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KOL KNOCKOUT™: OCULOPLASTICS EDITION

8 CASES OF TAILORED TREATMENT FOR THYROID EYE DISEASE


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Content Source

This continuing medical education (CME) activity captures content from two live-virtual symposia and one in-person symposium.

Activity Description

This supplement summarizes a discussion on thyroid eye disease (TED), including clinical findings, laboratory findings, medical and surgical treatments, and comanagment strategies used to ensure the best possible patient care and outcomes.

Target Audience

This certified CME activity is designed for oculoplastic surgeons, neuro-ophthalmologists, and general ophthalmologists.

Learning Objectives

Upon completion of this activity, the participant should be able to:

- **Conduct** comprehensive clinical assessments, including the appropriate use of laboratory tests and radiologic imaging, to recognize the heterogenous presentation of TED and ascertain potential thyroid dysfunction
- **Propose** medically relevant treatment regimens together with customized surgical approaches to address the physical burden and reduced quality of life due to TED
- **Formulate** effective comanagement strategies with relevant health care professionals to optimize treatment outcomes and manage adverse events

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PRETEST QUESTIONS

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1. Please rate your confidence in your ability to formulate effective thyroid eye disease (TED) comanagement strategies with relevant health care professionals (based on a scale of 1 to 5, with 1 being not at all confident and 5 being extremely confident).

a. 1
b. 2
c. 3
d. 4
e. 5

2. A 34-year-old woman with a history of Graves disease treated with methimazole presents with a 3-month history of bilateral eye pain, proptosis, diplopia, and eyelid retraction. Examination reveals 20/20 VA in each eye, full color plates, no afferent pupillary defect, and a Clinical Activity Score of 6. What is the most appropriate initial management strategy?

a. Orbital decompression
b. Orbital radiation
c. Selenium supplementation
d. Teprotumumab

3. A 54-year-old man with no significant past medical history presents complaining of bilateral eye pain and redness. Examination reveals right proptosis, right upper eyelid retraction, bilateral chemosis, and bilateral conjunctival injection. What laboratory and imaging tests would be most appropriate to aid in confirming a diagnosis of TED?

a. Orbital computed tomography (CT), thyroid-stimulating hormone (TSH), free T3, free T4, and thyroid-stimulating immunoglobulin (TSI)
b. Orbital CT, TSH, free T3, and free T4, and serum thyroglobulin (Tg)
c. Orbital ultrasound, TSH, free T3, free T4, and serum Tg
d. Orbital ultrasound, TSH, free T3, free T4, and TSI

4. What is the Kahaly protocol for corticosteroid treatment for TED?

a. 40 mg oral prednisone daily for 6 weeks, then tapered over 6 weeks
b. 500 mg intravenous methylprednisolone weekly for 6 weeks, then 250 mg weekly for 6 weeks
c. 60 mg oral prednisone daily for 6 weeks, then tapered over 6 weeks
d. 1,000 mg intravenous methylprednisolone weekly for 6 weeks, then 500 mg weekly for 6 weeks

5. Orbital radiation should be avoided in patients who are younger than 35 years of age and those who have _____.

a. Retinopathy, severe hypertension, or diabetes mellitus
b. History of cancer, severe hypertension, or diabetes mellitus
c. Retinopathy, glaucoma, or diabetes mellitus
d. History of cancer, retinopathy, or diabetes mellitus

6. Comanagement with which of the following specialties should be considered in the care of patients with TED undergoing treatment with teprotumumab?

a. Rheumatology
b. Endocrinology
c. Gastroenterology
d. Nephrology

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8 CASES OF TAILORED TREATMENT FOR THYROID EYE DISEASE

Thyroid eye disease (TED) is a heterogenous condition with a broad spectrum of severity and clinical findings. Treatments must be tailored to each individual patient to optimize outcomes, considering ancillary testing such as biomarkers and imaging, and often combining medical, surgical, and supportive therapies.[1] The approval of the only targeted therapy for TED, the insulin-like growth factor-1 (IGF-1) receptor inhibitor teprotumumab, has expanded the treatment options for patients.[2] However, this has also introduced an additional level of complexity to treatment decisions. As clinicians incorporate teprotumumab and other biologic medications into their clinical practices, they must consider their indications, efficacy, safety, how they are best combined with other therapies, and how to collaborate with other specialists to manage treatment-associated adverse effects.

The following series of case presentations are from three live-virtual "knockout rounds" in which experts in TED share their insights on how to navigate a rapidly evolving treatment landscape. They discuss the nuances of medical and surgical treatment regimens for TED, including the use of ancillary testing to guide patient care and the most effective comanagement strategies.

ROUND 1 | CASE 1: A 49-YEAR-OLD WITH PROPTOSIS AND PERIORBITAL EDEMA

Andrew R. Harrison, MD: Our first case is a 49-year-old male with a 3-month history of "red eyes" who was initially diagnosed with dry eye disease by his local optometrist and treated with artificial tears. One month prior to presentation to my clinic, he developed orbital pain and was treated with oral prednisone with minimal relief. Two weeks prior to presentation, he developed binocular diplopia. One day prior, his friend told him that his eyes "looked different."

His past medical history was significant for a diagnosis of Graves disease in 2017, for which he underwent radioactive iodine treatment and a subsequent thyroidectomy in 2019. His medications included levothyroxine. He stated that he was a former smoker and had quit in 1998. His most recent thyroid-stimulating hormone (TSH) level was elevated at 6.4 mIU/L.

On examination (Figure 1), marginal reflex distance 1 (MRD1) was 6 mm with 2 mm of superior scleral show and 1 mm of inferior scleral show on both sides. Hertel measurements were 24 mm on the right and 26 mm on the left. Slit lamp examination revealed periocular edema and mild erythema, lagophthalmos, and moderate chemosis but minimal conjunctival injection in both eyes. Strabismus examination demonstrated mildly reduced ocular motility, particularly in abduction and supraduction, with a small exophoria in near gaze. Clinical activity score (CAS) was 6.

Dr. Harrison: What would you do next in the management of this patient with TED?

(Images courtesy of Andrew R. Harrison, MD.)

Figure 1. The patient in Round 1 Case 1 presented with moderate proptosis and significant periorbital soft tissue edema.

Prem S. Subramanian, MD, PhD: You have several treatment options for this patient. But before I begin treatment, I want to first get his chemical hypothyroidism under better control. His TSH was somewhat high, and that could be stimulating the development of newly active TED with soft tissue manifestations. This patient has a CAS of 6 as well as proptosis and diplopia. Intravenous corticosteroids would likely help his pain, but are unlikely to improve the proptosis or diplopia although, they may stabilize the diplopia. Similarly, orbital radiation might stabilize the strabismus and decrease the soft tissue inflammation. He does not have any significant contraindications to these treatments such as diabetes mellitus or diabetic retinopathy.[1]

I would not recommend surgery yet, since he is still in an acutely changing phase. As far as biologic treatments, teprotumumab is US Food and Drug Administration (FDA)-approved for treating patients like this.[2] Proptosis was the primary outcome in the clinical trials for teprotumumab.[3] Tocilizumab and rituximab can also be considered but are off-label for this indication.[1] I would probably start by offering him teprotumumab because he has proptosis in addition to significant soft tissue signs.

(Images courtesy of Andrew R. Harrison, MD.)

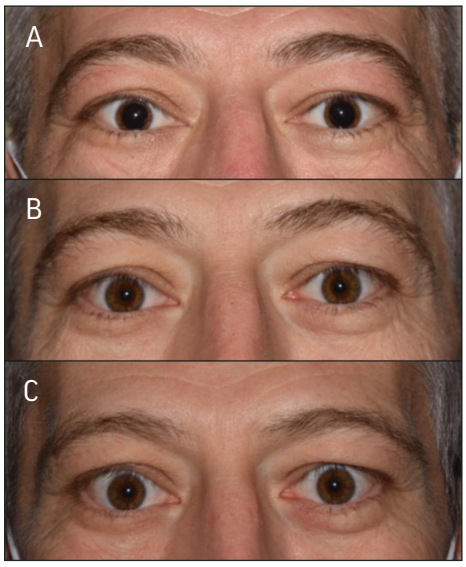


Figure 2. The patient in Round 1 Case 1 at baseline (A) and after four (B) and eight (C) infusions of teprotumumab.

In the majority of patients with active TED, teprotumumab will be beneficial.[3] However, I would start with trying to get his thyroid function under better control first.

Amina Malik, MD: This patient has active TED with pain, diplopia, proptosis, chemosis, and edema that are affecting his quality of life. I would offer teprotumumab as a first-line treatment. Corticosteroids can be helpful to decrease inflammation but are not as effective at improving proptosis.[1] Of course, I would also want to confirm that there were no relevant conditions in his medical history, such as diabetes or hearing issues, prior to starting teprotumumab.[2]

Nicholas Robert Mahoney, MD: I would agree that corticosteroids would be helpful, but teprotumumab is the better option to reduce the proptosis.[1,3] I find that patients that present with significant edema also respond well to teprotumumab. I would also agree with getting his thyroid levels under improved control. I would also check a thyroid-stimulating immunoglobulin (TSI) level to get a sense of his antibody productivity. I do not think it is necessary to obtain imaging at this point considering there is no doubt about the diagnosis.

