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KOL KNOCKOUT™: Oculoplastics Edition – Sculpting Sight For Patients With Thyroid Eye Disease - Round 2

Announcer:
This activity is supported by an unrestricted educational grant from Amgen. This content was captured during a live virtual symposium. Voting took place during the symposium.

Dr. Harrison:
Welcome to KOL Knockout: Oculoplastics Edition – Sculpting Sight for Patients with Thyroid Eye Disease. This is a CME event brought to us by Evolve Medical Education. I want to thank everybody for joining us this evening. This is Round 2. Round 1 was a similar program that was won by Nicholas Mahoney from the Wilmer Eye Institute in Baltimore.

I'm Andy Harrison. I'm your host for this evening. I work at the University of Minnesota, where I direct the oculoplastics division, and I'm the co-director for the Center for Thyroid Eye Disease. I'm joined today by these three amazing colleagues. In the red shorts on your far left, Kian Eftekhari, oculoplastic surgeon from the Eyelid Center in Utah; in the center, wearing the white shorts, Andy Lee, who is the Herb and Jean Lyman Centennial Chair of Ophthalmology, where he serves as the chair of Ophthalmology at the Blanton Eye Institute at Houston Methodist Hospital in Houston, Texas; and in the blue on the far right is my good friend Jeremiah Tao, Professor of Ophthalmology who's the Chief of Oculofacial Plastic and Orbital Surgery there at the Gavin Herbert Eye Institute in Irvine, California. We have a great group of contestants tonight, and I'm really excited about this program.

Here are the faculty disclosures that you can see up on the screen. So the staff and planners have reviewed and have no financial relationships with any of the ineligible companies, and Evolve has full policies in place that will identify and mitigate all financial relationships prior to this activity. And it's important to note, this activity is supported by an unrestricted educational grant from Amgen.

The learning objectives tonight are, first, to conduct a comprehensive clinical assessment, including the appropriate use of laboratory tests and radiologic imaging to recognize the heterogeneous presentation of thyroid eye disease and ascertain potential thyroid dysfunction; second, to propose medically relevant treatment regimens together with customized surgical approaches to address the physical burden and reduce quality of life due to thyroid eye disease; and finally, to formulate effective comanagement strategies with relevant healthcare professionals to optimize treatment outcomes and manage adverse events.

So let's begin. So I'm going to start with these cases, and I want to let you know these guys have not seen any of these cases. These are all new to them, as they are to you, and we'll get their input along the way, and you get to vote at the end of each case for who you think did the best job discussing and managing the case.

So let's start with Case 1. All right, this was a 49-year-old male. He had a 3-month history of red eyes. He was treated by his local optometrist for dry eyes. He described waking with eye pain, and this was initially treated with artificial tears. One month before I saw him, he developed orbital pain that was treated with orbital prednisone with some degree of relief. Two weeks prior to coming in, he developed binocular diplopia, and the day prior, a friend commented to him that his eyes looked different. So as far as his past medical history, he was diagnosed with Graves' disease in 2017 and treated with radioactive iodine at that time. And then subsequently, due to recurrent problems managing his thyroid levels, he was treated with a thyroidectomy 2 years later. You can see his laboratory tests

there that show that he's still probably mildly hypothyroid. He's on levothyroxine. He's a 10-pack-year smoker; he quit in 1998. Here's his eye exam pulled from the Epic note, and you can see he has some mild proptosis, more on the left than the right, actually probably moderate proptosis. He has periocular edema, mild erythema, some lagophthalmos, as well as chemosis in both eyes. These are done by our orthoptists in our thyroid clinic, and you can see he has some mild upgaze and a little bit of horizontal gaze issues, as well some restrictive extraocular muscle disease.

So here he is on his first visit, and you can see he has some mild lid retraction as well, some periocular fullness and erythema, and fairly white quiet eyes here in this picture, although it looks like he's had some dilating drops and so that might be obscuring his chemosis and erythema. Here's the up-the-nose view, a really nice way to see if somebody's proptotic. And you can again see his eyes are a little bit bulgy, and he has that very characteristic kind of thickening of the periorbital tissues. Here was his CAS score measured at that time. Each of these is given a point, as you all probably know, and a CAS score of 4 or more indicates active thyroid eye disease. He had a CAS score of 6.

So I want to go to our group, ask them about the case, and see what they will do. I'll start with Kian, because he's the first on the top of my screen.

Dr. Eftekhari:
Yeah. So, I mean, looking at a case like this, I think that the first thing you want to know is, how long has this been going on? And it sounds like, you know, the diplopia has been 2 weeks. And the question is, did it get better at all with the oral prednisone? It's a pretty mild amount of diplopia. It might be something that you'd be a little judicious about starting a biologic for something like this, but certainly a patient with diplopia with a CAS score of 6, I am certainly not likely to do surgery, and I am likely to initiate some form of treatment. I don't like to sit on somebody with a CAS score that high.

Dr. Harrison:
What would you consider for your first-line treatment in this guy?

Dr. Eftekhari:
I'd probably want to know a little bit more about his general health, if he's diabetic or if he has prediabetes, because that can affect your choice of whether you're going to do something like IV steroids or teprotumumab, both of which can raise the blood sugars. So that's an important consideration.

Dr. Harrison:
And for this guy, I'm going to tell you, he's nondiabetic and he's otherwise a healthy individual.

Dr. Eftekhari:
So I would offer this patient teprotumumab. I think that you could certainly offer IV steroids, because he will get better for a time on IV steroids. But there are side effects to IV steroids as well. And you know, in my experience, the effect is not going to be as durable, although, unfortunately, none of these medications and treatments have a truly durable effect in somebody with really active disease, but I would start with a discussion about teprotumumab, and have to kind of discuss the course of treatment, how many times he's going to have to go into an infusion center, and the risks and the likelihood of getting better.

Dr. Harrison:
Okay, Jeremiah, what do you think?

