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KOL KNOCKOUT™: Endocrinology Edition – Thyroid Titans Clash to Enhance Outcomes in Thyroid Eye Disease – Round 3

### Announcer:

Welcome to CME on ReachMD. This replay of a live broadcast titled KOL Knockout: Endocrinology Edition – Thyroid Titans Clash to Enhance Outcomes in Thyroid Eye Disease – Round 3, is provided by Evolve Medical Education and is supported by an unrestricted educational grant from Horizon Therapeutics.

### Dr. Gupta:

Good evening, everyone. I'm Malini Gupta. I'm an endocrinologist in Memphis, Tennessee, where I'm director of a practice called G2Endo. And I'm happy to be here for Round 3 of the KOL Knockout – Thyroid Eye Disease edition for endocrinologists. And today we have three really wonderful contestants: Dr. Woody Sistrunk from the Jackson Thyroid and Endocrine Clinic in Jackson, Mississippi, Dr. Sonalika Khachikian from Monument Health Rapid City - Clinic in Rapid City, South Dakota, and Dr. Kaniksha Desai, who is our Round 2 winner and coming in from the Endocrine Division of Stanford University School of Medicine. Welcome.

We have some faculty disclosures that you can read here. And this is a CME activity that's supported by an unrestricted educational grant from Horizon Therapeutics. The Evolve staff planners and reviewers have no financial relationships with ineligible companies. And Evolve has full policies in place that will identify and mitigate all financial relationships prior to this educational activity.

There are a few learning objectives through this program. We're going to be diagnosing thyroid eye disease based on clinical exam, appropriate testing to enable the assessment of disease activity, severity, and impact on quality of life; appraise the risk-benefit profile of medical and biologic therapies for TED; devise individualized treatment plans for patients with varying degrees of thyroid eye disease activity severity that prevent disease progression; and then establish a referral and comanagement protocols that ensure patient access to specialized and collaborative care.

Alright, so let's begin. We're going to start with Case 1. And Case 1 is a 36-year-old female who presented with swelling of her face and a tremor. She lost 20 pounds over 6 months, she had rapid heart rate, heat intolerance, hair loss, some irritability. She had a family history of celiac disease. She had some C-sections. She was on no medications and did not smoke.

Alright, I'm going to start with you, Dr. Desai. Is there anything that you would want to ask this patient just with this information?

### Dr. Desai:

Thank you. I actually wanted to start by saying thank you for having me today, Dr. Gupta. So, if I saw this patient in clinic, she is the age range and female, so they're high risk for thyroid disease. Since we are in this webinar, Graves' disease to be on the top of my differential just with her symptoms of heart rate, intolerance, and hair loss. I would want to ask her if there's any family history of other autoimmune conditions, including either Hashimoto's or Graves' disease. And then as far as the swelling of her face, would have to do like a proper physical exam, of course, when we're seeing her and kind of evaluate that a little bit more because I think that's the more concerning symptoms that she's having compared to some of these other symptoms, which can also be concerning, specifically the rapid heart rate.

**Dr. Gupta:**

Okay, that's great. We're going to move on to the next slide where you can see her face. She has some puffiness around the eyes. She had some pain on movement of her eyes. The eyes were watery. She had some itchiness, but she had no change in vision. Dr. Sistrunk, can you tell me what you see in this picture?

**Dr. Sistrunk:**

So, when I'm looking at her, I do see periorbital edema that is bilateral. And you know, whenever we're thinking about, like autoimmune thyroid disease and people talking about facial swelling, making sure it's not like an urticaria angioedema type situation. So, it is bilateral, so that first would be concerning for this being thyroid eye disease. The puffiness around the eyes, we do see a little bit of lid lag there. I do see the sclera are a little bit reddened. I see the pain on the movement is concerning to me. And I would probably want to ask a little bit more about that. I'd also want to probably test visual acuity as well with just a pocket card or something like that for acuity to see if she's having any difficulty with acuity. She notes no change in vision, but I think that can be subjective.

**Dr. Gupta:**

Okay. Dr. Khachikian, what do you see in this photo?

**Dr. Khachikian:**

So, thank you, again, for having me. It's really nice to be with this esteemed panel over here. I agree with most of the things they're saying. Oftentimes, that swelling above the eyelids is also called the rainbow sign. I think that's important. She almost looks like she has a little bit of ptosis. She also has some swelling of her lower eyelids, so I think that's important. If you look really closely at the light reflex, you'll notice it's not symmetric, which oftentimes points to the fact that she may have some double vision, if you look across. I think those are important. I think it'd be important to see if she's smoking. I don't know if you mentioned that or not, but I know smoking can be an exacerbating factor for patients who have any concern for eye disease or autoimmune disease in general. Let's see, I think that's the majority of what I see. I think Dr. Sistrunk pointed out all the other factors. I'm not close enough to her to see if she has any inflammation of the caruncle. Oftentimes, if they look laterally, you can see it. But I'd also like to ask her a little bit about when symptoms started, if they're around the same time, if thyroid disease started first, if she has any seasonal allergies, you know, I think it's important to look at all those factors. Oftentimes, when we're looking at this, it's also important, like Dr. Desai said, to ask about any other autoimmune conditions like Sjogren's if she has that, or lupus of any kind. Because if you look at her cheeks, she has a little bit of redness and who knows if it was a hot day, or if she has like a little bit of redness from having like any kind of malar rash. But those are some of the factors I'd look at.