Dr. Harrison: The patient was started on teprotumumab treatment, which is a monoclonal antibody against the IGF-1 receptor. Teprotumumab has been shown to decrease proptosis by 2 mm or more in patients with TED.[3] It is administered as an intravenous infusion every 3 weeks for eight doses, or a total of 24 weeks of treatment.[2] After the full course of teprotumumab treatment, the patient's CAS decreased to 0, and there were improvements in the soft tissue swelling (Figure 2). The proptosis also improved, with Hertel measurements of 21 mm in the right eye and 22 mm in the left eye.

Dr. Harrison: In your practice, what is the effect of teprotumumab on the surgical management of TED?

Dr. Mahoney: Some patients do have regression of the proptosis reduction or relapse after teprotumumab treatment, so we do not know how durable the response will be.[4-7] I would wait 6 months before performing any surgery. Assuming his thyroid levels remain well controlled, and his examination is stable, I would consider surgery after that time. I would also consider local and perioperative corticosteroids at the time of surgery.

Dr. Malik: This is a relatively new drug, so we are still learning as we go. There is no set amount of time that I wait before performing surgery. After the last infusion of teprotumumab, I typically have the patient return in 1 to 3 weeks. If I still see residual proptosis, I will offer surgical decompression. But it is really a discussion with the patient about how symptomatic they are from any residual proptosis they may have and whether they would want to consider surgery. Blepharoplasty is also sometimes needed after teprotumumab treatment, since edema can stretch the skin, and there can be residual fat prolapse. For this type of surgery, I usually wait 6 months to make sure there are no disease flares or reactivation. I would also like to see that the patient has been euthyroid for at least 6 months.

Dr. Subramanian: Addressing what bothers each individual patient is really key. So, I do not have a problem with doing an orbital decompression relatively soon after teprotumumab treatment is finished, if a patient has residual proptosis that is bothersome to them. The literature shows that if these patients are going to have regression of their treatment effect, it typically happens at about 9 to 12 months after treatment.[4,5] And we do not know if operating would actually reduce that risk. However, I do wait for 6 to 9 months before performing strabismus or eyelid surgery on these individuals because I have seen some paradoxical worsening of strabismus in the period after teprotumumab is administered. I think a fibrotic process can set in once the inflammatory aspect of the disease resolves from treatment.

ROUND 1 | CASE 2: A 49-YEAR-OLD WITH UNILATERAL PROPTOSIS AND LACRIMAL GLAND ENLARGEMENT

Dr. Harrison: The next case is a 49-year-old female who presented to an outside institution with left-sided proptosis, blurred vision, dryness, and a pressure sensation. She had no significant past ocular or medical history. On examination, VA was 20/15 in the right eye and 20/20 in the left eye. Intraocular pressures were 25 mm Hg and 28 mm Hg in the right and left eyes, respectively. Ishihara color plates and confrontational visual fields were full in both eyes. Extraocular motility was full in the right eye, and there was trace restriction in upgaze in the left eye. There was proptosis of the left eye, with Hertel measurements of 20 mm in the right eye and 22 mm in the left eye (Figure 3). MRD1 was 5 mm on the right side and 7 mm on the left side.

What additional testing would you obtain for this patient?

Dr. Malik: In a patient with no previous medical history and unilateral proptosis, TED is in the differential diagnosis, but I would definitely want to obtain additional workup. I usually start with computed tomography (CT) imaging of the orbits

(Images courtesy of Andrew R. Harrison, MD.)

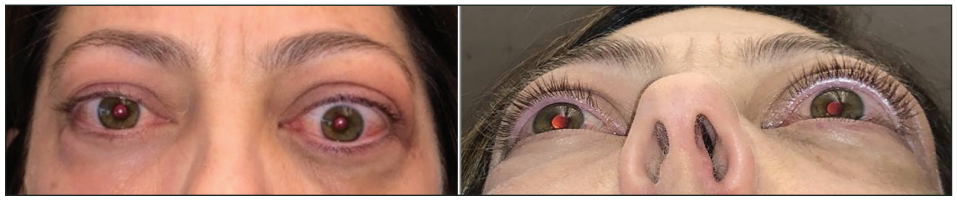


Figure 3. The patient in Round 1 Case 2 presented to an outside institution with proptosis of the left eye with an increased marginal reflex distance 1.

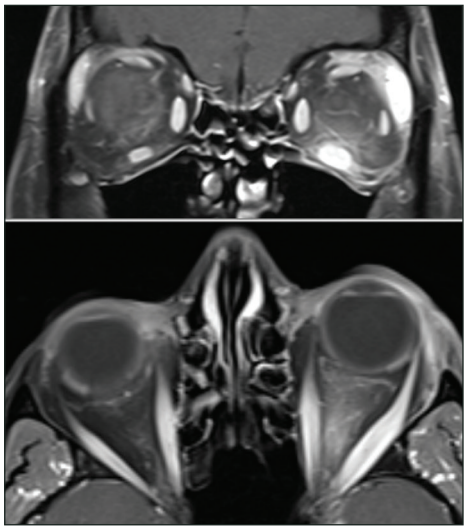


Figure 4. Magnetic resonance imaging (MRI) of the orbits of the patient in Round 1 Case 2, on presentation to the outside institution, showed enlargement and enhancement of the left lacrimal gland, lateral rectus, and inferior rectus.

without contrast to rule out other etiologies for the proptosis such as an orbital tumor. CT can also show classic signs of TED such as enlargement of the extraocular muscles and increased orbital fat. I would also want to obtain thyroid levels and antibodies.

Dr. Subramanian: I absolutely agree that further workup is needed. I would get magnetic resonance imaging (MRI) of the orbits instead of a CT in this patient. I often obtain a CT when TED is the most likely diagnosis. But in this case, I would like to look for alternative diagnoses as well. For example, I would like to be able to visualize the superior ophthalmic vein (SOV), because carotid-cavernous fistula is on the differential. MRI of the orbits will show if there is any abnormal enhancement. T2 or short tau inversion recovery (STIR) hyperintensity in the extraocular muscles can help to confirm a diagnosis of TED. I

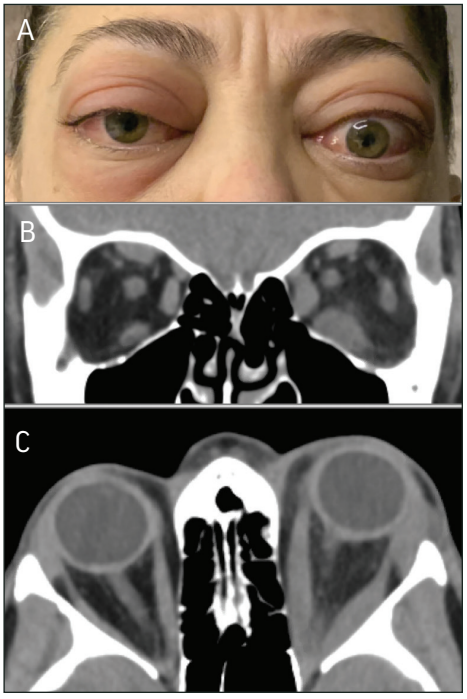


Figure 5. The patient in Round 1 Case 2 upon presentation to Dr. Harrison's clinic after being treated with oral prednisone for presumed orbital pseudotumor. There was significant periorbital erythema and edema and worsening of the left-sided proptosis (A). Computed tomography of the orbits of the patient in Round 1 Case 2 after treatment with oral prednisone. There was enlargement of the inferior, medial, and lateral rectus muscles on the left side with relative sparing of the muscle tendons (B).

also do not want to give iodinated contrast to patients with suspected TED because that can lead to worsening of their disease.[6] I would also obtain thyroid function tests, TSI, and thyrotropin receptor antibodies (TRAb) to confirm a diagnosis of TED. I would probably get a complete blood count (CBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) as well to look for inflammatory disease.

Dr. Mahoney: Clinically, this case is suspicious for TED. There is subtle lateral flare even on the right side. There is also enlarged retroorbicularis oculi fat (ROOF) and thinning of the brows.[9] To me, TED is high enough on the differential. There was nothing to indicate a carotid-cavernous fistula other than that the proptosis is unilateral—no bruit, decreased corneal sensation, sixth nerve palsy, or anything else localized to the cavernous sinus. The conjunctival injection does not look like episcleral flush. I would obtain a CT of the orbits without contrast, TSI, and CBC. I probably would not check ESR or CRP. If an inflammatory workup is needed, we can do that after the imaging is completed.

Dr. Harrison: At this point, the patient was still being managed at an outside institution. MRI of the orbits showed enlargement and enhancement of the left lacrimal gland, lateral rectus, and inferior rectus (Figure 4). TSH was low at less than 0.01 mIU/L, and free T4 and T3 were within normal limits. The patient was started on an oral corticosteroid taper.