Dr. Tao:
I'm a little more conservative. I don't know that you need to treat anything. I didn't hear anything about vision loss or optic neuropathy. I definitely would want to assess his optic nerve function, make sure there's no, you know, I'll call it, field defect. But you know, if I were to give you something, I probably might do a EUGOGO protocol, a little IV methylpred, I think it's 500 weekly, that's been shown to be pretty reasonably good and safe in terms of side effects. I think oral prednisone remains an option. You still have to, you know, with an infusion, you got to find an infusion center. You sometimes have to admit them. And there's additional layers of complexity. I hate writing orders for doing that kind of stuff, so I might just put him on some prednisone. I might not give him anything. I think he is in a situation where he could just burn himself out. And I think just watching and telling him sort of the parameters he needs to come back in for would be totally reasonable. I don't know that you have to prescribe anything.

Dr. Harrison:
Andy?

Dr. Lee:
Actually, with dolor, calor, rubor, or tumor, red, hot, swollen, painful, I think that's the tipoff that steroids might be useful. Intravenous

may be better than oral steroids, at least in some of the trials for thyroid eye disease. And I always, as a neuroophthalmologist, just want to a doctor first, and ophthalmologist second, and a orbit surgeon third. And that means controlling the thyroid, really making sure that they have stopped smoking, which, you know, if you've met any smokers, they quit and they start again, they quit and they start again. But controlling that thyroid.

And I do agree with Jeremiah that we don't have to do anything, but I think we would offer this guy IV steroids, and we would consider teprotumumab, and that's going to be a balance of the risks and benefits in the patient profile, but in a healthy person, probably would be observation, IV steroid offered, and consideration for teprotumumab.

Dr. Harrison:
All right. Let's see, what do we do? So we gave this guy tepro, and we can speak to this as we go on, but it's given, as you mentioned, by IV infusion, that they get eight infusions given every 3 weeks. So it's about a 6-month treatment, and that's what this guy went through. And here he is. You can see him at baseline after four infusions, and after eight infusions of teprotumumab he noticed marked improvement in the way he felt and looked. There's his Hertel and CAS scores before and after eight infusions.

And I guess my other question I wanted to ask to my oculoplastic colleagues, I'd be interested to see what Andy says as well, is, how does the treatment with teprotumumab affect your surgical management as far as, when do you operate on them? Because there is this theory, and we've all seen it now, where patients who are treated with teprotumumab, they start to drift back, and they get their max effect, and some of them start to drift back. So there's questions now about when to operate on these folks. I don't know, Jeremiah, do you want to take that one first?

Dr. Tao:
Yeah, we're still waiting and finding out. I think more and more patients are coming back with a rebound. I think we used to talk about reactivation, and it was like less than 5%. With tepro, it seems like it bottles it up, and then there's a lot of patients that, at a later date, they blow back up. So they get a second round of tepro, and they still blow up in some cases. So I don't think that tepro is a, you know, it's just in the same category, in my experience, as steroids, is sort of just disease modulating. It's really just putting out the fire. But having said that, there's another subset of patients that seem to be doing fine, and, you know, tepro has only been out for a couple of years. So are they going to come back in a couple years with their orbits blowing up? Who knows. But I think that's the struggle right now, finding out which patients really are going to get the home run out of it. But as time goes on, I feel like we're seeing less and less of the home runs; it's just a temporary, you know, base hitter, you know, it's just a temporary fix.

Dr. Harrison:
Right. Andy, so I know you don't do surgery, but when would you wait and say, hey, this guy needs to go to the orbital surgeon for a decompression or lid surgeon for lid surgery? How long do you wait after they've been treated?

Dr. Lee:
Yeah, so the thing that neurops are most worried about is just thyroid optic neuropathy. So we're going to be doing the field and the acuity, the color vision and OCT. So if they start to get signs of dysthyroid optic neuropathy, we're going to consider surgery. And I think that's not changed by teprotumumab. In terms of the timing of it, I think we do like to give the tepro a chance, but we're monitoring them. And this whole rebound thing, I think that is a real thing. So we are definitely going to be careful about dysthyroid optic neuropathy. In the traditional order, I think we still follow that for neurop, at least, orbital decompression, strabismus and lid las if they need all three. And so in a person who doesn't have dysthyroid optic neuropathy, I think we probably would wait. But if a cutter says, cut, you need a second opinion. If a cutter said, don't cut, they're telling you the God's honest truth, because cutters love cutting. So if my cutter says wait, I'm going to wait.

Dr. Harrison:
Kian, do you have any thoughts on when to cut or not to cut?

Dr. Eftekhari:
Yeah. So interestingly, a couple studies showed that teprotumumab actually sticks in the serum for up to 18 months after the last infusion. And so I think that's helpful as you think about surgical planning, especially if a patient's just gone through this for 6 months, getting all these infusions, they're not necessarily going to want to do surgery right away. And that's really important to know, because you have to follow them after teprotumumab, and you can't just, you know, turn them loose completely, because they might regress. And you might have a window there, I would say, up to 18 months even, but most people I'm going to be doing surgery within that first year after tepro, if we're going to do surgery. Because you probably will have some latent effects of it, before then, they might regress. And interestingly, some of the ones that regress, don't necessarily have a high Clinical Activity Score. They come back and they've got diplopia and proptosis, but not necessarily a high CAS if they've had tepro and it worked.

Dr. Harrison:
And I agree with all you guys, I usually wait like 3 to 6 months before I would do something, just because we've seen this drift, and sometimes it happens late and it sticks around. And I guess for those of you out there that aren't doing surgery, but are managing these patients, it's really important to know that just because they look like they're cured with teprotumumab, it seems like the more we know about this disease, it seems like it never goes away, right? It's always in there, and it might reactivate at some point.

Dr. Eftekhari:
I think the other thing that should be mentioned here also, is if this patient was in my clinic, I'm in a unique situation where I share office space with an ear, nose, and throat group, and we have audiology on staff, so I get audiograms on any patient that is potentially going to go on tepro, because it might actually affect whether you prescribe it. If they've got a baseline hearing loss, then you might be a little bit more on the side of Jeremiah and Andy with IV steroids or watchful waiting.

