Case Report

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The Effect of Colchicine on Thyroid Eye Disease: A Case Report

Kolşisinin Tiroid Göz Hastalığı Üzerine Etkisi: Bir Olgu Sunumu

Ali Saklamaz, Handan Bekdemir, Murat Uyar*, Murat Yalçın**, Halida Mammadova, Muammer Karadeniz

Şifa University Faculty of Medicine, Department of Endocrinology and Metabolic Diseases, İzmir, Turkey
*Şifa University Faculty of Medicine, Department of Ophthalmology, İzmir, Turkey
**Şifa University Faculty of Medicine, Department of Internal Medicine, İzmir, Turkey

Abstract

Thyroid eye disease (TED) is the most common extrathyroidal manifestation of Graves' disease (GD). Corticosteroids are mostly used drug for this complication. Can colchicine be used for the treatment of Graves' ophthalmopathy (GO)? A 49-year-old female, who suffered hyperthyroidism for 5 years, was admitted to our clinic for GO. Although the euthyroidism was achieved, there was no improvement in orbitopathy. Because of the patient's condition, we could not prescribe corticosteroids to our patient. TED improved after 3 months of colchicine treatment and the patient was found to be satisfied with her new appearance. No side effects related with colchicine treatment were observed. Colchicine can be used as an effective and safe drug in GO.
Keywords: Colchicine, thyroid eye disease, graves' disease

Öz

Tiroide bağlı göz hastalığı (TED) Graves' hastalığının (GD) tiroid dışı bulgularından en sık görülenidir. Bu komplikasyon için daha çok kortikosteroidler kullanılır. Graves orbitopatide (GO) kolşisin kullanılabilir mi? Beş yıldır hipertiroidi rahatsızlığı olan 49 yaşındaki kadın hasta polikliniğimize GO şikayeti ile başvurdu. Hipertiroidi kontrol altına alındığı halde orbitopatide olumlu bir gelişme olmadı. Hastanın şartlarının uygun olmaması nedeniyle kortikosteroid veremedik. Üç aylık kolşisin tedavisi ile göz bulgularında gerileme oldu. Hasta da bu durumdan memnundu. Kolşisine bağlı bir yan etki gözlenmedi. GO kolşisin etkili ve güvenli bir ilaç olarak kullanılabilir.
Anahtar kelimeler: Kolşisin, tiroid göz hastalığı, graves hastalığı

Introduction

Graves' disease (GD) is an autoimmune thyroid disease. About 60% of patients with GD may have thyroid eye disease (TED) (1). This is the most common extrathyroidal manifestation of GD. Thyroid-related ophthalmopathy occurs as chronic inflammation and scarring of the retro-orbital tissue. In this process, the humoral and cellular immunological pathways are responsible. In short period, the extraocular muscles and fat tissues are infiltrated with inflammatory cells, resulting in releasing of several cytokines, mostly interleukin-1, tumor necrosis factor-alpha and interferon-gamma (2). In addition, volume of the retro-orbital adipose tissue is increased by long-acting thyroid stimulators that are present in the environment. Later, in long-term, this inflammation causes the production of glycosaminoglycan by the fibroblasts. The infiltration of retro-orbital tissue by mucopolysaccharides and collagen causes fibrosis and, thus, distension of these tissues (2). In TED, inflammation of muscle and fat tissue can result in proptosis, compressive optic neuropathy and problems with extraocular muscle function. TED also may cause vision loss in some patients. Corticosteroids are used as the first-choice treatment for TED. The intravenous administration is more effective and has fewer side effects compared to per oral administration in reduction of inflammation. Sometimes, steroid use is not advantageous in TED patients, therefore, other options can be chosen. These options include radiotherapy, cyclosporine, somatostatin analogues, rituximab and anti-TNF-alpha antibody (1).

Can colchicine that has indication in gout and familial Mediterranean fever be used in the treatment of TED? Colchicine is an alkaloid and has anti-inflammatory effects. It inhibits motility, chemotaxis and phagocytosis of neutrophil cells. It also inhibits fibroblasts, lymphocyte function and proliferation (3). In the literature, there is only one randomized prospective study about the effect of colchicine on TED. In that paper, Stamato et al. (4) have reported that colchicine was effective and had fewer side effects compared to corticosteroid.

In this case report, we aimed to present the efficacy of colchicine in a TED patient in whom we could not use corticosteroid.

Address for Correspondence: Ali Saklamaz MD, Şifa University Faculty of Medicine, Department of Endocrinology and Metabolic Diseases, İzmir, Turkey
Phone: +90 232 446 08 80 E-mail: asaklamaz@hotmail.com **Received:** 26/12/2014 **Accepted:** 21/03/2015