Dr. Harrison: After the corticosteroid taper was completed, the patient returned for follow-up, and the left proptosis had worsened. A left orbitotomy with lacrimal gland biopsy was then performed. Pathology showed chronic inflammation and was negative for lymphoma or IgG4-related disease. The patient was diagnosed with orbital pseudotumor and was treated with oral prednisone.

At this time, the patient presented to my clinic. VA was 20/20 in both eyes. Motility of the left eye was limited in multiple directions of gaze, with esotropia and hypotropia in primary gaze. Hertel measurements were 23 mm on the right and 26 mm on the left. There was worsening of the periorbital and ocular edema (Figure 5A). CT of the orbits showed enlargement of the left inferior, medial, and lateral rectus muscles with relative sparing of the tendons (Figure 5B). TSI was pending.

Dr. Harrison: What is your working diagnosis at this point, and what would you do next?

Dr. Mahoney: It certainly could still be TED. There is enlargement of the medial and inferior rectus muscles with tendon sparing. Sometimes TED does involve the lacrimal gland, and it can involve any of the extraocular muscles. The SOV looks normal, and this does not look like a carotid-cavernous fistula. To me, this is still concerning for TED. TSI testing would be necessary and is a very sensitive test for this.[10] The patient's TSH is also low. In patients with suspected TED, if they have a hyperacute presentation and you are going to administer corticosteroids, the intravenous route is preferable. I usually give 500 mg of intravenous methylprednisolone weekly for 6 weeks and then 250 mg weekly for 6 weeks.[11]

Dr. Subramanian: I agree that the imaging is potentially consistent with TED. The lack of any significant response to corticosteroids also supports this, since other types of orbital inflammation such as orbital pseudotumor usually respond quite quickly to at least a reasonable dose of oral corticosteroid within a few days. TED treated with corticosteroids often takes a little bit longer to respond. I too would like to see a TSI and a TRAb to help cement a diagnosis. Intravenous steroids in a pulsed fashion at this point would make sense and might be diagnostically helpful. The only thing that is atypical from the external photograph is that there is more edema and almost ptosis on the right side, and that suggestion of lateral flare that was there previously is gone. It could just be because she is so inflamed. But that does concern me just a little bit that this could be an alternate diagnosis. I would not jump straight to another biopsy, though, at this point.

Dr. Malik: I agree that orbital inflammatory disease would typically respond to corticosteroids. Lacrimal gland involvement can occur in TED. I would also consider intravenous corticosteroids and obtaining TRAb as the next steps. In addition, some patients may not have serological evidence of TED, but clinically, they may still have the disease and may need treatment.

Dr. Harrison: The patient's TSI was elevated at 2.6 (reference index <1.3). Do you prefer to use TSI, TRAb, or both for your patients with TED?

Dr. Subramanian: There are two kinds of TSI assays. The real TSI is a cell-based bioassay and is reported as a percent of normal that is a little more variable. The one reported here is an immunofixation or binding assay. When it is positive like this, it is usually very helpful. However, it is an indirect assay that does not discriminate between blocking and stimulating antibodies.[12,13] There are some studies that suggest that TSI tracks with the progression or quiescence of TED.[12] However, many patients do not follow that rule, so I have found it not to be as helpful as I would like.

Dr. Mahoney: I absolutely obtain TSI if it has not been done when establishing care with a patient or for a new diagnosis. However, I no longer use it to track disease activity over time, as I have found that it fluctuates too much and tends to confuse things.

Dr. Malik: I obtain these tests at baseline as a diagnostic aid, and I do not follow them over time. I treat the patient and their symptoms rather than the antibody level, as it can be confusing and may not correlate with the clinical picture.

Dr. Harrison: What would you do next for the management of this patient?

Dr. Malik: I would start with pulsed intravenous corticosteroids only because there is not a clear-cut diagnosis of TED. I would also discuss teprotumumab with her as a potential option.

Dr. Subramanian: For similar reasons, I would start with intravenous corticosteroids. There is still some diagnostic uncertainty, and it is unknown whether biologics such as teprotumumab could have a beneficial effect. I would probably discuss teprotumumab as well if the other biochemical data and the overall clinical picture come together to make me more certain that she has TED.

Dr. Mahoney: Teprotumumab would be indicated, but it would take a bit of time to get it started, and her disease has already worsened. While getting the teprotumumab paperwork started, I would start her on intravenous corticosteroids.

Dr. Harrison: We decided to start teprotumumab because treatment with oral corticosteroids had already failed and had led to adverse effects for the patient. Upon follow up after the sixth infusion of teprotumumab, there was a very good response with improved periorbital edema and proptosis (Figure 6). The patient experienced some mild muscle cramps, but overall, tolerated the treatment well.

(Images courtesy of Andrew R. Harrison, MD.)

Figure 6. The patient in Round 1 Case 2 had marked improvement in the periorbital edema and left proptosis after six infusions of teprotumumab.

ROUND 2 | CASE 3: A 44-YEAR-OLD MAN WITH PROPTOSIS AND DIPLOPIA

Dr. Harrison: This case is a 44-year-old male patient who presented with dry eyes, tearing, grittiness, photophobia, pain, pressure, and diplopia that was worse in upgaze. The eye pain and tearing first began 8 months ago. His past medical history was significant for Graves disease for which he was taking methimazole.

Figure 7. The patient in Round 2 Case 3 presented with bilateral proptosis and restriction of ocular motility in upgaze.

He was also taking selenium, which was prescribed by his endocrinologist.

On examination, his VA was 20/25 in the right eye and 20/20 in the left eye. Pupils, intraocular pressures, and Ishihara color plates were normal. There was moderate proptosis with Hertel measurements of 25 mm in the right eye and 23 mm in the left eye. Motility examination showed restriction in upgaze in both eyes (Figure 7). CAS was 7, consistent with active TED.

I started the patient on initial treatment with intravenous corticosteroids, which was required by his insurance provider. Three months later, he reported emotional lability and suicidal ideation, so I stopped the corticosteroid infusions after four treatments.

The European Group on Graves Orbitopathy (EUGOGO) described the Kahaly protocol for intravenous corticosteroids, which consists of 500 mg methylprednisolone weekly for 6 weeks, followed by 250 mg weekly for 6 weeks.[11,14] This 12-week regimen has a fairly high success rate in active TED. Corticosteroids are 50% to 80% effective in halting the progression of TED.[1,14-16] Radiation is a viable option that has been reported to be 60% effective with 20 Gy administered during a 10-day period.[16,17] Radiation prevents the terminal differentiation of fibroblasts and blocks the inflammatory response.[18] In some studies, it has been shown to improve motility, but not proptosis.[1,19] However, radiation should be avoided in patients younger than 35 years due to the risk of secondary malignancy.[1] It should also be avoided in patients with diabetic retinopathy and severe hypertension.[1]

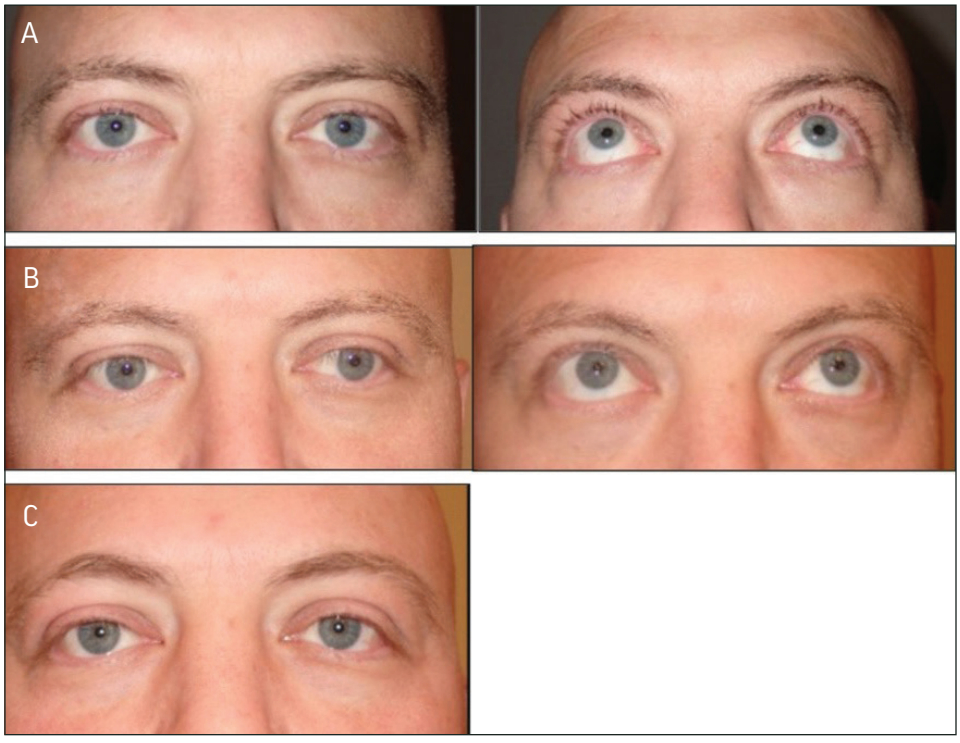
Dr. Harrison: This patient has already had intolerable adverse effects secondary to treatment with intravenous corticosteroids. What would you do next?