Dr. Harrison:
And I think that's important too. All patients who are treated with teprotumumab need to be monitored before, during, and after. And I can ask each of you guys how you do it. Kain, I know, because you have your audiologist in your office. Jeremiah, do you have a protocol for monitoring hearing in these folks?

Dr. Tao:
You know, we're increasingly getting it checked ahead of time. I typically comanage with my friendly neuro-ophthalmologist. There you go, Andy Lee, we like to, you know, I like to – I'm the cutter, and the neurologic ophthalmologist is sort of the thinker in the group, so they handle a lot of the symptoms that might come up from an audiologic standpoint.

But, you know, back to what Andy said earlier. Yeah, I mean, optic neuropathy changes the paradigm; of course we're going to operate if they have any signs of compressive optic neuropathy. But I will say, Andy, as a vote for the cutter, a lot of these patients that we call inflammation with a high CAS, having decompressed patients with an optic neuropathy on the table, their orbit just quiets down. All the chemosis goes away, their redness goes away on the table. So a lot of the things we call inflammation, I think, are misconstrued or misdiagnosed. They're actually just congestion from, I think, it's just vascular in the orbit. It just can't breathe. Everything's choked off. So that's one vote for cutting early.

My threshold to do a decompression is a little lower than perhaps others out there, but I still am old school. I think that's probably one of the most effective treatments, not really treating the underlying problem, we're not hitting the exact receptor that's going off, but we are modifying the orbit that has a durable anatomic modification that helps the eye and protects it. And so, you know, I always tell patients, I never mind having their orbit decompressed, because it creates a slip valve if they were ever to develop this, you know, acute worsening of the optic neuropathy. And so you knock out the floor and medial wall, which is pretty efficient and overall pretty safe if it's done properly, I think gives patients a lot of, you know, protective safety in terms of as the disease evolves.

Dr. Harrison:
So I'm going to keep going just in the interest of time, because you guys are hitting all these great points, and I have some of them in the cases to come. So let's move on to Case number 2. All these cases bring up kind of different things within thyroid disease. This is a complicated case. She's a 49-year-old who first presented to an outside institution with left-sided proptosis, blurry vision, dryness, and a pressure pain behind her left eye. She was otherwise healthy individual. Here's her exam. She has good vision. Her pressure's mildly elevated in primary gaze. Her pupils are normal. Ishihara color plates are normal. Confrontation visual fields are full. In the right eye she has full motility and the left she's restricted in upgaze. She has, I don't know that I believe these Hertels, but she has proptosis of the left eye for sure. Her palpebral fissure is slightly elevated in that side and her margin reflex distance, the distance from the corneal light reflex to her upper lid is elevated in the left eye, normal being around 4 to 5 or so.

So additional testing, and I'm going to go through some of this just to again, in the interest of time, because we have some good cases coming up. So this was an MRI scan that was ordered, again, this was all done in an outside institution, and it shows, as you can see, she has an enhancing inferior rectus muscle in the left orbit, and her lacrimal gland in the left side is enhancing as well on that coronal on your left. And then on the right side, this is, again, a fat-sat T1 with enhancement. You can see the enlarged lateral rectus, which almost kind of has a spindle shape to it, I would suggest. Here were the labs that were drawn. She had a very low TSH level, so she's hyperthyroid, even though her free T4 and free T3 are reading as normal.

So the plan at the outside institution was that this looks like thyroid eye disease, but there's some things that just don't smell thyroid, right? And Andy Lee, I know you always give those talks that when is it not thyroid, when it doesn't smell like thyroid. But this patient has large lateral rectus muscle, which is abnormal for thyroid, right? We know it's usually the inferior, medial, superior, lateral in that order, and she has no history of thyroid disease in the past, although she is quite hyperthyroid on their testing. So the outside physicians

treated her with an oral steroid taper, told her to start taking selenium. They got some thyroid antibody testing, and they said, come back in 2 months. Again, her optic nerve function is okay at this point we're assuming. Normal vision, normal pupils, confrontation visual field intact.

She comes back a month later, and now the proptosis is worse. So now she has 7 mm of proptosis. So now you have this 49-year-old female, newly diagnosed thyroid disease, progressive left proptosis, despite steroid use is – and this was their thought at the time, is this thyroid disease versus IgG4-related disease versus something else.

I think I'm going to stop there, just because I want to see what you guys would do. I'll start with Andy on this one.

Dr. Lee:
A neurop's going to get very nervous when it's lacrimal gland, lateral rectus and not the normal muscles, when it's markedly asymmetric or, frankly unilateral like this, and if you don't have the positive antibodies. But even though a common presentation of the common disease, thyroid eye disease, is the most common way we see TED, the uncommon presentation of TED is still more likely than the other diseases and IgG4. But we would definitely be testing this person for those things, and we would probably be doing a CT as well in this case, in addition to the MR, to look at it. But if it quacks like a duck and flies like a duck and looks like a duck, it's probably a duck. But this is quacking funny and flying funny and looking funny, so it's going to take a lot to not make me want to get tissue in a progressive case like this, especially if they start developing the optic neuropathy or the diplopia.

Dr. Harrison:
Jeremiah, what do you think?

Dr. Tao:
You know, thyroid eye disease is probably highest on the differential. But some weird other things to consider. The lacrimal gland does sort of not completely typical. Did she have any trauma? Did she ever bump her head or car accident, anything like that?

Dr. Harrison:
No history of trauma. Kian, what else? Anything else that you're thinking?

Dr. Eftekhari:
I think that it might be worth getting some other lab work, thinking about sarcoidosis. It is certainly in the differential especially within the large lacrimal gland. I was wondering if you mentioned if this was painful, because that might change some of how I approach it.

Dr. Harrison:
It was just pressure pain, but not like any abnormal pain, just pressure pain from having the proptosis.

Dr. Eftekhari:
And do you know what dose of steroids she was treated?

