

## DELAYED DIAGNOSIS GRAVES' OPHTHALMOPATHY: CASE REPORT

## TANIDA GEÇ KALINMIŞ GRAVES OFTALMOPATİSİ: OLGU SUNUMU

Tuğba BODUR<sup>1\*</sup> Hüseyin CAN<sup>2</sup><sup>1</sup>Manisa Yunusemre 13 Nolu Aile Sağlığı Merkezi, Manisa, Türkiye<sup>2</sup>İzmir Katip Çelebi Üniversitesi Tıp Fakültesi, Aile Hekimliği Anabilim Dalı, İzmir, Türkiye

\*Corresponding Author: Tuğba BODUR drtugba.bodur@gmail.com

Received : 29.01.2025

Accepted : 01.10.2025

Published: 30.04.2026

**How to cite:** Bodur T, Can H. Delayed diagnosis of Graves' ophthalmopathy: case report. SMJ. 2026;4(1):35-8.

## ABSTRACT

Thyroid diseases are common endocrine disorders worldwide. They may occur due to either increased hormonal activity or decreased hormone production. Thyrotoxicosis refers to the presence of elevated thyroid hormone levels in the blood, whereas hyperthyroidism refers to increased synthesis and secretion of thyroid hormones. Graves' disease is the most common cause of hyperthyroidism. Thyroid ophthalmopathy is the most common extrathyroidal manifestation of Graves' disease. Graves' ophthalmopathy is an autoimmune condition affecting the orbital and extraocular muscles, the pathogenesis of which is not fully understood. Management of Graves' ophthalmopathy should begin with achieving and maintaining euthyroidism. Accurate diagnosis of thyroid diseases relies on a careful medical history, physical examination, and laboratory evaluation. This article discusses the role of primary care and preventive approaches in a patient with delayed diagnosis of Graves' ophthalmopathy.

**Keywords:** hyperthyroidism, ophthalmopathy, TSH Receptor Antibodies (TRAb)

## ÖZET

Tiroid hastalıkları ülkemizde ve tüm dünyada yaygın olarak görülen endokrin hastalıklardandır. Tiroid hastalıkları ya artmış hormonal aktivite ya da hormon üretim azlığına bağlı olarak seyretmektedir. Çeşitli nedenlerle kanda tiroid hormonunun artmasına tirotoksikoz,; tiroid bezinin normalden çok çalışarak aşırı miktarda tiroid hormonu üretmesine ise hipertiroidi denir. Graves hastalığı ise hipertiroidinin en sık görülen nedenidir. Graves hastalığının en sık görülen tiroid dışı tutulumu tiroid oftalmopatisidir. Graves oftalmopatisi; patogenezi tam anlaşılmayan, orbita ve ekstraoküler kasları etkileyen otoimmün bir hastalıktır. Graves oftalmopati yönetimi eşlik eden tiroid hastalığının kontrolü ile başlamalıdır. Tiroid hastalıklarında doğru tanı dikkatli bir öykü, fizik muayene ve laboratuvar araştırması ile elde edilir. Yazımızda birinci basamak sağlık hizmetlerine başvuran, tanıda geç kalınmış graves oftalmopatisi olan hastanın problemlerine yaklaşım ele alınmıştır.

**Anahtar Kelimeler:** hipertiroidizm, oftalmopati, TSH Reseptör Antikoru (TRAb)

## Introduction

Graves' disease is a heterogeneous autoimmune disease affecting the thyroid gland, orbital tissues, and skin. TSH receptor autoantibodies (TRAb) cause hyperthyroidism by binding to thyroid-stimulating hormone receptor (TSHR) (1). Although the pathogenesis of the disease involves the interaction between genetic, environmental, and endogenous factors, studies have found that genetic inheritance is the most effective in the development of this disease (2). Signs and symptoms suggestive of Graves' disease include fatigue, irritability, palpitations, weight loss, dyspnea, intolerance to heat, increased appetite, oligomenorrhea, sweating, soft stools or diarrhea, muscle pain, weakness, and tremors. In addition, individuals may have ophthalmopathy findings such as periorbital edema, proptosis/exophthalmos, eyelid retraction and TRAb positivity in laboratory findings (3).