Andrew G. Lee, MD: As you mentioned, radiation is not very effective for proptosis.[1] This patient has a significant amount of proptosis, so teprotumumab is what I would offer, since it is effective for reducing proptosis.[3]

Jeremiah Tao, MD, FACS: I would monitor the patient closely. In most cases, the natural history of TED is that the disease will burn out. If at that point he still has proptosis or strabismus, we can perform surgery. Teprotumumab is also something to think about at this point.

Kian Eftekhari, MD: It is reasonable to discuss the option of observation. However, teprotumumab improves proptosis and is also indicated in patients with diplopia secondary to TED.[3] Some of my happiest patients are those who have been treated with a biologic and have had resolution of their diplopia.

Dr. Harrison: I decided to proceed with teprotumumab. The patient tolerated the treatment, but did have some adverse effects, including diarrhea, muscle spasms, and dry skin. He did not have any hearing issues. Upon follow up after four infusions, the restriction in upgaze, periorbital edema, and proptosis were all improving. After eight infusions, the clinical signs and



(Images courtesy of Andrew R. Harrison, MD.)

Figure 8. The patient in Round 2 Case 3 after four infusions of teprotumumab (A), eight infusions of teprotumumab (B), and 1 year later (C) with a stable treatment response.

symptoms continued to improve. One year after treatment, the patient was continuing to do quite well (Figure 8).

ROUND 2 | CASE 4: A 56-YEAR-OLD WOMAN WITH AN OPTIC NEUROPATHY

Dr. Harrison: This is a 56-year-old female with a history of Graves disease treated with radioactive iodine about 10 years ago. She presented with a 7-month history of diplopia and progressive redness, pain, tearing, and edema in the right eye. An optometrist had diagnosed allergies and dry eye disease and referred her to an ophthalmologist. The ophthalmologist diagnosed the patient with orbital pseudotumor and started her on oral prednisone 80 mg daily. Subsequently, upon presentation to my clinic, the patient had a right arcuate visual field defect, and CT of the orbits demonstrated enlargement of the extraocular muscles with apical crowding on the right side (Figure 9).

(Images courtesy of Andrew R. Harrison, MD.)

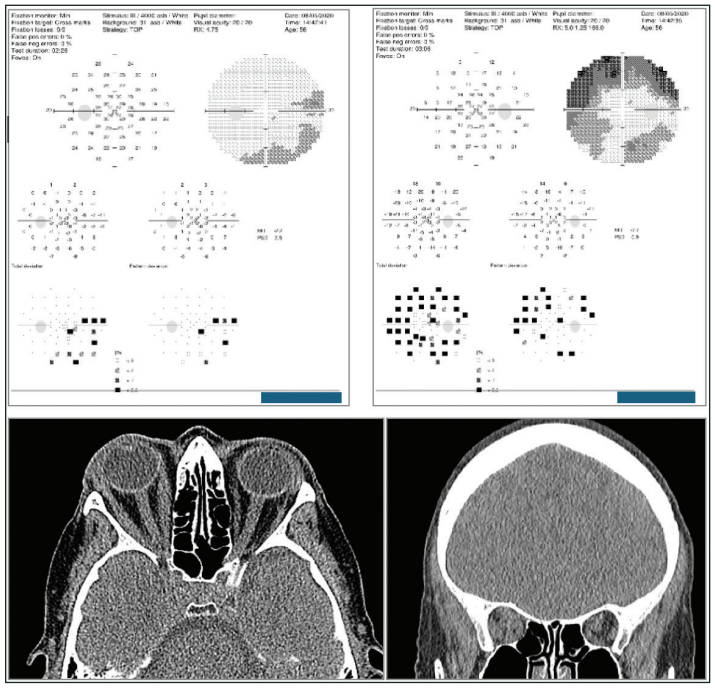


Figure 9. The patient in Round 2 Case 4 had an arcuate visual field defect in the right eye on presentation. Computed tomography revealed enlargement of the extraocular muscles and apical crowding on the right side.

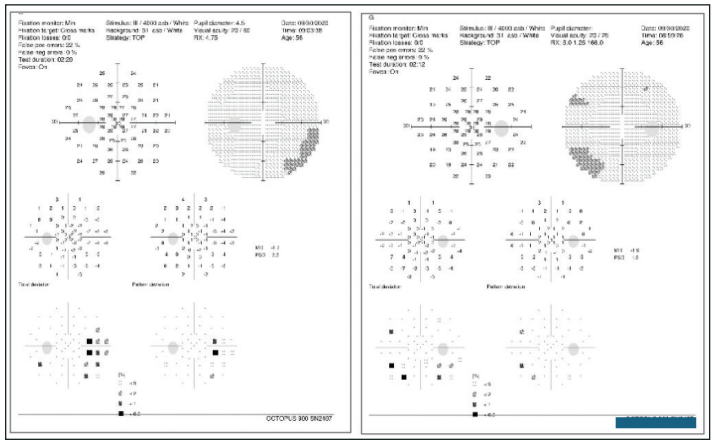


Figure 10. Visual field testing after right orbital decompression showed improvement in the right arcuate visual field defect.

Dr. Harrison: What would be your initial treatment for this patient with dysthyroid optic neuropathy secondary to TED?

Dr. A. Lee: I would give intravenous corticosteroids while waiting for surgery but would proceed with right optic nerve decompression.

Dr. Eftekhari: I would administer intravenous corticosteroids and monitor the patient very closely. I certainly think that there will be a role for surgery, but sometimes if you proceed to that without giving intravenous corticosteroids a chance, you may have a paradoxical increase in extraocular muscle size after decompression.

Dr. Tao: I would schedule the patient for the next available operating room date for orbital decompression, ideally within a week. In the meantime, I would give corticosteroids to reduce the inflammation. Orbital decompression is efficient and very safe overall.

Dr. Harrison: The patient underwent right medial orbital wall decompression and had resulting improvement in the visual field defect in the right eye (Figure 10).

Dr. Harrison: Three months later, the patient returned for follow-up and was noted to have worsening proptosis of the left eye, but no evidence of dysthyroid optic neuropathy. What would you do next?

Dr. Tao: I would observe and see how it evolves. Because we have decompressed the right orbit early in the active phase

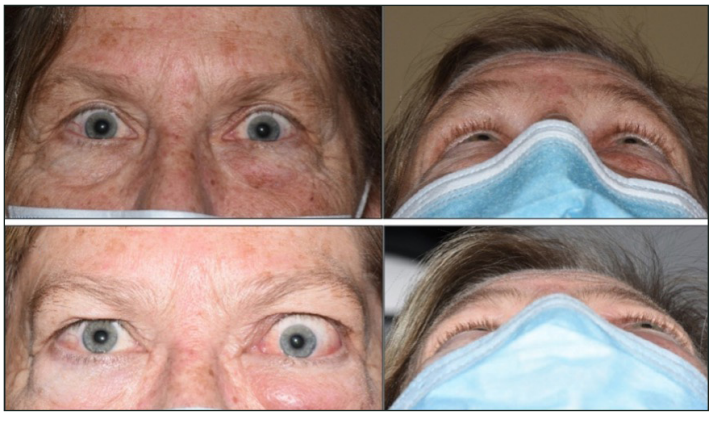


Figure 11. The patient in Round 2 Case 4 had clinical improvement following right orbital decompression and a full course of teprotumumab treatment (A). However, 3 months later, she presented with markedly worse left-sided proptosis (B).

(Images courtesy of Andrew R. Harrison, MD.)

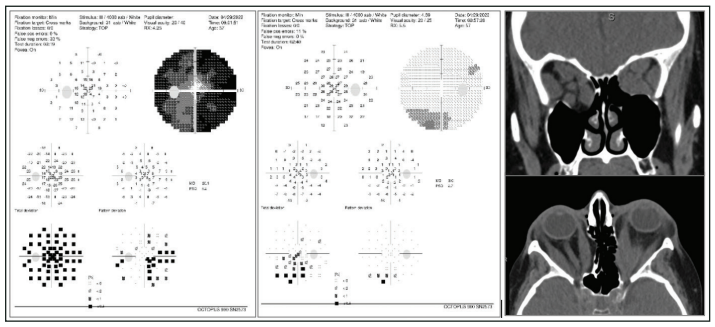


Figure 12. After right orbital decompression, teprotumumab, and intravenous corticosteroids, the patient in Round 2 Case 3 developed a dense left visual field defect consistent with dysthyroid optic neuropathy. Computed tomography at that time revealed apical crowding on the left side.

where the condition may be modifying, the right optic nerve is protected, but we need to monitor for stability. However, there is a very high risk of developing optic neuropathy on the left side due to the history of this on the right. Therefore, I would probably also offer left orbital decompression prophylactically.

Dr. A. Lee: Teprotumumab is also an option that has saved many patients from requiring surgery. I would offer this to her.

