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Case Report / Olgu Sunusu

Werner Sendromlu bir olguda sıradışı organ tutulumu: tiroid atrofisi
An unusual organ involvement in a case of Werner Syndrome: thyroid atrophy

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ABSTRACT

Werner Syndrome (WS) is a premature aging disease that begins in adolescence or early adulthood and results in the appearance of old age by 30-40 years of age. Some endocrinological abnormalities were manifested in this rare disease, such as hypogonadism, diabetes mellitus, hyperlipidemia. In this article, we present a nineteen years-old female patient who had been diagnosed as WS two years ago because of type 2 diabetes mellitus, osteopenia, hyperlipidemia, cataract, gray hair, and skin atrophy. Subclinical hypothyroidism was detected at her laboratory tests. Thyroid ultrasonography (USG) showed thyroid atrophy. Fine needle aspiration biopsy of both lobes confirmed this diagnose and excluded some infiltrative diseases such as amyloidosis. It should be kept in mind that thyroid atrophy could be seen in WS and, therefore, detailed thyroid examination including thyroid USG and close follow up should be performed in all patients with WS.

Key words: atrophy; thyroid; Werner syndrome

ÖZET

Werner Sendromu (WS) adölesan veya erken erişkin döneminde başlayan erken yaşlanmaya neden olan bir hastalıktır. Hastalar 30-40 yaşlarında yaşlı insan görünümündedirler. Bu nadir görülen hastalıkta, hipogonadizm, diabetes mellitus ve hiperlipidemi gibi bazı endokrinolojik anormallikler de olabilmektedir. Biz bu yazıda tip 2 diabetes mellitus, osteopeni, hiperlipidemi, katarakt, gri saç ve cilt atrofisi nedeniyle iki yıldır WS tanısı ile takip edilen 19 yaşında bir bayan hasta sunduk. Hastanın yapılan labotaruvar testlerinde subklinik hipotiroidi saptandı. Tiroid ultrasonografisinde (USG) tiroidin atrofik boyutlarda olduğu gözlendi. Her iki lobdan yapılan tiroid ince iğne aspirasyonu sonucu da atrofi ile uyumlu idi ve amiloidozis gibi bazı infiltratif hastalıklar dışlandı. WS'unda tiroid atrofisinin olabileceği akılda tutulmalıdır. Bu yüzden tüm WS'lu hastalarda tiroid USG'yi de içeren detaylı tiroid muayenesi yapılmalı ve bu açıdan yakın takip edilmelidir.

Anahtar kelimeler: atrofi; tiroid; Werner Sendromu

INTRODUCTION

Werner syndrome (WS) is an autosomal recessive disease characterized by premature aging, skin changes, gray hair, alopecia, muscle atrophy, osteoporosis, and cataracts and has a high frequency of association with rare neoplasms (1). Some endocrinological abnormalities were manifested in this rare disease, such as hypogonadism, diabetes mellitus, hyperlipidemia (2). In addition, atrophic changes of organs and systems such as skin, brain and genital organs were reported. There is a little knowledge about coexistence of WS with thyroid disease; only some thyroid function abnormalities and nodular goitre were described in WS cases (2). However, according to our knowledge, thyroid atrophy has not been reported in literature, yet. Here we present a case of WS who had diabetes, osteopenia, hyperlipidemia, cataract, gray hair, and skin atrophy together with the newly diagnosed thyroid atrophy.