Graves' disease usually begins between the ages of 30 and 50 and becomes more severe after the age of 50, affecting 3% of women and 0.5% of men throughout their lives. Thyroid ophthalmopathy is 2.5-6 times more common in women, while severe ophthalmopathy is more common in men. Clinical ophthalmopathy cases are classified according to the European Graves' Ophthalmopathy (GO) Group (EUGOGO) classification. The most useful method for assessing activity in practice is the clinical activity score (CAS), defined by EUGOGO. The clinical activity score determines the likelihood of disease response to anti-inflammatory therapy (4). Although symmetrical eye findings are more common in women, asymmetrical eye findings are seen especially in older men (5). In most patients, ophthalmopathy can be seen between 10 years before and 20 years after the onset of thyroid disease, but it is usually seen 18 months after the disease is diagnosed (6).

In mild and active ophthalmopathy, antithyroid drugs (ATD) or thyroidectomy should be preferred. If radioactive iodine therapy (RAI) is chosen, steroid prophylaxis should be considered. In moderate-severe and inactive ophthalmopathy, ATD or RAI therapy can be chosen. Moderate-severe and active ophthalmopathy and vision-threatening ophthalmopathy should be treated only with ATD. Patients should be strongly advised to quit smoking (7).

In our country, thyroid diseases are among the diseases that are frequently encountered and treated in primary health care institutions. Therefore, many thyroid diseases can be diagnosed early with a detailed history and a careful neck and systemic examination in primary care (8). It is important to refer Graves' patients, especially those suspected of ophthalmopathy, to an Endocrinologist without delay.

In our case report, it is aimed to discuss a patient with late-diagnosed Graves' disease and ophthalmopathy.

## Case

A 50-year-old married male patient, who applied to the outpatient clinic with complaints of headache and fatigue, stated in the detailed anamnesis that he had known hypertension, hyperthyroidism and glaucoma, but that he was not using any medications. There was mild cyanosis in the general physical examination. The patient did not have jaundice, clubbing of the fingers or lymphadenopathy. Blood pressure was 130/90 mmHg, oxygen saturation was 97%, pulse was 88 beats/min, and body temperature was 36.7 degrees. Ophthalmological examination revealed bilateral exophthalmos, swelling in the eyes and lack of adduction. The patient's ophthalmopathy was classified as sight-threatening according to the EUGOGO classification (Figure 1).

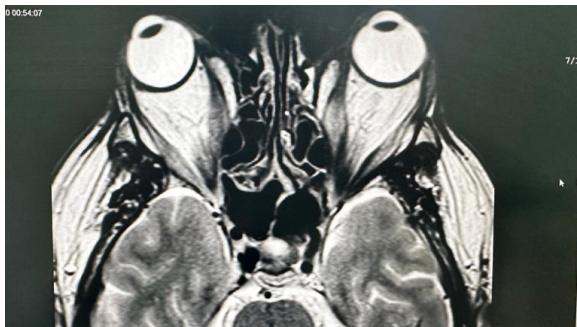


**Figure 1.** Ophthalmological examination revealed bilateral exophthalmos, periorbital swelling, and impaired adduction. Written informed consent for publication of the image was obtained from the patient.

It was learned that the patient had not undergone blood tests for several years before 2016 and gave a blood test after the eye findings emerged. Thyroid function tests (TFT), which were performed for the first time in 2018; TSH was 0.001  $\mu$ IU/mL (normal range 0.27-4.2  $\mu$ IU/mL), FT4 was 3.34 (normal range 0.93-1.7  $\mu$ IU/mL), Anti TPO was 28 U/ml (normal range), Anti TG was 150 U/mL (higher than normal). The last TFT tests performed were dated November 2024 and were TSH 0.005 IU/mL (normal range 0.27-4.2  $\mu$ IU/mL), FT4 was 2.67 (normal range 0.93-1.7  $\mu$ IU/mL). The patient's abnormal laboratory values in the same analysis were vitamin B12 level 195 pg/mL (normal range 197-771 pg/mL), Alkaline Phosphatase (ALP) value 248 U/L (normal range 40-129 U/L, fasting blood glucose 131 mg/dL (normal range 74-100 mg/dl). Other laboratory parameters were within normal limits.

