



Ocular Hypertension, Glaucoma or Compressive Neuropathy in Patient with Active TED

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Abstract

Introduction: Severe cases of thyroid eye disease with high intraocular pressure and visual field defects are a real diagnostic challenge requiring the exclusion of dysthyroid optic neuropathy and differential diagnosis with glaucoma.

Aim: To report a case of a patient with active thyroid eye disease (TED), decreased visual acuity and elevated intraocular pressure.

Materials and methods: We present a 52-year-old woman with TED in both eyes, class 2c3c4a6a (NOSPECS), with 6 points (by CAS) activity, who received corticosteroid therapy to a maximum cumulative dose of 5750 mg, with non-insulin-dependent diabetes mellitus and topical antihypertensive treatment with tapticom, brizadopt, and luxfen. The patient received full ophthalmological exam, tonometry, exophthalmometry, computer perimetry, optical coherence tomography (OCT) and computed tomography (CT) scan of orbits.

Results: The following results were obtained: BCVA of right eye = 0.6, BCVA of left eye = 0.3; TOD = 26 mm Hg and TOS = 21 mm Hg; exophthalmometry: 30 mm for the right eye and 31 mm for the left one; diplopia in all directions, edema and hyperemia of the eyelids and conjunctiva, eyelids retraction, sluggish pupil reactions, normal color vision, transparent ocular media, indistinct borders of the optic nerve disc, without glaucomatous excavation, tortuosity and dilation of the venules, retina - without diabetic changes, maculas - with normal reflex; CP data for a localized inferotemporal visual field defect, CT data for thickening of all extraocular muscles, soft tissue orbital edema, and optic nerves compression.

Conclusion: Our results confirmed the presence of dysthyroid optic neuropathy based on the decreased visual acuity, ophthalmoscopic evaluation of the optic nerve head, lack of glaucomatous OCT changes, atypical perimetric changes and the CT data. The optic neuropathy is the most severe complication in patients with TED which develops due to the compression of the optic nerve and/or its blood supply from the enlarged extraocular muscles and soft tissues in the orbital apex and due to the mechanical tension of the optic nerve in cases moderate or severe proptosis is present.

Keywords

thyroid ophthalmopathy

INTRODUCTION

Thyroid-associated ophthalmopathy (TAO) is a chronic au-

toimmune inflammatory disease affecting the soft tissues of the orbit, extraocular muscles, eyeballs, and ocular adnexa associated with thyroid autoimmune pathology. It is mostly associated with Graves' disease and hyperthyroid-

ism, but it can also occur in patients with euthyroidism or hypothyroidism due to Hashimoto's chronic autoimmune thyroiditis.¹ In pathogenesis, what is essential is a cell and humoral mediated autoimmune process against orbital antigens, leading to lymphocyte infiltration, fibroblast proliferation, adipogenesis, and accumulation of glucosaminoglycans in the soft tissues of the orbit. This is associated with an increase in their volume and a typical spindle-like thickening of the extraocular muscles.

The natural evolution of the disease includes an active inflammatory phase which takes 6 months to 5 years to go into an inactive fibrous phase. The use of the CAS (clinical activity score) allows clinicians to assess disease activity and NOSPECS classification – for the severity of the ophthalmopathy.^{2,3} Determining the phase of the disease is crucial to the right therapeutic approach.

Clinical signs are determined by the development of an autoimmune inflammatory process and include eyelid retraction, exophthalmos, edema and hyperemia of eyelids and conjunctiva, diplopia, spontaneous retrobulbar pain, pain upon eyeball movement. In 3%-8.6%, severe forms of TAO are observed with the development of dysthyroid optic neuropathy (DON) by compressing the optic nerve in the orbital apex by the enlarged extraocular muscles.⁴ DON signs include reduced visual acuity, changes in visual field, impaired color vision, changes in pupillary responses, edema or atrophy of the optic nerve disc.