Dr. Harrison: I started the patient on teprotumumab and she responded well, with improvement in the left proptosis and a CAS of 1 (Figure 11A). However, 8 months later, she returned for follow-up, and the proptosis of the left eye was markedly worse (Figure 11B). At that time, the CAS was 7. I then treated the patient with intravenous corticosteroids following the Kahaly protocol of 500 mg of methylprednisolone weekly for 6 weeks and 250 mg weekly for 6 weeks.[14] However, 3 months later, she developed left dysthyroid optic neuropathy (Figure 12).

Dr. Harrison: This patient has already been treated with right orbital decompression, teprotumumab, and intravenous corticosteroids, and has now developed left-sided dysthyroid optic neuropathy. What would you do next?

Dr. A. Lee: I would proceed with left orbital decompression.

Dr. Eftekhari: I would not do orbital radiation, because with apical crowding, you may get some edema of the extraocular muscles that would cut off the circulation to the optic nerve. But I agree, decompression is needed.

Dr. Harrison: We proceeded with medial orbital wall decompression on the left side, and the patient responded well with improvement in the visual field. What do you recommend in the setting of inadequate response or reoccurrence of disease after teprotumumab treatment?

Dr. Eftekhari: I would discuss retreatment with teprotumumab with the patient.[6] I would also offer the patient

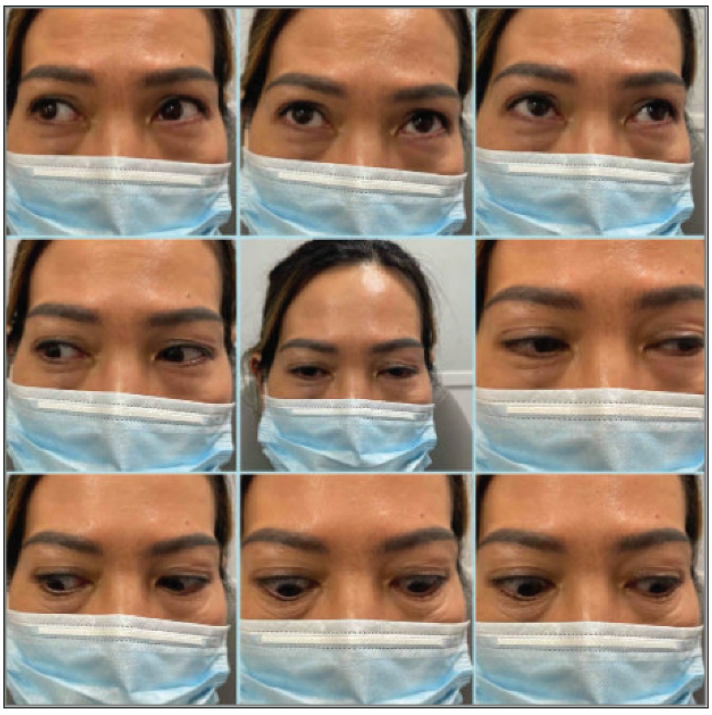


Figure 13. The patient in Round 3 Case 1 presented with eyelid retraction in downgaze and a CAS of 3.

off-label tocilizumab. It acts on a different target, interleukin-6 as opposed to the IGF-1 receptor.[1] However, we still do not have good answers for patients like this.

Dr. Tao: I am not inclined to retreat with teprotumumab due to the cost of treatment. Surgical decompression works and it saves vision, so that is my treatment of choice in this setting.

Dr. A. Lee: I agree that in the setting of failed medical therapy, that is an indication for surgery.

ROUND 3 | CASE 1: A 43-YEAR-OLD WITH EYELID RETRACTION IN DOWNGAZE

Dr. Harrison: This case is a 43-year-old female patient with a history of Graves disease, which was diagnosed 3 months ago. She began taking methimazole 2 months ago. She reported that she developed ocular pain 6 months ago and noticed progressive bulging of her eyes. She has also noted eyelid retraction on downgaze (Figure 13). Her most recent TSI was 4.4 mIU/L (reference range, < 1.0 mIU/L). On examination, Hertel measurements were 15 mm in both eyes, and CAS was 3.

Dr. Harrison: What would your initial treatment be for this patient?

Dr. Mahoney: With a positive TSI and eyelid retraction in downgaze, the diagnosis is clearly TED. You can also look at some of the more subtle features that are not included in

the CAS—for example, whether there is perhaps a little ROOF hypertrophy. This is a new diagnosis of TED, and the disease is fairly mild. This is somebody I would probably observe for the time being and ask to return in a few months. Teprotumumab may also be an option, but because there is not much impairment in the patient's function, I would hold off on treating her.

Wendy W. Lee, MD: I would want to know whether the TED was affecting the patient's quality of life. I agree that her disease is mild. At the very least, I would start some conservative treatment for the ocular surface and would monitor her. I do not think that corticosteroids or teprotumumab would be indicated yet.

Dr. A. Lee: I agree with observation of this patient.

Dr. Mahoney: Selenium could also be considered, but I would ask her to eat Brazil nuts rather than using supplementation. However, since the United States is probably not a selenium-deficient area, it may not be effective.[1]

Dr. Harrison: In the study of selenium for TED, 159 patients with mild disease received 100 µg twice daily for 6 months.[20] Selenium treatment significantly improved quality of life and symptoms and slowed disease progression. There was minimal downside. However, the main criticism of the study was that it was performed in a selenium-deficient area, and the results may not be generalizable to other populations.

I decided to observe the patient and offered selenium supplementation. Six months later, she returned with worsening diplopia and edema (Figure 14). CAS was 5, and Hertel measurements were 17 mm on both sides.

Dr. Harrison: What would you do next for this patient?

Dr. A. Lee: I would discuss with the patient how this was affecting her quality of life, and then offer treatment. Teprotumumab could be considered. I would not recommend radiation or surgery for this patient.

Dr. W. Lee: I would start the conversation about treatment with a biologic medication, specifically teprotumumab. I do not think that she is a candidate for orbital decompression surgery, radiation, or corticosteroids at this point.

Dr. Mahoney: I agree that it is too early for surgery and that there is no indication for intravenous corticosteroids. Radiation is perhaps an option, but teprotumumab is more effective. If any therapy is going to help this patient in the long run, the evidence suggests that it would be teprotumumab.[3]

Dr. W. Lee: If the disease is affecting the patient's quality of life, it is better to start treatment with teprotumumab earlier rather than later. I would also review her past medical history and discuss precautions and contraindications such as diabetes mellitus, inflammatory bowel disease, hearing loss, and current or future pregnancy.[2,21]

Dr. Harrison: The patient's insurance required step therapy with corticosteroids, so I started her on intravenous corticosteroids according to the Kahaly protocol.[14] Following this treatment, the patient's symptoms and signs resolved, and she had no residual diplopia or pain (Figure 15). She remained bothered by lower eyelid "bags."

Dr. Harrison: What is the available evidence for the use of corticosteroids for TED? Do you agree with the treatment plan for this patient?

Dr. W. Lee: The patient responded well to corticosteroids, which I would not expect very often. Her eyes look great, and the eyelids are no longer retracted. However, her disease was not very severe.

Dr. Mahoney: She still has some external signs beyond the proptosis. There is lateral flare and ROOF hypertrophy. Many people respond well to both oral and intravenous corticosteroid treatment.[1] However, the durability of the response is often not very good. There are also many adverse effects that outweigh the benefits of treatment for many people unless there is severe diplopia, pain, or dysthyroid optic neuropathy.[1]

(Images courtesy of Andrew R. Harrison, MD)

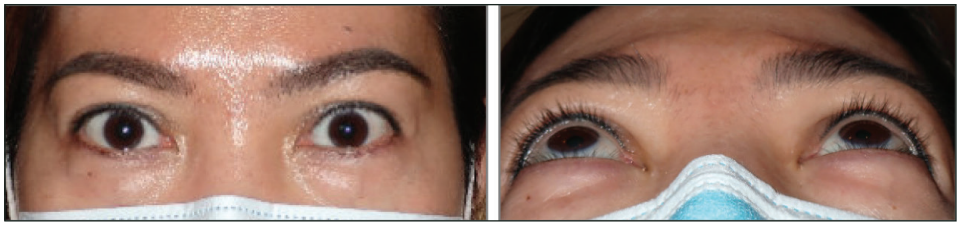


Figure 14. After 6 months of observation and selenium supplementation, the patient in Round 3 Case 1 returned with worsening diplopia and periorbital edema.