Dr. Harrison:
I don't. It was a quick oral taper, I believe, like a week or 2-week oral taper. I can't remember exactly.

Dr. Eftekhari:
That's important, because you can't say steroids failed if they started with a low dose.

Dr. Harrison:
So they decided to do a orbitotomy and get a piece of that lacrimal gland, and lateral rectus at the same time. The biopsy showed chronic inflammation. Was negative for lymphoma and IgG4-related disease. And it is, and I've definitely been in the same situation where it doesn't quite seem right, and you biopsy, but there's been several papers now that show you can have spillover inflammation into the lacrimal gland in thyroid eye disease. And sometimes, I know from decompression, when you're doing it, that lacrimal gland just wants to pop out laterally and can get quite large.

So does this change anything for you guys at this point now? Kian, we'll go up to down now.

Dr. Eftekhari:
Yeah, I mean, I think that if you've ruled out lymphoma, you could consider IV steroids at this point, especially with how proptotic she is. And I can't tell if you've seen her yet, Andy, but I'd be worried about this patient having some optic neuropathy. Although she is proposing out so that almost saves the optic nerve, but she's quite proptotic, so.

Dr. Harrison:
Andy Lee, he said the word optic nerve. What do you think

Dr. Lee:
We always want to check their field and acuity and color, even though my orbit people don't want to, but we check them all, because that's the thing we're worried about, optic neuropathy. Really, that's what worried about. We might have done a chest x-ray and a serum IgG4, just the easy things to make sure we're not missing something obvious. And once the steroid has been on board, it could modify the biopsy a little bit, so we still have to have that in mind as well. But I always say, if you're going to shoot the bear, shoot to kill, don't be poking it with oral prednisone 20; that's just going to make the bear mad, and then it's just going to come back worse. So I agree with what Kian said, that with that little dose, don't do that. Shoot to kill. Shoot to kill.

Dr. Harrison:
Jeremiah?

Dr. Tao:
Yeah, and this comment, so many of these biopsies come back just like this, showing just inflammation. I mean, I can't think of the yield on a case that I thought might not be thyroid, it's always just inflammation, and it hasn't been that helpful. So I think you're back to square one. I mean, I think it seems inflamed, so steroids, or maybe a steroid sparing, if she's not tolerant. I think, you know, some of the biologics would be certainly on the table at this point.

Dr. Harrison:
Right. And I don't know about you guys, and this isn't in there, but I'm always worried when I biopsy extraocular muscles. Always. Right? That I'm going to cause more harm than good, unless there's something that really pushes me. A lumpy, bumpy muscle, that's one thing, but this kind of looked smooth. And it's easy to Monday quarterback for Sunday and say, well, maybe they didn't need to get the piece of muscle, but I don't know. What do you guys – do you guys have thoughts on that? It just always makes me super nervous.

Dr. Lee:
Yeah, my pathologist is always going to complain that we didn't send enough specimen or we send not a representative. And the most common reason for not enough and not the right is nobody wants to really biopsy the muscle. So unless I see in the specimen that muscle was in there, or lacrimal gland was in there, I'm going to get nervous that what exactly did you biopsy? So I totally get where you're coming from. Nobody wants to cut on muscle.

Dr. Harrison:
Jeremiah. Do you just take a big –

Dr. Tao:
Well I mean, the problem is, if you want to do – I think what might be useful if you send it for flow cytometer gives you some specificity on, you know, CD, whatever, and that can guide which biologic might help. But you need a pretty decent sized sample, I think, a 0.5 or 1 cubic centimeter sample, but so you're not going to get that amount out of the muscle. Yeah, I find it to be pretty low yield, and I'm not so worried about damaging the muscle; I just think it's kind of hard to get a specimen that shows anything, and you're kind of diving longitudinally along that muscle posteriorly. It's a little bit blind. And I don't disagree with anybody who wants to biopsy, but I would say the yield is pretty low.

Dr. Harrison:
Yeah. What about Kian? You're the cutter, so?

Dr. Eftekhari:
Totally agree. The only time I would biopsy a muscle is if it's got an area where it's a little bit hypodense, where you are worried about like a carcinoid tumor or another kind of rare cancer that might be metastatic, then your differential is quite dependent on the biopsy of the muscle, and you're not going to get much from the lacrimal gland if it was just diffusely hyperintense. But I didn't see that on the MRI you showed, so I agree I would probably have avoided the muscle biopsy here.

Dr. Harrison:
All right, I'll keep moving on. So they diagnose this patient and treat them with oral pred, kind of as suggested. This was again done outside. So then she came. This is when she came to see us. So this is post oral prednisone treatment. You know, you can see our exam here. Vision's still good. Pupils are still. Okay, pressure's still a little bit elevated, and you can see she has a restricted upgaze and lateral and medial gaze in that left eye. And you saw the exam. I mean, she's very swollen, especially on the left side, with 2+ chemosis. Her Hertel readings at this point are 23 in the right and 26 in the left. And we did get a CT at this point. I think, you know, and let's ask you guys, what thoughts on CT, MRI, and what about this case at this point? I'll start with Kian, since I ended with you last time.

Dr. Eftekhari:

Yeah, I think CT is a great way to look at the muscles. And you can see how the tendons are slightly spared in terms of the muscle thickening, and that is more representative of thyroid eye disease. And I think that, you know, the number one cause of bilateral proptosis is thyroid eye disease, and the number one cause of unilateral proptosis is thyroid eye disease. So I would still favor thyroid eye disease for this case.

Dr. Harrison:
Andy?

Dr. Lee:
Yeah, I think the CT is actually more like thyroid, and that MR kind of made it look scarier probably than it was. And I like CT. We don't want to give the iodine when we have CT scans, because that can make thyroid disease worse if they're Graves, because it's the same in the contrast material. That's the Jod-Basedow effect, but a non-contrast CT here, I think it did help you, and it is heading more towards thyroid.

Dr. Harrison:
JT, are you MRI guy or a CT guy?