**Dr. Gupta:**

Okay, great. So, had some labs drawn and ordered a CMP, CBC, TSH, free T4, free T3, thyroid stimulating immunoglobulin, and a TPO antibody. Do you guys order anything else besides this panel for thyroid, Dr. Desai?

**Dr. Desai:**

Specifically, I wouldn't have ordered any. I mean, you could actually order a TRAb antibody if you wanted to. Sometimes you can see a TRAb antibody being positive when the TSI was negative. As far as other things, if we're really focusing on her eyes, and she's having a lot of pain, you could consider imaging of the eye. I didn't see a lot of proptosis, but I mean, we would have to do a side view to confirm but if she was having proptosis, you could also get imaging of a CT or an MRI of her orbital area.

**Dr. Gupta:**

Do you guys have any trouble getting the TRAb antibody? Because I'm from the south and we do sometimes have some difficulty getting that level drawn in a cost-effective manner.

**Dr. Sistrunk:**

It takes about a week but you can get it, but it takes about a week to get back.

**Dr. Khachikian:**

You know, that's exactly what I also do. Like, I will order TRAb antibodies because I've had situations where I've just relied on the simulating immunoglobulins which you think would be positive, and for whatever reason they're not. The other thing I would do with somebody like this especially in the office if I have the ability to do it is to throw an ultrasound on her neck because if I see a lot – I mean, you know, I was always taught in training that eye disease is pathognomonic for Graves' disease. And you look at her, and I think in the clinical picture, for sure, you're like, Wow, this, you know, this is yeah, I can see all the different signs. But if she didn't come to you with those classic symptoms that would go along with Graves' disease, I mean, if you looked at her, you would also think, oh, does she have a Cushingoid face? You know, like, it doesn't jump out at you. It's not like that proptosis where her eyeballs are, like, bulging out of her head. So, I think it's oftentimes, if I'm a little bit concerned about a patient, and they don't have overt eye disease that

you can see before they even come into the room, or if there's any question about what the diagnosis is, oftentimes, I'll put an ultrasound on their neck, because if you see increased blood flow, I mean, right there, you have a pretty good idea of what could be happening.

**Dr. Sistrunk:**

The other thing too, is that, you know, there – I have seen a number of people with profound hypothyroidism with this degree of periorbital edema as well. You know, I'm sure you all have as well.

**Dr. Khachikian:**

Right. That's a really, really good point. That's exactly right. Yeah.

**Dr. Desai:**

Well, I think you covered both ends of the spectrum with the TPO and a TSI antibodies, because very few people, about like 5% of people actually do have hypothyroidism. Even with TED, you can have hypothyroidism you can have euthyroidism, majority obviously your Graves' disease but it's important to remember that you can also have other conditions with TED.

**Dr. Sistrunk:**

Would you get a thyroglobulin antibody as well?

**Dr. Khachikian:**

I hate that test.

**Dr. Gupta:**

I get that. I actually do.

**Dr. Sistrunk:**

I get it. Yeah, I mean, I would say with Hashimoto's, I always – and Graves', I always get both because, you know, the discordance between the two is profound at times.

**Dr. Khachikian:**

So, if you got a thyroglobulin antibody, like, are you just adding it just in case the TSI or TPOs are negative? Or you feel like if you had a TSI that was positive and TPO that was positive or negative, then would you retrospectively go back and get a thyroglobulin?

**Dr. Sistrunk:**

I can get a thyroglobulin antibody inside of 45 minutes in my lab.

**Dr. Khachikian:**

Okay.

**Dr. Sistrunk:**

And so, if you had this picture and a suppressed TSH, you know, and the TPO and thyroglobulin antibody, one or both are positive, it's Graves' disease until proven otherwise, and you're having that discussion before they leave.

**Dr. Desai:**

I don't actually have that thyroglobulin antibody available readily in our facility, so it would be not very cost effective to get it.

**Dr. Khachikian:**

My TPO antibodies come back really, really fast. The TSI or, you know, okay the TRAb are what take the longest time, so.

**Dr. Gupta:**

Okay, so, the results show that she had a TSH of 0.00 which obviously is very low, the free T4 and free T3 were elevated. She was started on methimazole 20 mg BID and when propranolol was needed, advised her to increase your water intake. After 2 months, the thyroid function improved but her eyelid swelling did not. She was placed on a short course of steroids and referred to ophthalmology.

So, my next question is for Dr. Khachikian. Do you use steroids? And when you do use steroids, do start with an oral dose or an IV dose?

