantial diagnosis of conditions associated with an elevated free T_4 with non-suppressed TSH: Thyroid hormone resistance, thyroxine replacement theraphy, drugs (amiodarone, heparine, clofibrate, 5-fluorouracil, oral contraceptives), amphetamine and heroine abuse, TSH secreting pituitary tumor, liver diseases and familial dysalbuminaemic hyperthyroxinaemia[5].

We should consider autoimmunity and TSH secreting adenomas at first in our differential diagnosis in case of high thyroid hormone levels especially when the patients do not have a family history or when they do not use an offending agent. Our patient did not use an offending agent and did not have a family history. We excluded TSH secreting adenoma with a normal hypophyseal appearance in MRI. And also we rulled out autoimmunity and Graves disease with negative antibody titres.

We measured peripheral effects of thyroid hormone with echocardiography by systolic time interval index measurement because he had not got any symptoms. According to systolic time interval index he had peripheral thyrotoxicosis. He had a very low systolic time interval index that increased near to normal euthyroid ranges with antithyroid treament.

We treated the patient with methimazole but also TRIAC (3,5,3'triiodothyroacetic acid) could be used. TRIAC has similar affinities for both wild type TR-β1 and mutant TR-β1. TRIAC is also able to inhibit the secretion and biological activity of TSH with very little thyromimetic effects of thyroid hormone at the level of peripheral tissues[6]. Beta blockers can be used when patients reveal symptoms like tachycardia and tremor. Ablative therapy and thyroidectomy may also be used in rare circumstances like life threatining thyrotoxic cardiac failure associated with THR[7].

Conclusion

THR is a rare syndrome and clinical presentation of THR is heterogenous. Most of the patients might be mistakenly diagnosed as thyrotoxic and may even be treated when in fact they might be euthyroid.

Systolic time interval index measurement is a reliable way to follow-up of treatment. And, treatment for THR can be attempted with supraphysiological L-T_4 in clinically hypothyroid patiens, while clinically hyperthyroid patiens may be treated with TRIAC, beta blockers, methimazole, somatostatine analogs and D-T_4[2].

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