



## LAPORAN KASUS—CASE REPORT

# THYROID-ASSOCIATED OPHTHALMOPATHY WITH SUSPECTED SECONDARY GLAUCOMA

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### Abstract

**Introduction:** Thyroid-associated ophthalmopathy (TAO) is a thyroid hormone imbalance that manifests in the eye. The most common TAO is in Grave's Disease. TAO could increase the intraocular pressure and could cause a glaucoma optic neuropathy and therefore secondary glaucoma could happen.

We are reporting a 26 years old male came to the West Nusa Tenggara Eye Clinic both eyes bulging since 10 months ago. This patient's complain happens with red eyes, dirt around the eyelashes, pain around the eye, feeling tired, heart beats faster, and no weight gain. This patient came again after not taking his usual medicine for one month.

Based on the eyes examination, this patient had lagophthalmos and proptosis on both eyes, palpebra oedema, hyperaemia on tarsal conjunctiva, conjunctiva injection, corneal infiltrate, limited eyeball movement for both eyes, and increased intraocular pressure. The laboratory result shows hyperthyroid and head CT scan shows medial lateral rectus muscle hypertrophy. This patient was given timolol maleate eye drop 0,5% and levofloxacin eye drop 0,5%.

Early identification of the diagnosis and controlled therapy of TAO could prevent the secondary glaucoma.

**Keywords:** *Thyroid-associated ophthalmopathy, secondary glaucoma, Grave's Disease, steroid.*

## INTRODUCTION

Thyroid-associated ophthalmopathy (TAO) is a thyroid hormone imbalance that manifests to the eye which could happen because of an increase in free thyroid hormone and suppressed thyroid stimulating hormone (TSH). TSH could increase in Grave's Disease (80%) which is the most common cause of hyperthyroidism. It is estimated that 16 per 100,000 women in the general population and 2.9 per 100,000 men in the general population suffer from TAO. TAO can be demonstrated by clinical symptoms in the eye such as corneal irritation, chemosis, extraocular muscle dysfunction, proptosis, strabismus, and eyelid

retraction. TAO is a disease that needs to be controlled medically, not taking medication for a long time can worsen TAO and can develop secondary glaucoma.<sup>1,2</sup>

Secondary glaucoma is a form of glaucoma in which there is an identifiable cause of increased intraocular pressure (IOP), and could result in optic nerve damage and vision loss. IOP increase could happen in TAO. Consequently, it can lead to glaucomatous optic neuropathy because (according to European Glaucoma Society guidelines) ocular hypertension is the most important risk factor for glaucoma development. Increased IOP is determined by aqueous humour production, aqueous humour outflow, and episcleral venous

pressure level. In TAO, increased orbital pressure results in increased episcleral venous pressure leading to an increase in IOP. Glaucoma can occur in the course of TAO in 0.8 – 13% of patients.<sup>3,4</sup>

We report a case of thyroid-associated ophthalmopathy in a 26 years old male that develops a secondary glaucoma.

## CASE ILLUSTRATION

A 26 years old male from Mataram, West Nusa Tenggara, works in the parking lot came to Ophthalmology Outpatient Clinic at the West Nusa Tenggara General Hospital (RSUDP NTB) on March 10, 2022. This patient came with the complaint of watery eyes since one month ago. This complaint is accompanied by protrude eyes, sore especially when exposed to dust, red, and lots of dirt like pus around the eyelashes, especially after the patient wakes up. The patient feels this complaint throughout the day. Initially in May 2021, the patient complaint were protrude eyes, feeling tired easily, easily hungry and thirsty, sweating frequently, palpitating frequently, and losing weight despite eating a lot. Then the patient feels both eyes protrude and it is difficult to blink and could not close his eyes completely so that the eyes become dry, red, and sore. Then the patient checked himself into the Ophthalmology Outpatient Clinic of the RSUDP NTB with these complaints and was diagnosed with TAO. The patient has received several medications such as Cendo xitrol eye drops, Cendo Lyteers eye drops, methylprednisolone 40 mg tablet since May 2021 until August 2021, and gentamicin eye ointment. The patient has been always came to the Ophthalmology Outpatient Clinic to evaluate his complaints every month since May 2021, but the patient has missed a month of control so that the patient does not take medication during January 2022 until February 2022. Currently, the patient is coming back to the Ophthalmology Outpatient Clinic of RSUDP NTB because of complaints of watery, red, sore eyes and are currently more severe. The patient's eyes are still protrude. The patient also complains of headaches and neck pain which is often felt every time he wakes up.