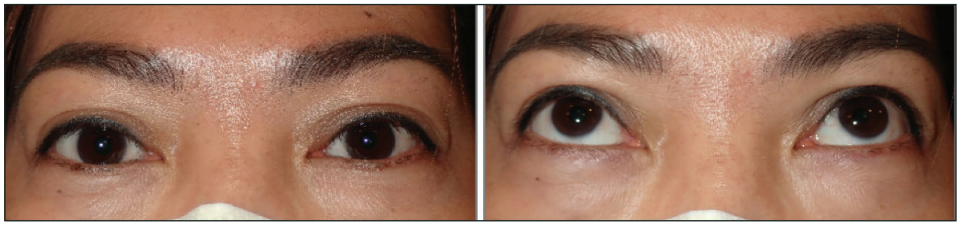
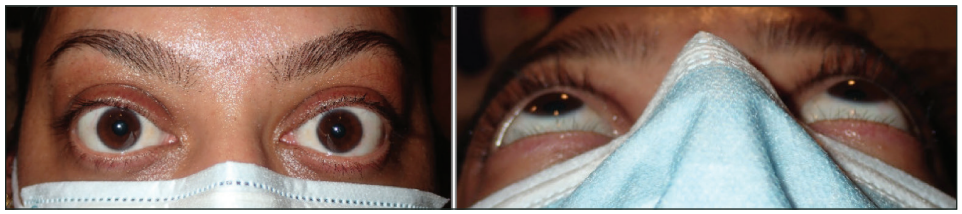


Figure 15. After treatment with intravenous corticosteroids according to the Kahaly protocol,14 the patient in Round 3 Case 1 had resolution of the diplopia and edema.



(Images courtesy of Andrew R. Harrison, MD.)

Figure 16. The patient in Round 3 Case 2 presented with bilateral proptosis.

ROUND 3 | CASE 2: A 33-YEAR-OLD WITH BILATERAL PROPTOSIS

Dr. Harrison: This is a 33-year-old female patient with a history of Graves disease that was diagnosed 6 months ago. She complained of progressive eye bulging and pain for the past 10 months (Figure 16). Her medications included methimazole, and her most recent TSI was 12.4 mU/L (reference range, < 1.0 mU/L). Hertel measurements were 26 mm on both sides, and CAS was 5.

Dr. Harrison: What would you do for the initial treatment of this patient?

Dr. A. Lee: This would be a similar discussion as for the last case, but there is more proptosis here. Therefore, teprotumumab could be considered sooner.[3]

Dr. W. Lee: There is significant proptosis, so I would definitely discuss teprotumumab.[3]

Dr. Harrison: I was able to get teprotumumab approved by the patient's insurance and proceeded with this treatment. The patient's past medical history is important to consider prior to starting teprotumumab.[2] Her last hemoglobin A1c was 5% and there was no history of inflammatory bowel disease.[2] She was not pregnant and reported no chance that she could become pregnant. I recommended using birth control before, during, and for 6 months after teprotumumab treatment.[20]

In the phase 2 and 3 clinical trials for teprotumumab, 10% of patients experienced hearing impairment, including hearing loss (Table 1).[22] It is recommended to assess each patient's hearing before, during, and after teprotumumab treatment and consider the benefits and risks.[2] Patients should be instructed to contact their doctor if they develop symptoms of hearing loss.

Dr. Harrison: How do you discuss teprotumumab with patients, and how do you monitor for adverse effects?

Dr. W. Lee: I try to make the initial discussion fairly basic, because there is a lot of information about teprotumumab. I talk about how it has been shown to decrease proptosis and diplopia, but for her I would focus on proptosis because that is her main issue.[3] And then I would explain some of the more common adverse effects, including hearing issues and muscle spasms (Table).[22] I also counsel patients to hydrate before, during, and after treatment. I obtain a baseline hearing test and repeat it midway through treatment and again at the end, unless there are abnormalities.[2] I monitor patients either after every or every other infusion.

Dr. Mahoney: I dwell on the common adverse effects. Many people have hair loss and muscle cramps, and those usually get better when the treatment ends. If the patient has diabetes or prediabetes, I focus on hyperglycemia. If they are female, I ask them to take a home pregnancy test before each infusion. I obtain an audiogram before treatment, after the fourth infusion, and toward the end of treatment, or if they develop any hearing-related symptoms.[2]

Dr. A. Lee: I differentiate hearing impairment versus loss because hearing impairment can be mild, moderate, or severe. It also can be reversible.[23] I frame it as, hearing impairment is an adverse effect. Permanent hearing loss is an uncommon adverse effect but can occur.[23] I also obtain a screening audiogram before, during, and after treatment. I involve endocrinology for hyperglycemia. And we have a

TABLE: ADVERSE EVENTS OCCURRING IN 5% OR GREATER OF PATIENTS TREATED WITH TEPROTUMUMAB IN A POOLED SAFETY ANALYSIS OF THE PHASE 2 AND 3 CLINICAL TRIALS.[22]

Adverse reactions	Teprotumumab (n=84), n (%)	Placebo (n=86), n (%)
Muscles spasms	21 (25%)	6 (7%)
Nausea	14 (17%)	8 (9%)
Alopecia	11 (13%)	7 (8%)
Diarrhea	10 (12%)	7 (8%)
Fatigue	10 (12%)	6 (7%)
Hyperglycemia	8 (10%)	1 (1%)
Hearing impairment	8 (10%)	0
Dysgeusia	7 (8%)	0
Headache	7 (8%)	6 (7%)
Dry skin	7 (8%)	0
Weight decreased	5 (6%)	0
Nail disorder	4 (5%)	0
Menstrual disorder (n=22 and n=25, respectively)	5 (23%)	1 (4%)

CTCAE4.03 Scale Grade:

**Grading based on comparison to patient's baseline audiogram (on a 1, 2, 3, 4, 6, and 8 kHz audiogram) dated 11/28/2022.*

- RIGHT: No Grade, stable
- LEFT: No Grade, stable.
  - ***Please note:** Patient had experienced a significant shift/decrease in their extended high frequencies in the left ear; however, this does not fit the criteria to change their Grade at this time.

Figure 17. Audiology report from a screening audiogram obtained after the sixth teprotumumab treatment.

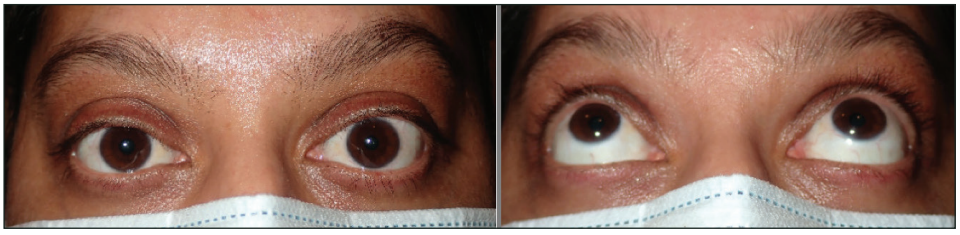


Figure 18. Following eight infusions of teprotumumab, there was improvement in the patient's proptosis and eyelid retraction.

partner audiology facility and ear, nose and throat (ENT) specialist available for consultation for all our patients who start teprotumumab.

Dr. Harrison: After the sixth infusion, the patient had a good response to teprotumumab treatment. She underwent audiology testing, which was interpreted as no grade and stable (Figure 17). However, there was a note at the bottom that stated that the patient had experienced a significant decrease in their extended high frequencies in the left ear. According to the audiologist, this did not meet the criteria to change the grade, but there was some hearing change present.

Dr. Harrison: In the setting of this hearing change, would you continue teprotumumab infusions?

Dr. Mahoney: I would discuss with the patient and say, this sounds concerning, but in our experience, it is often reversible. If she was otherwise having a positive response to the treatment, I would recommend continuing.

Dr. A. Lee: You would need to have a conversation with the patient, and in a case like this, ENT would need to be involved, not just audiology.

Dr. W. Lee: I would discuss with the patient whether she would like to continue and whether there was enough improvement in her TED that it was worth it to her. I would monitor her more closely and repeat the audiogram after every infusion. I would also get ENT involved.

Dr. Mahoney: You can also talk about treating with oral corticosteroids, as there is some suggestion that they might have a role in treating teprotumumab-associated hearing loss.[24]

Dr. Harrison: After eight infusions of teprotumumab, the patient returned for follow-up. There was improvement in the examination, with a CAS of 3 and Hertel measurements of 25 mm in both eyes (Figure 18). There was residual proptosis and retraction of the left upper eyelid. However, the patient was happy and did not want any further treatment. Her hearing returned to baseline and she denied any hearing-related symptoms.

ROUND 3 | CASE 3: A 35-YEAR-OLD WOMAN WITH CHRONIC THYROID EYE DISEASE

Dr. Harrison: This case is a 35-year-old female with TED who complained of eye bulging and retraction of the left upper eyelid. She also reported a 4-year history of eye pain and irritation that was worse in the morning. Her past medical history included a diagnosis of Graves disease 6 years prior, treated with antithyroid medications. Two years after this diagnosis, she gave birth to a child and the Graves disease stabilized. On examination, CAS was 0, and Hertel measurements were 20 mm in the right eye and 21 mm in the left eye (Figure 19).

Dr. Harrison: What would your initial treatment be for this patient with longstanding TED?

Dr. A. Lee: Patients with unilateral or asymmetrical disease tend to be more symptomatic as they notice the changes more. What is the patient's chief complaint? If it was, "I do not like the way this looks," then we would discuss teprotumumab.[25] Surgery would be another option.

Dr. W. Lee: I would want to know if she was interested in having more children, because that would play into my discussion about biologic therapies. If she was planning to become pregnant, we could consider more conservative treatments, such as botulinum toxin for the eyelid retraction. I would have the discussion of what we can do to fix the eyelid retraction alone, because that would disguise the 1 mm of relative proptosis she has on that side.