A number of studies have indicated a higher risk for individuals with thyroid disease of having ocular hypertension or glaucoma.^{5,6} Approximately 25% of patients with TAO have elevated intraocular pressure (IOP). The main reason for this is the increased intra-orbital pressure from the increased volume of soft tissues, resulting in disturbances in venous circulation and increased episcleral pressure. Long-lasting ocular hypertension can lead to the development of glaucoma with definitive impairment. Cases of severe TAO with high IOP and visual field defects requiring shutdown of DON and differential diagnosis of glaucoma are diagnostic challenges. The presence of ocular hypertension or glaucoma requires continuous IOP monitoring and treatment review whereas the presence of dysthyroid optic neuropathy determines a severe TAO grade with vision-threatening signs and requires immediate therapeutic intervention. Computed tomography shows extraocular muscle enlargement, the extent of the proptosis, and allows the calculation of the Barrett's risk assessment index of DON.

The aim of this study is to present a patient with an active thyroid-associated ophthalmopathy which has high IOP values, visual field defects and reduced visual acuity.

CASE REPORT

A 52-year-old patient with autoimmune thyroid disease (Hashimoto's thyroiditis) since 2010, on hormone replacement therapy with levothyroxine, with non-insulin depen-

dent diabetes mellitus since 2013, a smoker, with no family history of thyroid pathology. In 2017 she noticed edema on the eyelids, conjunctival hyperaemia, bilateral exophthalmos with burning and tearing. In hormone testing hypothyroidism was found (TSH 6 μ IU/l, range 0.34-5.6 μ IU/l) and elevated TRAb 13 IU/l (range 0-1.75 IU/l), anti-thyroglobulin antibodies (anti-TG) 1107 IU/ml (range 0-115 IU/ml), anti-thyroid peroxidase antibodies (anti-TPO) 1721 IU/ml (range 0-34 IU/ml). Diagnosed active TAO 2b3b, CAS 5 points.

From April to August 2018, a pulse therapy with corticosteroids to a cumulative dose of 5750 mg was administered without affecting the activity of TAO and retaining high immunological activity (April 2018 TRAb - 17.54 UI/l, August 2018 TRAb - 18.69 UI/l). A total thyroidectomy was performed in November 2018 with a histological result of colloid nodular goiter with focal lymphocytic thyroiditis. Due to high IOP values, anti-hypertensive treatment with a carbonic anhydrase inhibitor started in June 2018, subsequently a prostaglandin preparation, a beta-blocker and an alpha-agonist were added. The patient entered an eye clinic in March 2019 with complaints of decreased vision for a month, diplopia, exophthalmos, edema and redness of the eyelids and conjunctiva. The clinical examination showed hypermetropic astigmatism in both eyes with best corrected visual acuity for right eye 0.6 and left eye 0.3, upper and lower eyelid retraction with pronounced lid edema and hyperemia, conjunctival and caruncular hyperemia and chemosis, transparent ocular media, sluggish pupil reactions to light (**Fig. 1**). In ophthalmoscopy, the optic nerve disc borders were veiled, without glaucoma excavation, pronounced tortuosity and dilation of the venules, retina - no change from diabetes, macules - with a clear reflex. Colour vision was preserved for both eyes. The degree of exophthalmos, measured by Hertel's exophthalmometry, showed 30 mm for the right eye and 31 mm for the left eye. The intraocular pressure was high, despite the thera-



Figure 1. Image of our patient showing active disease as manifested by eyelid hyperemia, eyelid edema, conjunctival injection, and caruncular edema.

py, and showed values of 26 mm Hg for the right eye and 21 mm Hg for the left eye, measured by Goldman tonometry in the first position of the eyeball. Upon looking upwards at 30°, higher IOP values were found (27 mm Hg for the right eye

and 23 mm Hg for the left eye). The central corneal thickness of the right eye was 593 μm and of the left eye it was 604 μm . Diplopia was found in all viewing directions with a slight limitation of the left eye's motility nasally (mild abduction deficiency).

A computer perimetry for visual field examination (Humphrey Field Analyzer II 30-2, Threshold Test) was performed, which showed a localized defect in the lower-left temporal quadrant of the left eye and points with diminished light sensitivity of the right eye (Fig. 2). Optical coherent tomography of optic nerves and macules did not show any changes.