Physical examination was done in this patient. He shows good general condition, compos mentis, the blood pressure was 130/80 mmHg, HR 83x/minutes, RR 15x/minutes, and axillary temperature 36.6oC. Ophthalmological examination revealed that the visual acuity of right eye was 6/18 and left eye 6/15 (Snellen chart) and could achieve 6/6 with S-1,25 and S- 1,00 for right and left eyes respectively. There is a limitations in moving the eyeball to all directions with no pain and narrowed field of view. The patient's eyes had exophthalmos and lagophthalmos for both eyes, oedema on both superior palpebra, and dirty on both eye's cilia. For the conjunctiva, we could see hyperaemia on superior and inferior tarsal conjunctiva for both eyes. Conjunctival injection, ciliary injection, peri corneal injection, and chemosis could be seen in bulbi conjunctiva for both eyes. There is infiltrate in this patient's cornea for both eyes (Figure 1). The IOP is measured with non-contact tonometry (NCT) and is measured 26.8 mmHg and 28.3 mmHg for right and left eyes respectively. Ophthalmoscopy examination are normal for both eyes. The patient had checked for his thyroid level and the result for his TSH was 0.11 uIU/mL (Normal = 0.27 – 4.7 uIU/mL) and FT4 64.09 Pmol/L (Normal = 10.60 – 19.40 Pmol/L). Head CT scan was done in this patient and the result was medial lateral rectus muscle hypertrophy for both eyes superior and inferior.



**Figure 1.** Patient's eyes that shows hyperaemia, oedema, conjunctival injection, proptosis, and lagophthalmos.

Patient was diagnosed with TAO with moderate to severe European Group of Graves' Orbitopathy (EUGOGO) classification and Clinical Activity Score (CAS) 6 and suspected secondary



glaucoma for both eyes. The therapy given to this patient was Cendo lyteers eye drops every hour 1 drop for both eyes, levocin eye drop 4 times a day 1 drop for both eyes, chloramphenicol eye ointment, and Cendo timolol 0,5% eye drop 2 times a day 1 drop for moth eyes.

## DISCUSSION

Grave's disease is the most common cause of bilateral protruding eyes. Usually, the diagnosis of Grave's disease is clinically made. The symptoms for Grave's disease are weight loss despite of increased appetite and increased amount of intake, protruding eyes, eyelid oedema, decreased vision acuity, decreased eyeball motility, palpitations, fatigue, weakness, tremor, excessive sweat. For the physical signs of Grave's disease are prominence of eyes, lid lag, globe lag, exophthalmos, lid oedema, chemosis, extraocular muscle weakness, decreased visual acuity, and tachycardia. In Grave's disease, the pituitary gland will try to compensate for the excess T3 and T4 hormones in the blood and it could stop the production of TSH, so in Grave's disease the TSH level in the blood would be very low and high FT4 level.<sup>5,6</sup>

Thyroid-associated ophthalmopathy is characterized by enlargement of the extraocular muscles as well as an increase in orbital fat volume. Although the exact mechanism is unknown, antibodies to TSH appear to cross-react with antigens in the orbit resulting in infiltration by activated T lymphocytes, with subsequent release of inflammatory mediators. Muscle is infiltrated with inflammatory cells (lymphocytes, macrophages, plasma cells, and eosinophils), and mucopolysaccharide deposition is increased. Extraocular muscles that are involved are levator palpebra superioris muscle, inferior rectus muscle, medial rectus muscle, superior rectus muscle, lateral rectus muscle. oblique muscles. The increase in orbital fat volume is the result of venous congestion from compression of the superior ophthalmic vein by enlarged muscles and/or intrinsic adipose inflammation. This pathophysiology of Grave's disease could result in