Dr. Tao:
I'm usually CT just because it's quick and I'm a cutter, and so I'm just looking at it from the anatomic standpoint of decompression landmarks. In this case, I will disagree, that medial rectus on the left, the tendon does look a little bit involved. So that's the one feature of this scan that kind of doesn't look like thyroid to me. But, you know, that's a soft kind of – I wouldn't hang the diagnosis on that left medial rectus tendon at all, but that's the only thing that I didn't really notice on the MRI.

Dr. Harrison:

So we kind of touched on this. CT versus MR? I'll give you guys - just one or the other? Kian?

Dr. Eftekhari:
CT.

Dr. Harrison:
JT?

Dr. Tao:
CT.

Dr. Harrison:
Andy?

Dr. Lee:
CT, but in this case, I think you needed both.

Dr. Harrison:
Okay.

Dr. Lee:
Because of weird muscle, lacrimal gland, making sure it's not lymphoma; all that was from the clinical stem. It was the atypical. So I think the answer for us would have been both here, because neurops are always going to choose MRI.

Dr. Harrison:
I think so too. I mean, I do CT as well.

All right, so any other testing you guys would do at this point? I'll start with Andy, since I ended with you last.

Dr. Lee:
So of course, we want to make sure about the dysthyroid optic neuropathy thing every single time. I think the antibody testing, I don't know if we had that or not, that would help make us better about it. If it was autoimmune thyroid disease, I think those things make us feel better. Serum IgGs, look for sarcoid, the chest x-ray, what we would call the usual suspects. But yeah, I think we're getting ready for treating this as thyroid eye disease.

Dr. Harrison:
JT?

Dr. Tao:
Yeah, I kind of, I'm lazy. So in Epic, there's like, this uveitis inflammatory workup, so I just sometimes click on that, or have somebody do that, and it just looks for Lyme and all these weird, oddball things. And again, the yield on that's pretty low, but I think it's not invasive to just check blood. So that, I might just go fishing for something odd, but no other, nothing. And then I agree with Andy, just optic nerve function, kind of visual field, and OCT optic nerve, although I don't even know how to interpret that, I don't have neurop.

Dr. Harrison:
What's an OCT? Kian?

Dr. Eftekhari:
Yeah, green is good, Jeremiah, green is good. The only other thing that you might consider, if you have this available, which I don't, and it's really far between nowadays in the modern era of ophthalmology, but a really talented ultrasonographer could probably give you some really helpful information on delineating some of those things in the differential with the extraocular muscles, but that's very person dependent.

Dr. Harrison:
Yeah, for sure, and institution dependent. So we did a TSI that popped up positive, so I think now we've kind of clinched the diagnosis, and I'm not going to belabor TSI and TRAb and TED, because I think that's a discussion that could go on forever. And I have some other great cases. But somebody wanted to know, though, Andy, before I move to the next slide, can you expand upon the comment that contrast dye makes TED worse?

Dr. Lee:
So the dye in CT scan is iodinated contrast. That's the same thing that goes to your thyroid. So if you give a big, high iodine load to people who are Graves disease, you might flip them into thyrotoxicosis. That's called the Jod-Basedow effect. So we don't want to give iodine to hyperthyroid people, and it can cause the opposite effect that can go low thyroid, which is called the Wolff-Chaikoff effect. So that is one vote for having an MR, where the contrast material is gadolinium and is non-iodinated. So we prefer a non-contrast CT of the orbit or gadolinium MR if you're looking for contrast for thyroid disease.

Dr. Harrison:
Thanks. All right. Now, guys, treat. Okay, hey, I'm telling you, patient definitely has thyroid eye disease. What would you do for this patient now? They've been treated with steroids. They got oral steroids, they got worse, and now you know, she has this massive proptosis, restrictive strabismus, and is pretty miserable. So what would you do? Jeremiah, I'll start with you.

Dr. Tao:
Yeah, I mean, while we're waiting for her to stabilize, I think IV steroids would probably be first line. I always forget about radiation. It's actually a great option. It's really, it sounds scary, but it's super, you know, I'm told that the dose that they give is really low risk for causing any secondary cancers or other side effects. So IV steroids and radiation remain sort of probably gold standard for me. The biologics, I think are nice to talk about. I'm not sure they've, they've established themselves as, you know, the gold standard, yet I think they're in the Olympic terms silver and bronze for right now.

Dr. Harrison:
Kian?

Dr. Eftekhari:
Yeah, I agree, Jeremiah. I mean, interesting thing about this case is, as bad as she looks, she doesn't really have optic neuropathy, and she does have some restrictive strabismus. So I would be having a discussion with her about a biologic, I'd get an audiogram. And I think the one thing to point out with orbital radiation, as Jeremiah said, it's 20 Gy. You know, the cancer dose for orbit is like 60 Gy. My wife's a radiation doctor, so that's the only reason I know that kind of junk. But basically, the risk to having a cataract or to having radiation retinopathy is quite minimal at that dose. Importantly, though, if you are going to consider radiation, you have to also do IV steroids, in my opinion, because some folks can get worse for a little bit on radiation, and if they have some optic neuropathy or some crimping of the nerve towards the orbital apex, then that little bit of worsening can be a lot of vision loss. But I would probably be having a discussion with this patient about biologics, but I think it's worth doing some IV steroids to just see if we can cool them off first.

Dr. Harrison:
Andy?

Dr. Lee:
I think that the fact that it's a female and some of her problems are probably from the two courses of steroids, she probably is not going

to do the IV steroids for the esthetic appearance. I think this is someone we would offer the teprotumumab first in. My patients don't like that radiation word, and they get scared by it. So I teprotumumab might be a good choice here.