Thyroid USG performed in 2020 revealed a right lobe of 26x17x55 mm, a left lobe of 19x20x48 mm, and an isthmus thickness of 2 mm. Thyroid gland

parenchymal echogenicity was decreased and slightly heterogeneous; no nodules or lymphadenopathy were detected. Orbital Computed Tomography (CT) performed in the same year showed a hypertrophic appearance of the bilateral extraocular muscles and findings compatible with exophthalmos, reported as 'consistent with Graves'. Magnetic Resonance Imaging (MRI) confirmed the CT findings and additionally showed increased volume and contrast enhancement in the bilateral extraocular muscles, with no optic nerve pathology. Furthermore, a mucus retention cyst was observed in the patient's maxillary sinus (Figure 2).



**Figure 2.** The magnetic resonance image of the patient

The patient was started on propylthiouracil (PTU), steroid and medication for hypertension in 2018, and surgery was also recommended due to decreased visual acuity in the left eye and increased complaints of eye pain in 2019. The patient did not want to have surgery for 2 years. The patient underwent orbitotomy and cyclophotocoagulation surgery in 2021 after two years. Despite the surgery, the patient lost vision in his left eye, and therefore it was deemed appropriate to have a tomography scan. CT performed in 2021, it was reported as “significant thickness increase in the extraocular muscle bodies in both eyes, retroorbital fat tissue increase, bilateral advanced exophthalmos developed. There is also a depression fracture at the lamina papyracea level in the ethmoidal left bone”. The patient did not comply with the medication treatment regularly both at the beginning of the diagnosis and today and continued to smoke 1 pack of cigarettes per day. Effective patient-doctor communication was established, the risks of the disease and not using the medications regularly and the importance of lifestyle changes in chronic diseases were explained, and an agreement was reached for referral to a higher level, and the patient was directed to Endocrinology and Ophthalmology specialists. The patient is still under our follow-up.

## Discussion

Thyroid diseases should be included in routine screening during primary care visits. Individuals with suggestive symptoms or a family history of thyroid

disease should be evaluated at the initial examination. In addition, screening with thyroid function tests every five years is recommended for adults over the age of 35 for early detection of thyroid dysfunction (8). In patients with symptoms/findings related to hypothyroidism, it is recommended that TSH and fT4 levels be checked for diagnostic purposes. In patients with symptoms/findings related to hyperthyroidism, T3/fT3 levels should be requested in addition to TSH and fT4 for diagnostic purposes. The early diagnosis of Graves' disease can be made clinically in a patient with elevated serum thyroxine (T4) and suppressed TSH values. If uncertainty persists after initial evaluation, the 2016 American Thyroid Association (ATA) Guidelines for the Diagnosis and Treatment of Other Causes of Hyperthyroidism and Thyrotoxicosis recommend that one or more of three methods be used, including TRAb testing, radioactive iodine uptake (RAIU), or demonstration of diffusely increased vascularity on Doppler flow ultrasonography (9). The modern TRAb test has high sensitivity and specificity of 97% and 99%, respectively, for the diagnosis of Graves' disease (10). Therefore, TRAb should be requested in patients suspected of hyperthyroidism. The prevalence of GO among Graves' patients is around 30% (11). In a single-center study of more than 300 consecutive patients with recent onset Graves' hyperthyroidism, 74% had no signs/symptoms of GO, 20% had mild GO, and only 6% had moderate-to-severe or, rarely, sight-threatening (12). Magnetic resonance imaging. MRI provides better imaging of the optic nerve, orbital fat, and extraocular muscle and also allows for identification of active inflammation within the orbital tissues, but CT scans provide better views of the bony architecture of the orbit (13). Early diagnosis is important in patients to prevent eye symptoms. In addition, since smoking increases the severity of ophthalmopathy and decreases the response to treatment in patients with eye symptoms, patients who smoke should be encouraged to quit smoking (14). Euthyroidism should be achieved and maintained as soon as possible, as thyroid dysfunction, especially hypothyroidism, negatively affects the course of ophthalmopathy. In mild disease, topical lubricants, use of sunglasses, elevation of the head of the bed, use of prismatic glasses in the presence of diplopia, or botulinum toxin injection into the Müller muscle can provide relief from symptoms (15). Our patient's failure to take a blood test for many years delayed the diagnosis, and his failure to receive regular medical treatment and continued smoking caused the eye symptoms to worsen. Despite many reports in the literature, underdiagnosis of this disease is still very common in clinical practice and the importance of this situation should be emphasized.