Case Report

A 49-year-old female, who suffered TED, was admitted to our outpatient clinic. Her history revealed a diagnosis of GD established 5 years ago, when she had weight loss, palpitations and anxiety for 4 weeks. She was first given propylthiouracil for 1 year. She did not use the drug as prescribed and did not attend follow-up visits. The patient had last been seen by a doctor 8 month ago. There were some symptoms of hyperthyroidism; increased fatigue, palpitation, loss of energy and irritation. Thyroid hormone levels were at the upper limit of the normal range (free thyroxine=1.3 ng/dl; normal range: 0.7-1.45 ng/dl, and thyroid-stimulating hormone (TSH): <0.05 µIU/mL; normal range: 0.35-4.9 µIU/m). She was prescribed methimazole 10 mg daily. On those days, she attended our ophthalmology outpatient clinic because of bulging eyes. The right eye was more bulging than the left eye. There was no complaint of headache or pressure behind the eyes, but she reported periorbital puffiness and eye irritation. She was very unhappy with her appearance and fearful about the possibility of progressive disfigurement. It was observed that the vision and eye movements were normal bilaterally, the pupils were equal and reactive, the fundi were normal, and bilateral exophthalmos (R>L) was determined. Hertel measurements were done and 22 mm (right eye) and 21 mm (left eye) were recorded. Clinical activity score was found to be 3. The patient was evaluated by our endocrinology department and it was found that the thyroid was slightly enlarged but no nodules were palpated. The TSH receptor antibody level was 0.607 IU/l (normal: <1.2 IU/l). Thyroid scan showed high uptake (36.4%) and thyroid ultrasound demonstrated two nodules (5 mm and 6 mm). The patient was started on metoprolol and methimazole. The initial dose of methimazole was 10 mg/day. Her TSH normalized one month later, but the bulging eyes were the same although the thyroid function tests were normal three months later. Though we planned to prescribe prednisolone, we could not prescribe intravenous corticosteroid due to a recent history of peptic ulcer. Considering the fact that the patient lives in a rural area and has difficulty to reach any medical aid, we prescribed colchicine (0.5 mg tablet 3 times a day) for TED. Three months later, her thyroid function tests were still within normal limits and Hertel measurements of the eyes were 20 mm (right), 19 mm (left). Clinical activity score was reported as 1. Her complains about her eyes were better and she was referred for thyroidectomy. Although euthyroidism was achieved, she was still using anti-thyroid treatment and had TED. She continues to take colchicine two times a day until thyroidectomy. She is very happy with her appearance and does not feel fear about her eyes now (Figures 1, 2, 3) (The informed consent has been taken from the patient).

Discussion

Patients with GO may have mild symptoms, such as proptosis, redness, swelling of the eyelids and serious complains like loss of vision. The infiltration of retroorbital tissue with lymphocytes and secretion of cytokines stimulate fibroblasts. Fibroblasts secrete glycosaminoglycans which cause edema and swelling of the muscles and adipose tissue resulting in exophthalmos (5).

Corticosteroids are the most commonly used anti-inflammatory drugs. However, it has some well-known side effects and recurrences may occur after withdrawal. When high-dose corticosteroids are administered intermittently, the side effects may be less (6). If TED does not respond to corticosteroids, radiotherapy, immunoglobulin, cyclosporine A, octreotide, azathioprine, cyclophosphamide and pentoxyfylline can be used (7).

Figure 1. Photograph of the patient from the front view after the colchicine treatment

Figure 2. Photograph of the patient's right eye after the colchicine treatment

Figure 3. Photograph of the patient's left eye after the colchicine treatment

Colchicine is indicated for familial Mediterranean fever and gout. It is also used for the treatment of Behçet's disease and pericarditis (8,9). In the literature, there is only one randomized prospective trial on colchicine treatment for TED. In that study, 22 patients with TED were divided into two groups; one group was treated with prednisone (7.5 mg/kg/day) and the other group with colchicine (1.5 mg/day) for 3 months. The patients were monitored by an ophthalmologic assessment [clinical activity score (CAS)], magnetic resonance imaging of the eyes and signal intensity ratio (SIR) of the recti muscles in comparison to the cerebral substantia alba. At the end of the study, the two treatment modalities achieved the same reductions in SIR and CAS. The patients of prednisone group had weight gain, edema, gastric complains, hirsutism, weakness, depression and alterations in blood pressure. However, these side effects were not seen in colchicine group (4).

Our patient had mild thyroid ophthalmopathy. There was no improvement in TED although euthyroidism was achieved with anti-thyroid treatment. Since the patient was living in the suburb with difficulties to reach medical support and the diagnosis of peptic ulcer was established recently, we decided to try colchicine for TED. The patient received 1.5 mg of colchicine for 3 months. Hertel measurements were done by the same ophthalmologist before and after treatment. The Hertel measurements, redness and swelling of the eyes were improved with the colchicine treatment (clinical activity score decreased from 3 to 1). We could not have taken orbital MRI before and after colchicum treatment.

Our patient did not experience any side effects when using colchicine. The patient was euthyroid in the 6th month. Laboratory examinations showed no abnormality. Thyroidectomy was recommended for permanent treatment of TED.

In patients with thyroid ophthalmopathy, who are not suitable for corticosteroid treatment, colchicine can be effective in suppressing inflammatory reactions and in improving clinical activity scores. Since colchicine is well tolerated, it can be used for longer durations than corticosteroids.

Authorship Contributions

Informed Consent: Consent form was filled out by the patients, Concept: Ali Saklamaz, Muammer Karadeniz, Design: Ali Saklamaz, Handan Bekdemir, Murat Yalçın, Data Collection or Processing: Murat Uyar, Analysis or Interpretation: Ali Saklamaz, Handan Bekdemir, Literature Search: Halida Mammadova, Murat Yalçın, Writing: Ali Saklamaz, Muammer Karadeniz, Peer-rewiev: External and Internal peer-reviewed, Conflict of Interest: No conflict of interest was declared by the authors, Financial Disclosure: The authors declared that this study has received no financial support.

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