Dr. Harrison:
I agree. You know, we didn't radiate this patient. But I think there are certain cases where radiation is still a reasonable alternative, you know, to help Kian make his boat payment. But I think there are patients that are active, you know, where you might want to - but you do have to give steroids concurrently, I think, to get a good effect. But in this patient, we decided to give teprotumumab again. And actually, she did – this was – and I want to tell you guys as a disclaimer, these were all kind of in the early 2020s. I'm going to guess 2021-22, so we're still – teprotumumab was pretty new. We were all very excited about it. Hence, you know, you see, in not all our cases, we give teprotumumab so that's what you're going to think after tonight. But she had a really remarkable response. Here she is before. There she was when she first presented outside. Here she is when she came to see us. And here she is after treatment with teprotumumab. So, you know, there's some patients like, I can't remember Jeremiah or Kian said, where these patients have these dramatic responses to the drug for whatever reason. And she did. She did. You know, to talk about some of the adverse events that you can see with this drug, cramping is by far the highest, I'd say, in our experience at University of Minnesota and in the studies. I think it's 25-30%, I would say it's pretty typical. It might be even higher than that. You know, there's the other things, nausea, headache, some patchy alopecia, it can push the sugar up in diabetics and prediabetics, so we need to be aware of that. And then, as mentioned, the hearing, we need to monitor that throughout. But fortunately, this woman tolerated it with some mild cramping and did quite well.

Any other thoughts, you guys while we wait on teprotumumab and side effects and things like that? Because I didn't really put a slide to –

Dr. Lee:
Yeah, I tell them about the cramping so that they know it's coming. It's kind of like with Diamox, we always tell them they're going to get the paresthesia, otherwise they're going to call. So to prevent the call, you have to tell them this is known adverse effect, don't call me for the cramping. But the sugar thing, the hyperglycemia and the hearing loss, those we do tell them they should call us, and we're always comanaging with their primary care physician or the endocrinology. Luckily, endocrine kind of can do both. And those are the things we're afraid of with the drug.

Dr. Harrison:
Right.

Dr. Tao:
I don't have a ton of experience, but there is some pretty good data on tocilizumab, and it's actually really comparatively cheap compared to tepro. And so, you know, I think what we really need is a head-to-head. I mean, it's sort of the retina world, where you had, you know, the on-label and an off-label Avastin. But I think people forget that tocilizumab has been around, and it's shown some decent effect, and all these may be just temporizing. So I would, I would vote for that if you're considering one of the biologics.

Dr. Harrison:
I think that's a great point, Jeremiah. And unfortunately, I haven't had a lot of experience with tocilizumab, but I'm really impressed by the data that's out there. And I think you're right, we need some more head-to-head studies now that we have all these drugs coming out on the market.

All right, we've got to move along, because we're getting close. This is a 44-year-old, dry, grittiness, photophobia, constant pressure, pain, diplopia, especially with upgaze. So 8 months ago, he noticed the eye pain in the watering, 6 months prior to us seeing him, his eyes didn't look normal. He does have a history of Graves' disease. Otherwise, he's on methimazole for his Graves' and selenium, started by his endocrinologist. Somebody started him on loteprednol for his red eyes. So here he is. His vision's 20/25 OD, 20/20 OS. Pupils are normal. His pressures are normal. Ishiharas are normal as well. He has moderate proptosis, 25 and 23 normal fields at this point. So here's his motility. You can see he's fairly significantly restricted in upgaze in both eyes. So in this case, I think, you know, it's pretty clear what's going on. He's swollen, periocular swelling and edema and erythema, injected and chemotic. He has a CAS score measured at 7 at this point, so clearly active thyroid eye disease.

So I'm going to scoot along just so we can get - because the last case has a lot of issues as well. But he was treated initially with IV steroids. It was dictated by his insurance carrier. And as we talked about, there's lot of steroid protocols out there. Three months later, he came in. He stopped after four infusions, he had emotional liability and became suicidal, and now actually, his eyes are worse. So, you know, steroids have 70+% effectiveness, this IV steroid protocol. But in this guy, unfortunately, it really didn't work.

So I just wanted to just touch on steroids in thyroid eye disease. I think we've hit a lot of it. I think most of us consider the Kahaley protocol, as Jeremiah mentioned, the EUGOGO group out of Europe described this, 500 mg IV weekly, followed for 6 weeks, followed by

250 IV weekly for 6. So it's a 12-week regimen that has a fairly high success rate with active thyroid eye disease.

Radiation in TED, again, we kind of mentioned. I don't have a ton of experience with radiation. We've used it as last resort in a lot of patients and had some success. But it is a viable option. And there are some people that that's a first-line option. So just about radiation quickly. Radiation has been reported to be 60% effective with 20 Gy per an orbit over a 10-day period. It's given Monday through Friday 2 weeks in a row. Works well, I think, in active, progressive disease, and correct patient selection is critical. The way radiation works, we really don't know. This is all theoretical, that it induces terminal differentiation of the fibroblasts and blocks the inflammatory response. And in some studies, it's been shown to improve motility, but not proptosis. And it's important, I guess, whenever you're considering radiation for anything, for that matter, to avoid in younger patients so as not to create a secondary malignancy in patients with retinal disease, severe hypertension, or diabetes, so that you don't create a radiation retinopathies issue.

So and then, as far as steroids are, you know, 50 to 80% effective in halting or progression of disease. Radiation we talked about, it's about 60%. Combining the two seems to be more effective. So in this dude, what would you guys do next? How would you manage this guy that's already been treated with IV steroids, had a terrible side effect, suicidal side effect. So what would you do at this point? I'll start with Andy. We haven't started with you for a while.

Dr. Lee:
So as you mentioned, the radiation isn't that great for the proptosis. He's got a significant amount of proptosis. I think the teprotumumab is going to be something we would offer here. I think Jeremiah's point about the other biologics and the point about the step therapy being required by the insurance carrier, we see that all the time, so they're going to make us go through and try steroid first. So I think this is where we would end up with in our practice as well. But I think teprotumumab is really good for proptosis.

Dr. Harrison:
Okay. Jeremiah?