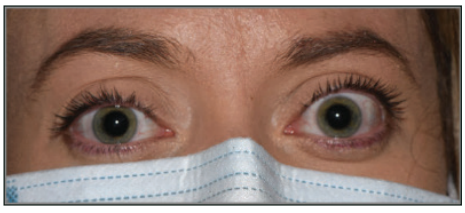
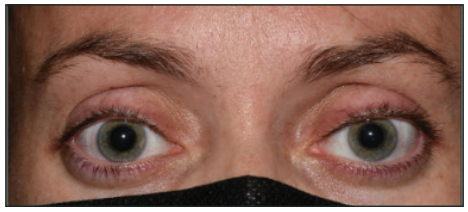


Figure 19. The patient in Round 3 Case 3 presented with bilateral proptosis and left upper eyelid retraction with a CAS of 0.



(Images courtesy of Andrew R. Harrison, MD.)

Figure 20. The patient in Round 3 Case 3 following bilateral lateral orbital decompression and left upper eyelid recession.

Dr. Mahoney: I would not discuss teprotumumab with her. Her disease is quiet, she is comfortable and functioning well. It is an aesthetic problem. I would ask her to return in a few months to verify that the disease is stable. I would obtain a CT scan, and if she did not have diplopia, I would do a decompression of the left lateral orbital wall. I might also repair the eyelid retraction at the same time. If the CT scan indicated that she was not a good candidate for lateral orbital decompression, I may just repair the eyelid. I agree that the TED might reactivate with her next pregnancy or in menopause. That may be where teprotumumab treatment would be indicated. But I would not give it to her otherwise.

Dr. A. Lee: From a neuro-ophthalmology standpoint, when we see this asymmetry, it is important to consider that a ptotic right eyelid may be causing a pseudoretraction of the left upper eyelid. It is also important to consider concomitant myasthenia gravis, because the two disorders occur together between 5% and 15% of the time.[26] If there was any component of variability, ptosis, or pseudoretraction, I would screen for myasthenia gravis. If the ophthalmoplegia was an exotropia rather than an esotropia or hypotropia, that is also a sign that it could be myasthenia gravis. I agree with Dr. Wendy Lee that botulinum toxin could be given for the eyelid.

Dr. Harrison: Would you consider imaging in this patient, and if so, what type?

Dr. Mahoney: I would obtain a CT scan for surgical decompression planning. If I was worried about the extraocular muscles or the diagnosis, I would get an MRI.

Dr. A. Lee: MRI is more informative for T2 hyperintensity and disease activity. This is all evolving, and you may need both types of imaging—CT for surgical planning, MRI for disease activity and muscle enlargement.

Dr. W. Lee: I would obtain a CT as well if I were planning to perform an orbital decompression. However, I would not choose decompression for her, because she is only 1 mm more proptotic on the left side. I feel that she would get more benefit from correcting the eyelid retraction.

Dr. Harrison: I proceeded with bilateral lateral orbital decompression and left upper eyelid recession. Upon follow up after surgery, Hertel measurements were 18 mm in both eyes with good symmetry of the eyelids (Figure 20).

ROUND 3 | CASE 4: A 45-YEAR-OLD PATIENT WITH PROPTOSIS AND STRABISMUS

Dr. Harrison: This case is a 45-year-old female patient with a history of Graves disease diagnosed 2 years ago and a most recent TRAb of 7.31 IU/L (reference range, < 1.75 IU/L). She reported progressive bulging of the left eye and turning in of the right eye, along with worsening periocular edema. On initial examination, CAS was 4. Hertel measurements were 19 mm on the right side and 23 mm on the left side. Strabismus examination indicated a right esotropia that was worse in right gaze (Figure 21).

Dr. Harrison: What would you do for the initial management of this patient?

Dr. A. Lee: I would definitely want to obtain imaging. This is the perfect example where I would get both a CT and an MRI to try to assess disease activity and extraocular muscle enlargement. This patient is likely to require treatment. I would discuss teprotumumab with her as well as other options.

Dr. W. Lee: I agree, but my decision would also depend on what the imaging looked like.

Dr. Mahoney: I concur, but I would also probably obtain a TSI. It is more sensitive than TRAb.[12,13,27] The patients who I have seen benefit the most from teprotumumab are those that are more

(Images courtesy of Andrew R. Harrison, MD.)

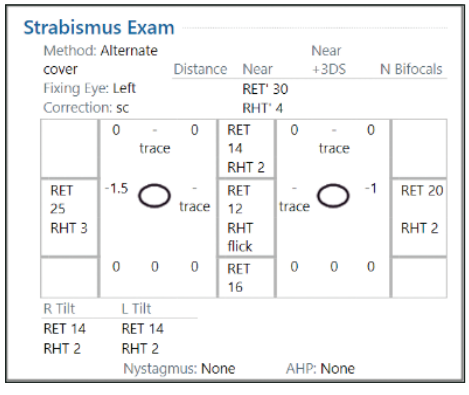


Figure 21. Strabismus examination indicated a right esotropia that was worse in right gaze.

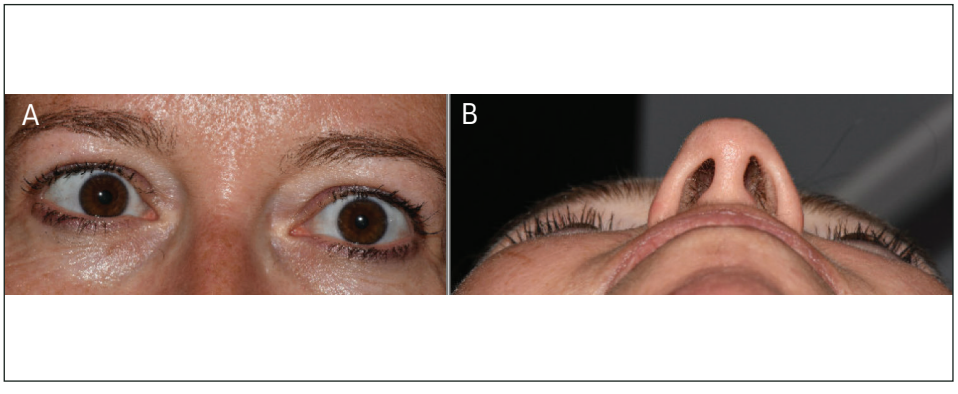


Figure 22. The patient in Round 3 Case 4 after the fifth infusion (A) and eighth infusion (B) of teprotumumab.

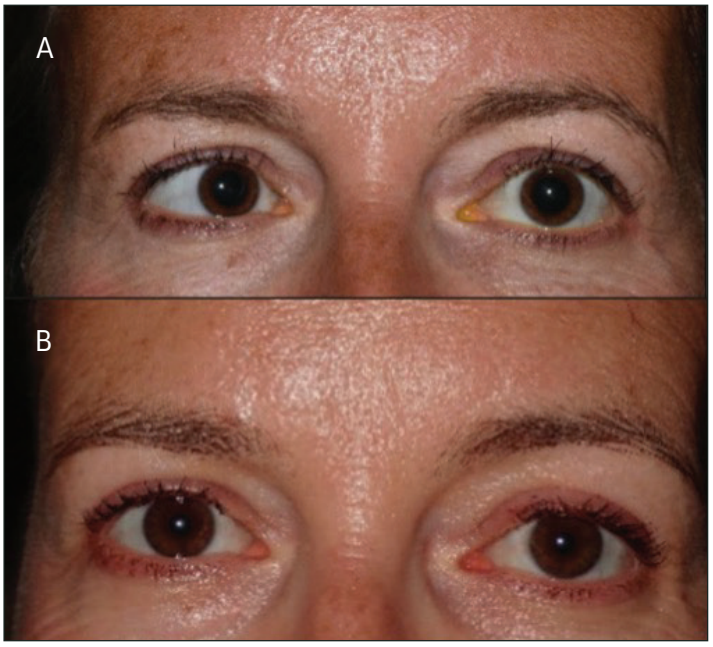


Figure 23. The patient in Round 3 Case 4 presented with worsening right esotropia following left orbital decompression (A). She then underwent strabismus surgery, and 4 years after her initial presentation, she was doing well (B).

inflamed-looking—a little bit more edematous and uncomfortable. I am a little worried that she may be past the window where I have seen teprotumumab to be the right option. On the other hand, she has diplopia, and any improvement in that would be a real win. So, I am hoping that teprotumumab would be an option for her.

Dr. A. Lee: I would also add that for the Hertel measurements, it is difficult to get a real measurement when a patient has esotropia, because the cornea is not aligned with the mirror.

Dr. Harrison: After discussing the options with the patient, I started her on teprotumumab treatment. Upon follow-up, there was improvement in the strabismus and proptosis, and CAS was 0 (Figure 22). She experienced muscle cramps, diarrhea, blocked ears, and fatigue secondary to the treatment. Three months following the completion of the course of teprotumumab, the examination was stable. However, the patient remained bothered by the proptosis of the left eye, which measured 2 mm greater than the right side.