Computed tomography (CT) of orbits carried out on a 16-slice computer tomograph (Bright Speed, General Electric) identified bilateral exophthalmos, edema of the soft orbital tissue, thickening of all extraocular muscles of both eyes,

and compression of the optic nerves (Fig. 3). The thickness of the extraocular muscles was measured in axial and coronal scans and the Barrett's index (BI) was calculated for each orbit (Table 1, Figs 3 and 4).

Table 1. Thickness of extraocular muscles and BI for both eyes

Indicator	Right eye	Left eye
Medial rectus	10.2 mm	12 mm
Lateral rectus	10.9 mm	8.4 mm
Superior Muscle Complex	4.8 mm	4.7 mm
Inferior rectus	10 mm	8.9 mm
Barrett's Index	62%	51%

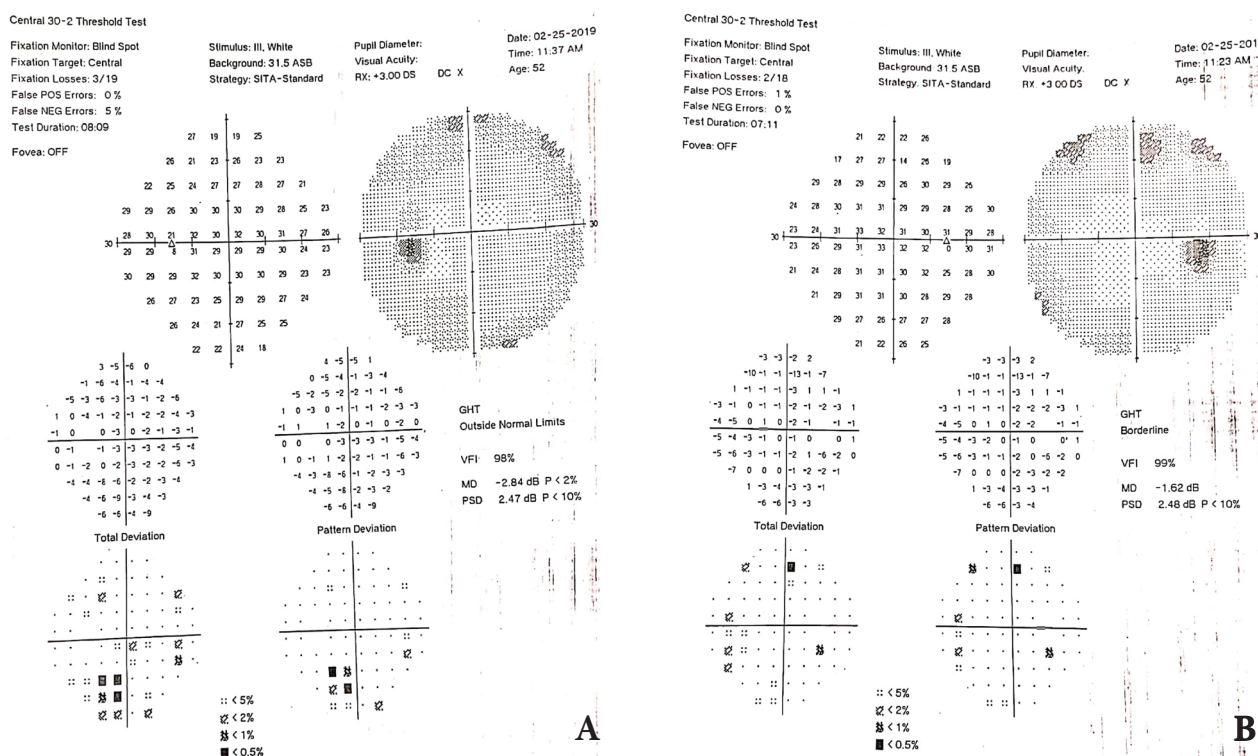


Figure 2. Visual field examination showing a localized defect in the lower-left temporal quadrant of the left eye (A) and points with decreased light sensitivity of the right eye (B).