Dr. Tao:
Yeah, like I said earlier, I wouldn't hesitate to just monitor him closely, just let him burn himself out. I think most of these cases do have a finite life natural history. And you know, if he if his eyes are still proptotic, and he's needs for strabismus surgery, I think surgery, we're just buying time until we can offer him surgical interventions that give him some structural changes that do improve quality of life. But, yeah, tepro again is definitely something to think about at this point.

Dr. Harrison:
Sorry. Kian?

Dr. Eftekhari:
Yeah, I agree with Jeremiah that, especially since he's orthophoric in primary, at least from what I can see in this picture, and maybe from your exam, it's reasonable to discuss with him the option of observation. But in my clinic, if somebody comes in with diplopia from thyroid eye disease, I am having the discussion about teprotumumab, because it does improve proptosis, but I think it was 45% do have some improvement in either extraocular muscle size or diplopia. And those have been some of my happiest patients that have gotten a biologic is when their diplopia goes away after like one or two infusions. And sometimes it's even a consideration to not do all the infusions in those patients, depending on how they're responding. That is off label, but it's something that can be a discussion depending on their side effects.

Dr. Harrison:
Those are great. So we did decide tepro in this guy again. He noticed that he felt better, the diplopia went – and this is one of those, as I call it, slam dunks with teprotumumab, where everything kind of worked. It doesn't always work. For sure, he did have some side effects, diarrhea for a couple days, he had these muscle spasms following a week after infusion, dry skin. And fortunately, he did not have any hearing issues. And just to show, here he is after four infusions, you can see his upgaze is starting to improve and that periorbital edema is starting to lessen, his Hertel is better. He was about 25 OU at the beginning. Here he is, eight infusions. And then just he's one that actually had this great, long-lasting response. So we actually just saw him recently. This is a year out from treatment, and he's still doing quite well, and you can see the improvement there on the before and after.

And again, thanks everybody for coming out tonight. This is always – I always learn so much on these and it's a blast.

So I'm going to move on, because this case is another one that's quite complicated and brings up a lot of issues. So this is a 56-year-old woman. She was treated with radioactive iodine about 10 years prior. Seven years, comes in with progressive redness, pain, tearing, swelling, and double vision. She was diagnosed with allergies and dry eye and then by an optometrist who subsequently sent her to the ophthalmologist, who diagnosed her with orbital pseudo tumor and started her on 80 mg, a fairly healthy dose of prednisone.

I'll let Andy Lee, he's been asking for visual fields, and I finally have some visual fields to show what's going on here on this woman here.

Dr. Lee:
Yeah, so black is bad. So we've got arcuate field defects. It's bilateral, asymmetric. We've got apical crowding on the CAT scan, so not a lot of space back there. So this is the person we're worried that sometimes you just need hot and cold steel to touch this person. But we're going to do the IV steroid thing. And I think we would go through all the motions, control the thyroid, do everything we normally would do, but sometimes you just need the knife.

Dr. Harrison:
So Andy says – Andy, you would recommend optic nerve decompression, orbital decompression surgery to decompress the nerve?

Dr. Lee:
Yeah. Normally we give the IV steroid to get started while we're waiting for the surgeon. I think there are some cases where teprotumumab has been used in patients who are not candidates or who just refuse surgery, but sometimes the old ways are still good.

Dr. Harrison:
Kian, what's your protocol here?

Dr. Eftekhari:
I'd give this patient IV steroids and watch them really closely. I didn't see the initial vision that you sent, but I certainly think that there's going to be a role for surgery. But I worry sometimes that if you jump right in without giving IV steroids a chance, you might have proptosis right into your decompression defect, and sometimes you can even have paradoxical increase in the muscle size even after the decompression, because you've tickled the bear.

Dr. Harrison:
How long for the steroids?

Dr. Eftekhari:
I would see them in my clinic pretty often to just monitor, but I would give it even a week or two and just see.

Dr. Harrison:
Jeremiah?

Dr. Tao:
I'd probably take it a little quicker. I'd probably just schedule next available. I wouldn't, you know, go to the emergency room type of thing and go tonight, but I would just say, let's find the next available within a week. And then, in the meantime, I agree steroids to cool things down. I wouldn't be so concerned about, you know, secondary issues. Decompression is a great surgery, and I like the floor, medial wall, and it's efficient and pretty safe overall.

Dr. Harrison:
So here's that patient. I agree. I'm still a cut, insecure. I'm a cutter. Andy Lee calls me the evil Andy. He's the good Andy. But I think patients with compressive neuropathy, I'm not convinced. Or I'm so worried, I want to protect that nerve, I'm not willing to wait. And we do steroids, surgery as soon as possible. So this is a right medial wall decompression. So now the fields are improving.

She comes back 3 months later. Now the left eye, the opposite eye, is getting worse. So what would you do at this point? I'll start with Jeremiah.

Dr. Tao:
I'd want to see what's going on with her imaging. But you know, same thing as before, right, steroids and radiation would be first line. But I'm going to know what's going on. No worsening neuropathy or recurrence of neuropathy? So just proptotic?

Dr. Harrison:
Worsening proptosis at this point.

Dr. Tao:
Just sit on it and just watch and see it evolve. Because, you know, we've decompressed somewhere early in the active phase where the condition may be modifying, and so, you know, we've given this slip valve of decompression. So the nerve is protected, but we need to monitor for stability. So I'd want to see her a couple times with stable measurements in terms of diplopia and proptosis over, I'd say, like a 6-month period before we do anything surgical. But in the meantime.

Dr. Harrison:
She's only had decompression on the right. Her left is still not decompressed at this point. Would you decompress the left or still watch?

Dr. Tao:
If she's changing, I probably wouldn't, if no neuropathy, but if she's been stable, if the Hertel is stable, and the motility and the duction seems similar, I'd probably consider decompression or start scheduling it.

Dr. Harrison:
Kian, what would you do?