proptosis, restrictive myopathy, and exophthalmos.<sup>1,7</sup>

This patient's complaints are both eyes protruding, the eyelids could not cover the entire eyeball, causing the eyes to feel red and sore when exposed to the dust. From systemic complaints, symptoms show hyperthyroid which are feeling tired easily, easily hungry and thirsty, sweating frequently, palpitating frequently, and losing weight despite eating a lot. The laboratory shows low TSH and low FT4 which strengthen the hyperthyroid diagnosis. In the head CT scan that this patient's did, the result showed was medial lateral rectus muscle hypertrophy for both eyes superior and inferior. Based on the history, physical examination, the eye manifestation of Grave's disease is shown, which are decreased vision acuity, extraocular weakness which is shown in patient's inability to look to all directions and narrowed visual field, protruded eyes, exophthalmos and lagophthalmos, and oedema on both superior palpebra. Patient's lagophthalmos caused conjunctivitis for both eyes. Based on patient's history, physical examination, laboratory result, and head CT scan could be concluded that this patient is diagnosed with thyroid-associated ophthalmopathy.

Based on the 2021 EUGOGO guideline, patient with thyroid-associated ophthalmopathy should be classified into CAS and EUGOGO severity classification. CAS (Table 1) is used for assessing patient's activity and EUGOGO severity classification (Table 2) is used for determine patient's management.<sup>6</sup> This patient's CAS score is 6 and considered as active Grave's orbitopathy because there is redness of conjunctiva, swelling of caruncle or plica, swelling of eyelids, swelling of conjunctiva, a decrease in eye motility of >80, and a decrease in visual acuity in the last 1 – 3 months. For the EUGOGO classification, this patient is in moderate-to-severe Grave's orbitopathy because there is a moderate soft-tissue involvement and exophthalmos. So, this patient is diagnosed with TAO with moderate to severe EUGOGO classification and CAS 6.



**Table 1. Clinical Activity Score.6**

<b>For initial CAS score items 1 - 7</b>	
1.	Spontaneous retrobulbar pain
2.	Pain on attempted upward or downward gaze
3.	Redness of eyelids
4.	Redness of conjunctiva
5.	Swelling of caruncle or plica
6.	Swelling of eyelids
7.	Swelling of conjunctiva (chemosis)
<b>Follow-up after 1 - 3 months score items including 8 - 10</b>	
8.	Increase in exophthalmos of $\geq 2$ mm
9.	A decrease in eye motility of $\geq 8^\circ$
10.	A decrease in visual acuity in the last 1-3 months
CAS < 3 = inactive GO; CAS $\geq 3$ = active GO	

**Table 2. Classification of severity of Grave's Orbitopathy.6**

Classification	For initial CAS score items 1 - 7
Mild GO	<p>Patients whose features of GO have only a minor impact on daily life that have insufficient impact to justify immunomodulation or surgical treatment. They usually have one or more of the following:</p> <ul style="list-style-type: none"> <li>• minor lid retraction (&lt;2 mm)</li> <li>• mild soft-tissue involvement</li> <li>• exophthalmos</li> <li>• &lt;3 mm above normal for race and gender</li> <li>• no or intermittent diplopia and corneal exposure responsive to lubricants</li> </ul>
Moderate-to-severe GO	<p>Patients without sight-threatening GO whose eye disease has sufficient impact on daily life to justify the risks of immunosuppression (if active) or surgical intervention (if inactive). They usually have two or more of the following:</p> <ul style="list-style-type: none"> <li>• lid retraction <math>\geq 2</math> mm</li> <li>• moderate or severe soft-tissue involvement</li> <li>• exophthalmos <math>\geq 3</math> mm above normal for race and gender</li> <li>• inconstant or constant diplopia</li> </ul>
Sight-threatening (very severe) GO	Patients with dysthyroid optic neuropathy and/or corneal breakdown