Case

Nineteen years-old female patient had been diagnosed with WS for 2 years. She had type 2 diabetes mellitus, osteopenia, hyperlipidemia, cataract, gray hair, and skin atrophy. She had been treated with insulin aspart and glargine, metformin, gemfibrozil, calcium and vitamin D. At the time of routine outpatient clinic control, her glucose was unregulated and she was hospitalized for regulation of the blood glucose. Short stature, light body weight (BMI: 17,6 kg/m^2) and bird-like appearance was detected at her physical examination. Her thyroid was not palpable on examination. Her secondary sex characters and menses were normal. Her laboratory tests were as follows; glucose 245 mg/dL, HbA1c 7.9 %, thyroid stimulating hormone (TSH): 6.5 uIU/mL (0.6-4.8), free T3: 3 pg/mL (2.3-4.2), free T4: 0.8 ng/dL (0.74-1.52), anti-thyroglobulin antibody: 50.7 (0-64) U/mL, anti-thyroid peroxidase antibody: 33.7 U/mL (0-57), serum thyroglobulin: 7.3 (1,6-59,9) ng/mL. Thereafter, thyroid USG was performed and bilateral parenchymal heterogenity and very low thyroid volume were detected (right lobe dimensions were 26x10x8 mm, volume was 1 cm^3 and left lobe dimensions were 19x10x7 mm, volume was 0.6 cm^3). The patient approved the FNA biopsy of both lobes for exception of some infiltrative diseases. Decreased follicular epithelium cells were detected in specimens and there was not any thyroiditis or fibrosis sign. Because of having no symptoms and signs of hypothyroidism she was followed up without treatment.

DISCUSSION

In 1904, Otto Werner reported 4 cases of brothers and sisters with symptoms and signs including premature aging of the face, small stature, juvenile cataract, pachyderma-like alteration of the extremities, juvenile grey hair, and genital hypoplasia (1). In 1934, Werner's syndrome was described by Oppenheimer and Kugel as an independent disease, with additional endocrine abnormalities (1).

Werner Syndrome is a premature aging disease that begins in adolescence or early adulthood and results in the appearance of old age by 30-40 years of age. Its estimated incidence is one case per a million individuals. Disease is more prevalent in Japan, US and Germany (1). Werner Syndrome is inherited and transmitted as an autosomal recessive trait and results from a mutation at WS gene belonging to RecQ type DNA/RNA helicase (WRN). The most important theory explaining the development of the disease is abnormal metabolism of connective tissue showing itself by abnormal mucopolysaccharides and fibroblasts in pathological and biochemical studies in WS. Fibroblasts show a mutator phenotype, replication fork stalling, increased rates of mean telomeric loss and accelerated cellular senescence. Senescence has been proposed as a candidate mechanism for the

aging of mitotic tissue (3,4). Cells from WS patients have a shorter lifespan in culture than do normal cells (5). In disease mean survival time is 46 years and death is mostly due to atherosclerosis and malign tumors (1,2).

Werner Syndrome is also characterized with certain endocrine defects, such as abnormal production of the hormone insulin by the pancreas and resistance to the effects of insulin (non-insulin-dependent diabetes mellitus), impaired functioning of the ovaries in females or testes in males, hyperlipaemia, hyperuricaemia, and osteoporosis from the age of 30 years. Hypogonadism (80%), type 2 diabetes mellitus (70%), secondary sexual underdevelopment (50%) are the most common endocrine disorders which occure in WS (1,6). However, hypergonadotrophic hypogonadism, adrenal cortical hypofunction and GH deficiency was reported previously (7). In addition, some postmortem studies revealed findings of atrophy of the endocrine glands including the genital organs (8,9). The exact mechanisms which induce these clinical manifestations are still unclear.

Thyroid dysfunction, either hyper- or hypo-functioning, is observed in 15 % of WS patients (2) . Nodular goiter, subclinical primary hypothyroidism and lower serum triiodothyronine levels in patients with Werner syndrome were reported (7,10), and it is well known that those who have WS may be at increased risk for thyroid cancer. Follicular type is the most common type of thyroid carcinomas (11). According to our knowledge, there is no report of thyroid atropy in WS in the literature.

In our case, the patient was diagnosed as WS at seventeen years old. She had type 2 diabetes mellitus, osteopenia, hyperlipidemia, cataract, short stature, gray hair, and skin atrophy. Subclinical hypothyroidism was detected at her laboratory tests. Thyroid USG showed thyroid atrophy and FNA biopsy of both lobes confirmed this diagnose. Because of having no symptoms and signs of hypothyroidism she was followed up without treatment.

In conclusion, thyroid atropy can be seen in WS and, therefore, detailed thyroid examination including thyroid USG and close follow up should be performed in all patients with WS.

The authors declare that they have no conflict of interest.

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