Dr. Eftekhari:
Interesting thing about our field right now is that nothing that you have on this list has a really good evidence base for this case. So all of them would be valid. I think it would kind of depend on how they tolerate the IV steroids. Another thing you could consider, or you could have considered right off the bat, is, instead of the Kahaly protocol, for somebody with optic neuropathy, you could do a gram of Solumedrol med drill for 3 days every day and see how they do before you, you know, instead of doing the 500 up front weekly, and just see if you can quiet things down and make the neuro-ophthalmologist a little happier. But I do think that if they're having optic neuropathy in that other eye, your best bet is going to be a decompression somewhere along.

Dr. Harrison:
But she's just proptotic, no optic neuropathy at this point.

Dr. Tao:
I think she's super high risk of getting neuropathy on the left side because she had it on the other side. Obviously, you know, having it on one side's the strongest predictors. I would tell her that. And I take it back, I probably would offer a decompression sort of prophylactically, but I think there is a high degree of probability that the left orbit is going to do the same thing as the right side.

Dr. Harrison:
Andy, what do you think?

Dr. Lee:
So I think that we don't know is, as Kian said, but teprotumumab, I think, has saved a lot of patients from surgery. So I think it's an option here. And even though we know what the other side did, I'd offer it to her.

Dr. Harrison:
We offered. So we did offer teprotumumab on this lady, and she did great. Right now, CAS score's 1, Hertel's back, you know, and she's looking pretty good and happy. Eight months later, she came back, and now her proptosis is markedly worse in that left eye. So again, she's been decompressed on the right, teprotumumab, 8 months later, you know now she's got CAS scores 7 and massive proptosis on the left. And, you know, what would you do at this point here?

Dr. Lee:
I guess we should have done what Jeremiah said.

Dr. Harrison:
So Andy. Andy says, decompress. Jeremiah, decompress. Kian?

Dr. Eftekhari:
This is tough. I mean, it's interesting, because when people get really proptotic, they might be given some stretch on their optic nerve, so you may not have as much of the worry for apical crowding. So her risk of optic neuropathy might be a little bit less by actually proptosing out. But this is a tough one. I don't – getting that much proptosis, I don't know if you're going to get as good a result from just a one wall decompression like you did on the right side. So you're going to have to go for a bigger surgery with a little bit more risk the more walls you do. So this is a tough one, I would probably consider, at least talking about another treatment with a biologic or decompression.

Dr. Harrison:
She got the Kahaly. This lady got the Kahaly protocol at this point, and she got worse. So you can see her decompressed side on the right, you know, nice black around the optic nerve. And now on her left, this is 3 months after the Kahaly protocol. So now she said decompression on the right, teprotumumab, 12 infusions of steroids, and this is what her left eye looks like. You know, so she's got severe extraocular muscle enlargement, and she's got a black is bad visual field.

Dr. Tao:

Cut, cut, cut, cut, cut.

Dr. Harrison:
JT said cut.

Dr. Tao:
I'd cut her slides ago.

Dr. Harrison:
He'd cut her slides ago.

Dr. Tao:
Day zero I'd cut her.

Dr. Eftekhari:
The one thing I wouldn't do here is radiation, because of apical crowding, you might get some swelling of the muscles, and you might cut off her optic nerve, which apparently is important to Andy. But yeah, I think you have to do some form of surgery to get her orbit opened up a little bit here.

Dr. Harrison:
Yeah, so this lady had a decompression on the left eye, and so thankfully, she did well with it. And this was just, you know, when they're hot – I don't know how you guys feel about this, but I'm a just get the wall that's causing the problem, I'll deal with the rest of it later. I don't know if you guys are just like, go for it when you go for it and not do a second decompression. But in this lady, we just did medial wall. So she's had media walls OU at this point.

So I just briefly, we're kind of at the end of our time, and this is the last slide, and then we can vote, and can crown the winner. Teprotumumab failures, you know, do you retreat? Do you do steroids? Do you do surgery? I'll let each of you guys answer that, and then you can give your final parting thoughts. Kian, I'll start with you.

Dr. Eftekhari:
I would talk about a retreatment, but I would also offer the patient off-label tocilizumab. It's a different target. It's IL-6 as opposed to the IGF1 receptor, and they might just respond better to it. You don't have – this is a good way to end this discussion, because we are at the frontier of this treatment, we don't have good answers for patients like this still.

Dr. Harrison:
Jeremiah?

Dr. Tao:
Yeah, I mean, I was initially excited about teprotumumab, but I'm a little bit more of a skeptic. And, you know, I think I'm not inclined to give somebody a second $400,000 course of drugs that already didn't work. And so I see a lot of patients that have had two rounds. And not to be hypercritical of people who prescribe that, you know, I think we do have to be responsible, you know, to society when we spend this kind of money on treatments. And, you know, we've had a treatment. It's not treating the exact underlying disease, it's not targeting the underlying pathophysiology, but decompression works, and it saves people. And so just a vote for the cutter.

Dr. Harrison:
Andy?

Dr. Lee:
I concur. If you fail medical therapy, I consider that an indication for surgery.

Dr. Harrison:
It's always a blast doing these cases, and hopefully taught some folks about thyroid eye disease, the heterogeneity of the disease, the heterogeneity of the treatment across the country. We had Jeremiah in California, Kian in the kind of middle of the country in Utah, Andy in Houston, and I'm up north. We just don't have the east coast on this group, but we got everybody.

So I think we'll go to the champion on this one, and I'll just tell you the champion, so again, Nick Mahoney was the champion of Round 1, and this will be the champion of Round 2. Round 3 will be done live Friday over lunch time at the ASOPRS meeting at the Palmer House Hotel in Chicago.

So let's do the winner. Open the envelope. So the winner tonight is Dr. Andrew Lee from Houston Methodist is the champion of KOL Knockout 2.0. So, Andy, you get to join Nick Mahoney and myself in Chicago for Round 3.

But I think that was an awesome discussion. I want to thank all my participants, Kian, Jeremiah, and Andy, for doing this with me tonight. It's been a riot and educational, and it's always a lot of fun. And thanks to Evolve and Amgen for sponsoring this event. Hope everybody has a good night, and we'll see you later. Take care.