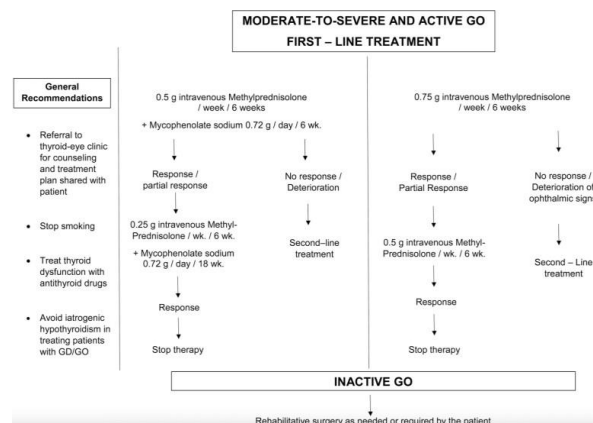
One of uncontrolled TAO's complication is secondary glaucoma. Excessive or underactivity of the thyroid can be associated with problems in and around the eyes. The socket in which the eye is located can be affected by inflammation; fluid and white blood cells can collect in the tissue behind and beside the eye, causing swelling. This swelling pushes the eye forward so that it protrudes, the blood vessels around the eye open wide making it look red and angry and the eyelid is pulled back. All of this makes it very difficult to close the eyes

properly. The front window of the eye (cornea) cannot be protected adequately and roughness or even ulcers may form. These can become infected, and may heal leaving scars. In addition to pushing the eye forward, swelling of the tissue behind and to the side of the eyeball increases the pressure inside the eye in at least three ways: first, by simply pressing the back of each eyeball, and second, by making the tissue less elastic. So, when the tiny muscles on the side of the eye try to contract and move the eye from one position to another (an important part of being able to see efficiently), they have to pull against tight resistance and third, the pressure in the blood vessels around the eye. eyes up. It is into these veins that fluid from inside the eye flows, so if the venous pressure rises, so does the eye pressure upstream. Eye pressure can fluctuate widely, with maximum pressures even reaching the range of 40 – 50 mm Hg. The pressure can cause damage to the optic nerve fibers in exactly the same way as in other glaucoma. This type of glaucoma is known as "secondary", because we can identify the cause of the increased eye pressure.8

This patient missed his one-month medication because he did not go to the Ophthalmology Outpatient Clinic to receive his medication. This causes his eyes to stay medically uncontrolled for one month which causes the development of secondary glaucoma. It is seen based on the increased IOP and narrowed visual field.

Based on EUGOGO guideline, the medication for moderate-to-severe TAO is as shown in Figure 2.6 This patient already had steroid before. So, for this time's treatment, the patient needed Cendo lyteers eye drops every hour 1 drop for both eyes, Levocin eye drop 4 times a day 1 drop for both eyes, Chloramphenicol eye ointment, and Cendo timolol 0,5% eye drop 2 times a day 1 drop for moth eyes. Conjunctivitis in patient could be caused by lagophthalmos. This condition is exacerbated with patient's daily work in the parking lot which exposed to dust all day. Antibiotic eye drop and topical antibiotic are

effective to treat conjunctivitis and so the patient was given both.9 Cendo Lyteers was given to reduce the dry eyes syndrome in patient. Levocin eye drop and chloramphenicol eye ointment are topical antibiotic and was given for the conjunctivitis caused by patient's lagophthalmos. Timolol maleate is a nonselective beta-blocker that could reduce IOP. It is suggested that timolol could reduce the formation of aqueous humour in the ciliary body in the eye.10 Cendo timolol 0.5% was given to reduce patient's increased IOP.



**Figure 2.** Algorithm for the first-line management of moderate-to-severe and active Graves' orbitopathy.

## CONCLUSION

A 26 years old male was diagnosed with TAO with moderate to severe EUGOGO classification and CAS 6 with suspected secondary glaucoma. Uncontrolled medication could exacerbate patient's condition and could develop secondary glaucoma. By identifying risk factors, management will be more effective and efficient.

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