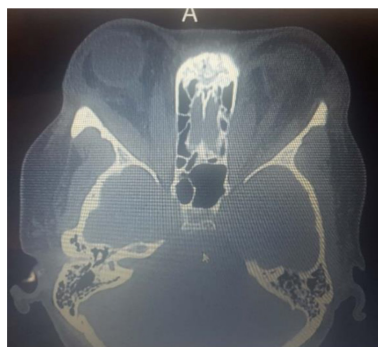


Figure 3. CT imaging identifying enlarged extraocular muscles and proptosis.



Figure 4. Coronal CT with Barrett's index calculation.

Laboratory studies showed normal values of TSH and high values of TRAb - 20.2 IU/l.

Using the scale for clinical activity (CAS) we determined a TAO activity of 6 points, and under NOSPECS classification - severity 2c3c4a6a.

Our results confirmed the presence of dysthyroid optic neuropathy based on decreased visual acuity, ophthalmoscopic evaluation of the optic nerve disc, lack of glaucoma OCT changes, atypical visual fields changes and CT data.

DISCUSSION

Thyroid-associated ophthalmopathy is the most common extrathyroidal disorder in patients with Graves' disease and occurs significantly less frequently (5%-10%) in patients with autoimmune Hashimoto's thyroiditis. Although TAO is observed more often among females, in the severe forms of ophthalmopathy the relative share of men increases.⁷ Smoking is the most important risk factor, both related to the development and worsening of TAO.⁸ Smoking slows down and worsens the effect of immunosuppressive treatment in already established TAO. Poorly controlled thyroid function (both hyper- and hypothyroidism) aggravates ophthalmopathy. Therefore, the aim is to timely restore and maintain euthyroid state in all patients with TAO. High titres of thyrotropin-receptor antibodies (TRAb) are a risk factor for the occurrence of TAO, and their high retention has a poor prognosis with regard to ocular manifestations. A correlation between titres of TRAb and TAO activity has been determined. Mouritis and Gerding report a strong correlation between the TRAb and CAS ($p=0.54$) as well as between the proptosis and the TRAb levels.⁹ Eckstein et al. have recognized the role of TRAb for predicting the response to anti-inflammatory treatment and have established the persistence of antibodies in 93% of patients with a poor therapeutic response.^{10,11} TRAb are considered to be an independent risk factor for TAO, and their study supports the diagnosis, prognosis and follow-up during TAO treatment. In our clinical case, an increase in TRAb titres was observed despite the immunosuppressive treatment with corticosteroids.

Dysthyroid optic neuropathy belongs to the most severe manifestations of TAO and occurs in 3-8%. A EUGOGO study found that in 33% of cases of DON there was no evidence of proptosis greater than 21 mm.¹² In these cases, when increasing the volume of soft tissues of the orbit, the rigid and non-elastic structures of the anterior orbital septum do not allow spontaneous decompression with bulb protrusion, which results in the optic nerve compression. For the development of DON in our patient, both the nerve compression of the thickened muscle in the orbital apex and the mechanical stretching of the nerve at the extreme exophthalmos are responsible. It is believed that advanced age and the accompanying diabetes are risk factors for the development of DON, probably due to the accompanying vasculopathy and more pronounced susceptibility to dam-

age to the optic nerve from mechanical factors in TAO.

CT gives us a diagnostic opportunity for DON risk assessment by calculating the Barrett's index (BI), which takes into account the percentage of muscular occupation from the height/width of the orbit.¹³ In patients with DON, BI is found to be greater than 50%, and Barrett assumes that a 67% muscle index can be practically diagnosis for DON.¹⁴ In our case, the BI for the right eye is 62%; left eye - 51%.