Dr. Harrison: What would you do next for this patient?

Dr. W. Lee: At this point, this is a great result from teprotumumab. The proptosis is almost even between the sides. I would treat her conservatively for the left upper eyelid retraction, either with botulinum toxin or steroid injection. I would wait before considering a surgical eyelid procedure, because I would want to ensure that the disease was not going to relapse.

Dr. Mahoney: I would want to make sure that the improvement was maintained, so I would not rush into surgery. Once I had ensured the examination was stable, I would do a lateral orbital wall decompression on the left side, because the left eye is 2 mm more proptotic than the right eye.

Dr. A. Lee: From a neuro-ophthalmology standpoint, if there is not extraocular muscle enlargement on the imaging to correlate with the ophthalmoplegia, that is another reason to consider a workup for myasthenia gravis.

Dr. Harrison: We proceeded with a left orbital decompression. What is your approach to decompression surgery in patients who have been treated with teprotumumab? How long do you wait before performing surgery, and do you do anything differently?

Dr. W. Lee: I do not think that you have to wait. Some clinicians are now moving toward performing decompression surgeries either while on teprotumumab or shortly after. The surgeries may actually seem a bit easier, with less inflammation in the orbit and less fibrosis in the extraocular muscles.

Dr. Mahoney: I usually wait at least two visits, which are 3 months apart, to make sure the measurements are stable and that the disease does not reactivate. I would also give corticosteroids intraoperatively and postoperatively. In cases like this, I would prefer not to remove too much intraconal fat. I would ultrasonically aspirate the lateral wall, open the periosteum, and keep everything on the bone rather than in the orbit. I would hope to not stir up as much inflammation that way. But there is also something to be said for doing the surgery while the patient is on the medication, because I think the surgery is potentially problematic.

Dr. Harrison: Following the left orbital decompression, the patient presented with worsening right esotropia (Figure 23A). Do you feel that this is a recurrence of the TED, or is this just a drift of the eye back to its "steady state"? How would you proceed?

Dr. W. Lee: I would obtain imaging to evaluate whether the extraocular muscle sizes have changed.

Dr. Mahoney: It is possible that the preexisting strabismus has decompensated since you last saw her due to fatigue or another reason. It does not look like there is much inflammation, so I feel that this is not reactivation of TED, but rather that the strabismus was just never really fully fixed. Now that the decompression has been completed, she can see a strabismus surgeon.

Dr. A. Lee: This is where MRI can help. It can show enhancement patterns such as T2 hyperintensity that you cannot see on a CT.

Dr. Harrison: The patient underwent strabismus surgery. Four years later, she is doing quite well with resolution of the esotropia (Figure 23B).

Thank you to everyone who participated in these programs. ■

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KOL KNOCKOUT™: OCULOPLASTICS EDITION

8 CASES OF TAILORED TREATMENT FOR THYROID EYE DISEASE

Release Date: February 2025
Expiration Date: February 2026

INSTRUCTIONS FOR CREDIT

To receive credit, you must complete the attached **Pretest/Posttest/Activity Evaluation/Satisfaction Measures Form** and mail or fax to Evolve Medical Education LLC, 353 West Lancaster Avenue, Second Floor, Wayne, PA 19087; Fax: (215) 933-3950. To answer these questions online and receive real-time results, please go to https://evolvemeded.com/segment/32750/. If you experience problems with the online test, email us at info@evolvemeded.com. NOTE: *Certificates are issued electronically.*

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DEMOGRAPHIC INFORMATION

Profession
___ MD/DO
___ OD
___ NP
___ Nurse/APN
___ PA
___ Other

Years in Practice
___ >20
___ 11-20
___ 6-10
___ 1-5
___ <1

Patients Seen Per Week
(with the disease targeted
in this educational activity)
___ 0
___ 1-15
___ 16-30
___ 31-50
____ >50

Region
___ Midwest
___ Northeast
___ Northwest
___ Southeast
___ Southwest

LEARNING OBJECTIVES

Did the program meet the following educational objectives?	**Agree**	**Neutral**	**Disagree**
Conduct comprehensive clinical assessments, including the appropriate use of laboratory tests and radiologic imaging, to recognize the heterogenous presentation of thyroid eye disease (TED) and ascertain potential thyroid dysfunction	_____	_____	_____
Propose medically relevant treatment regimens together with customized surgical approaches to address the physical burden and reduced quality of life due to TED	_____	_____	_____
Formulate effective comanagement strategies with relevant health care professionals to optimize treatment outcomes and manage adverse events	_____	_____	_____

POSTTEST QUESTIONS

Please complete at the conclusion of the activity.

1. Based on this activity, please rate your confidence in your ability to formulate effective thyroid eye disease (TED) comanagement strategies with relevant health care professionals (based on a scale of 1 to 5, with 1 being not at all confident and 5 being extremely confident).

a. 1
b. 2
c. 3
d. 4
e. 5

2. A 34-year-old woman with a history of Graves disease treated with methimazole presents with a 3-month history of bilateral eye pain, proptosis, diplopia, and eyelid retraction. Examination reveals 20/20 VA in each eye, full color plates, no afferent pupillary defect, and a Clinical Activity Score of 6. What is the most appropriate initial management strategy?

a. Orbital decompression
b. Orbital radiation
c. Selenium supplementation
d. Teprotumumab

3. A 54-year-old man with no significant past medical history presents complaining of bilateral eye pain and redness. Examination reveals right proptosis, right upper eyelid retraction, bilateral chemosis, and bilateral conjunctival injection. What laboratory and imaging tests would be most appropriate to aid in confirming a diagnosis of TED?

a. Orbital computed tomography (CT), thyroid-stimulating hormone (TSH), free T3, free T4, and thyroid-stimulating immunoglobulin (TSI)
b. Orbital CT, TSH, free T3, and free T4, and serum thyroglobulin (Tg)
c. Orbital ultrasound, TSH, free T3, free T4, and serum Tg
d. Orbital ultrasound, TSH, free T3, free T4, and TSI

4. What is the Kahaly protocol for corticosteroid treatment for TED?

a. 40 mg oral prednisone daily for 6 weeks, then tapered over 6 weeks
b. 500 mg intravenous methylprednisolone weekly for 6 weeks, then 250 mg weekly for 6 weeks
c. 60 mg oral prednisone daily for 6 weeks, then tapered over 6 weeks
d. 1,000 mg intravenous methylprednisolone weekly for 6 weeks, then 500 mg weekly for 6 weeks

5. Orbital radiation should be avoided in patients who are younger than 35 years of age and those who have _____.

a. Retinopathy, severe hypertension, or diabetes mellitus
b. History of cancer, severe hypertension, or diabetes mellitus
c. Retinopathy, glaucoma, or diabetes mellitus
d. History of cancer, retinopathy, or diabetes mellitus

6. Comanagement with which of the following specialties should be considered in the care of patients with TED undergoing treatment with teprotumumab?

a. Rheumatology
B. Endocrinology
C. Gastroenterology
d. Nephrology

ACTIVITY EVALUATION

Your responses to the questions below will help us evaluate this activity. They will provide us with evidence that improvements were made in patient care as a result of this activity.

Rate your knowledge/skill level prior to participating in this course: 5 = High, 1 = Low____

Rate your knowledge/skill level after participating in this course: 5 = High, 1 = Low____

This activity improved my competence in managing patients with this disease/condition/symptom. _____ Yes _____No

Probability of changing practice behavior based on this activity: _____High _____ Low _____No change needed

If you plan to change your practice behavior, what type of changes do you plan to implement? (check all that apply)

Change in pharmaceutical therapy _____
Change in nonpharmaceutical therapy _____
Change in diagnostic testing _____
Choice of treatment/management approach _____
Change in current practice for referral _____
Change in differential diagnosis _____
My practice has been reinforced _____
I do not plan to implement any new changes in practice _____

Please identify any barriers to change (check all that apply):

_____ Cost
_____ Lack of consensus or professional guidelines
_____ Lack of administrative support
_____ Lack of experience
_____ Lack of time to assess/counsel patients
_____ Lack of opportunity (patients)
_____ Reimbursement/insurance issues
_____ Lack of resources (equipment)
_____ Patient compliance issues
_____ No barriers
_____ Other. Please specify: _____

The design of the program was effective for the content conveyed	___ Yes	___ No
The content supported the identified learning objectives	___ Yes	___ No
The content was free of commercial bias	___ Yes	___ No
The content was relative to your practice	___ Yes	___ No
The faculty was effective	___ Yes	___ No
You were satisfied overall with the activity	___ Yes	___ No
You would recommend this program to your colleagues	___ Yes	___ No

Please check the Core Competencies (as defined by the Accreditation Council for Graduate Medical Education) that were enhanced through your participation in this activity:

_____ Patient Care
_____ Practice-Based Learning and Improvement
_____ Professionalism
_____ Medical Knowledge
_____ Interpersonal and Communication Skills
_____ System-Based Practice

Additional comments:

_____

_____

This information will help evaluate this activity; may we contact you by email in 3 months to inquire if you have made changes to your practice based on this activity? If so, please provide your email address below.

_____

_____