## Disclosures

**Peer-review:** Externally peer-reviewed.

**Informed Consent:** Written informed consent was obtained from the patient.

**Acknowledgements:** None

**Conflict of interest:** None

**Funding:** None

## REFERENCES

1. Hoang TD, Stocker DJ, Chou EL, Burch HB. 2022 Update on Clinical Management of Graves' Disease and Thyroid Eye Disease. *Endocrinol Metab Clin North Am.* 2022; 51(2): 287–304.
2. Lane LC, Wood CL, Cheetham T. Graves' disease: moving forwards. *Arch Dis Child.* 2023;108 (4):276-81.
3. Lee SY, Pearce EN. Hyperthyroidism: A Review. *JAMA.* 2023;330(15):1472–83.
4. Barrio-Barrio J, Sabater AL, Bonet-Farriol E, Velázquez-Villoria A, Galofré JC. Graves' Ophthalmopathy: VISA versus EUGOGO Classification, Assessment, and Management. *J Ophthalmol.* 2015;249125.
5. Panagiotou G, Perros P. Asymmetric Graves' orbitopathy. *Front Endocrinol (Lausanne).* 2020;11:611845.
6. Bartalena L, Marcocci C, Pinchera A. Graves' ophthalmopathy: a preventable disease? *Eur J Endocrinol.* 2002; 146: 457-61.
7. Burch HB, Perros P, Bednarczuk T, Cooper DS, Dolman PJ, Leung AM et al. Management of Thyroid Eye Disease: A Consensus Statement by the American Thyroid Association and the European Thyroid Association. *Thyroid.* 2022;32(12):1439-70.
8. Republic of Turkey Ministry of Health, Public Health Institution of Turkey. Periodic health examination and screening tests recommended in family medicine practice. Publication No: 991. Ankara: Republic of Turkey Ministry of Health; 2015.
9. Schübel J, Stahl A, Feldkamp J, Werner F, Uebel T, Voigt, K. Thyroid Nodules: Diagnosis and Treatment in Primary Care. *Dtsch Arztebl Int.* 2025;112(13):341-7.
10. Kahaly GJ, Diana T, Olivo PD. TSH receptor antibodies: relevance & utility. *Endocr Pract.* 2020;26(1):97–106.
11. Ippolito S, Cusini C, Lasalvia P, Gianfagna F, Veronesi G, Gallo D, et al. Change in newly diagnosed Graves' disease phenotype between the twentieth and the twenty-first centuries: meta-analysis and meta-regression. *J Endocrinol Invest.* 2021; 44:1707–18.
12. Tanda ML, Piantanida E, Liparulo L, Veronesi G, Lai A, Sassi L, et al. Prevalence and natural history of Graves' orbitopathy in a large series of newly diagnosed Graves' hyperthyroidism seen at a single center. *J Clin Endocrinol Metab.* 2013; 98:1443–9.
13. Wagner RS. Diagnosing and Treating Thyroid Ophthalmopathy. *J Pediatr Ophthalmol Strabismus.* 2018;55(6):355.
14. Bartalena L, Kahaly GJ, Baldeschi L, Dayan CM, Eckstein A, Marcocci C, et al. The 2021 European Group on Graves' orbitopathy (EUGOGO) clinical practice guidelines for the medical management of Graves' orbitopathy. *Eur J Endocrinol.* 2021; 185:43–67.
15. Şahlı E, Gündüz K. Thyroid-associated Ophthalmopathy. *Turk J Ophthalmol* 2017;47: 94-105.