Elevated intraocular pressure is a common symptom in TAO patients and is due to increased intraorbital and episcleral venous pressure, which worsening outflow of the aqueous humor as well as the accumulation of mucopolysaccharides in the trabecular meshwork. In a retrospective study of 482 TAO patients, Kalmann and Mourits found ocular hypertension in 3.9% of cases compared to the general population, where the rate was 1.6%.¹⁵ Another mechanism for increasing IOP is the pressing of the eyeball from the enlarged extraocular muscles. In the interpretation of IOP values, the position of the eyeball should be taken into account when conducting the study. A number of studies have reported higher IOP values when deflecting the eyeball 30° upwards due to its compression from the rigid and enlarged lower right muscles.¹⁶ When examining patients with TAO and IOP measuring, the presence of disease activity as well as the conducted treatment should be taken into account. Behrouzi examined 117 TAO patients and found that in patients with ocular hypertension, the active forms predominate. In the study group he established a rate of ocular hypertension of 8.5% and 2.5% of cases with glaucoma.¹⁷ Determining the activity and severity of TAO is important for the choice of treatment. Patients with disease activity are indicated for corticosteroid therapy, which may affect IOP values.

In patients with TAO who have high IOP, decreased vision and visual field defects, DON should be suspected and differential diagnosis of glaucoma should be made. In these cases, decreased visual acuity, changes in pupil reaction to light, impaired color vision, ophthalmoscopic evaluation of the optic disc, the lack of glaucoma OCT changes, atypical perimetric changes and CT data are important to support the diagnosis of DON.

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Глазная гипертензия, глаукома или компрессионная нейропатия у пациента с активным ТАО

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Резюме

Введение: Тяжёлые случаи тиреоид-ассоциированной офтальмопатии (ТАО) с внутриглазным давлением и дефектами поля зрения представляют собой реальную диагностическую проблему, требующую исключения дистиреоидной оптической нейропатии (ДОН) и дифференциальной диагностики глаукомы.

Цель: Сообщить о пациенте с активной ТАО, снижением остроты зрения и повышением внутриглазного давления.

Материалы и методы: Мы представляем случай 52-летней женщины с ТАО обоих глаз, класса 2с3с4а6а (NOSPECS), с шестью точками активности (согласно CAS), которая прошла курс лечения кортикостероидами с максимальной кумулятивной дозой 5750 мг, с инсулиннезависимым сахарным диабетом и местное антигипертензивное лечение таптикам, бризадопом и люксфеном. Больная прошла полное обследование глаза, тонометрию, экзофтальмометрию, компьютерную периметрию, оптическую когерентную томографию (ОКТ) и компьютерную томографию (КТ) глазных орбит.

Результаты: Были получены следующие результаты: коррекция остроты зрения (BCVA) на правом глазу = 0,6, BCVA, на левом глазу = 0,3; TOD = 26 мм mm Hg и TOS = 21 мм mm Hg; экзофтальмометрия: 30 мм для правого глаза и 31 мм для левого; диплопия во всех направлениях, отёк и гиперемия век и конъюнктивы, ретракция век, вялые зрачковые реакции, нормальное цветовое зрение, ясная глазная среда, нечёткие границы диска зрительного нерва, отсутствие глаукоматозной экскавации, перекручивание и дилатация венул – отсутствие диабетических изменений, макулы – с нормальным рефлексом; Данные компьютерной периметрии на наличие дефекта поля зрения нижневисочной области коры. Данные КТ на наличие утолщения экстраокулярных мышц, отека мягких тканей и сдавления зрительного нерва.

Выводы: Наши результаты подтвердили наличие дистиреоидной оптической нейропатии, основанной на снижении остроты зрения, офтальмоскопической оценке головки зрительного нерва, отсутствии глаукоматозных изменений при ОКТ, атипичных периметрических изменениях и данных КТ. Оптическая нейропатия является наиболее тяжёлым осложнением у пациентов с ТАО, которое развивается вследствие сдавления зрительного нерва и / или его кровоснабжения увеличенными экстраокулярными мышцами и мягкими тканями на вершине орбиты и в результате механического напряжения зрительного нерва, в случае наличия умеренного или тяжёлого проптоза.

Ключевые слова

тиреоидная офтальмопатия