**Dr. Khachikian:**

So, this is a little bit of a trick question. So, I think it depends on what you're wanting. I mean, I think you can use steroids. I think if you want to see the most efficacious result with steroids, you want to use methylpred and you want to use high doses. Do I use steroids? Sure, I'll use steroids. Do I use a very conservative dose of steroids? Yes, because typically when I give patients steroids, they may get better initially, but the majority of my patients may also have compounding factors that will make one thing worse. So, oftentimes, you

can use, you know, like Medrol Dosepak or you can use prednisone. My experience is that patients may notice a little bit of improvement initially because it helps with inflammation, and as soon as you withdraw them, they have a rebounding effect. So, that is my truth.

**Dr. Sistrunk:**

Back to the other slide, I've got to ask about the water. Increase water intake, tell me a bit, just maybe I'm missing something but I –

**Dr. Gupta:**

She had a little bit of dry mouth and she had a really high BUN to creatinine ratio.

**Dr. Sistrunk:**

Okay. Alright. Okay, I missed that. Yeah.

**Dr. Gupta:**

Okay, so she was sent to oculoplastics and then she was started on teprotumumab and finished the 24-week course. So, there were eight infusions, one infusion every 3 weeks. She developed some tinnitus that she did not have before treatment. She had audiology testing after treatment and was found to have some sensorineural hearing loss. She had some lagophthalmos after 24 weeks but had improvement in proptosis and lid swelling. And so, here you can see the before and the after pictures. Dr. Desai, when do you get your audiology testing done?

**Dr. Desai:**

So, ideally, we would like to do an audiology testing prior to starting treatment. And then when you are doing all of the courses every 3 weeks, you could theoretically get one intermediately halfway through the treatment, especially if you ask her has there been a change in your hearing. Or she, at the time of reporting the first episode of her tinnitus, I would have definitely considered getting an audiology screening at that time, rather than just doing it after treatment, partly because if she had already had this hearing loss prior to getting treatment, then we might not have considered this medication. And then she is 36, so the chances of her having hearing sensorineural hearing loss would have been less. But I still think it's something important to consider because this medication does cause a lot of hearing issues. I believe that tinnitus should have gotten better after stopping the treatment, but I'm not – it's kind of iffy with the sensorineural hearing loss would have improved, or if this is something that she's going to have long-term wise. But I think she has improved a lot. I would hope that her ocular pain has improved as well with this treatment. And if she had severe visual acuity or visual field defects, probably they would have improved as well.

**Dr. Gupta:**

Great. I think we're ready to vote. So, while we're voting, would you guys have - when do you guys start selenium? And how do you do it? Dr. Sistrunk?

**Dr. Sistrunk:**

So, I usually – if you see somebody with eye disease, that's the first thing that I usually go over with them about, you know, taking care of the eyes, making sure that they are not outside running the weed eater or causing anything that could cause them harm. So, protection of the eyes. So, you know, wraparound sunglasses, if they can. I talk to them about selenium. And usually, I will Google the paper that talks about selenium in thyroid eye disease and show them that just as proof that I'm just not throwing herbs, you know, and then I usually will talk to them about that.

And I talk to most Graves' patients about that on every first visit that I'm aware of that being the diagnosis. And I usually will have them do – I know that the study used 100 mg twice a day, but knowing that you can get 200-mcg tablets at Walmart or wherever you shop, I usually just say 200 mcg per day, and have them get it going. And most of them will but some won't. And some don't stop smoking either. You know? Yeah.

**Dr. Gupta:**

Okay, great. We're ready to move on to Case #2. So, this is a woman who was 57 years old and presented to her ophthalmologist with blood in her eye. You can see that in the left eye. She's rubbing her eyes a lot from the dryness. She smokes one pack per day, as we were just talking about smoking. She had a past medical history of Graves' disease treated with radioactive iodine many years ago. Is currently euthyroid on levothyroxine, has a family history of thyroid disease and lupus. So, her eye findings are here. Dr. Khachikian, what do you see?

**Dr. Khachikian:**

So, when I'm looking at her eyes, I am noticing that she has proptosis bilaterally. She has a little bit of scleral show on the right eye. She has increased edema or that rainbow sign above both eyelids. She definitely has a little bit of lid retraction. She has lid lymphedema on

the upper and lower lid. It's hard to tell if you see a little bit of chemosis or not, but maybe in that right eye, but I can't tell. You can definitely notice in the left eye that she has inflammation of the caruncle and the plica. Those are things that I'm noticing. She has, I mean, she has almost all the symptoms.

**Dr. Gupta:**

Dr. Desai, do you see anything else that you would – that's different?

**Dr. Desai:**

Yeah, so the only other thing is that under the right eyelid, maybe from excessively rubbing her eyes, and she has a lot, it looks like a pretty bad bruise or maybe like under-skin hematoma, particularly on the right side. And then I know we already talked that she had the conjunctival hemorrhage on the left side. But other than that, I agree with everything else Dr. Khachikian had said.

**Dr. Gupta:**

Great. So, she had been sent to audiology for baseline testing, and started on the teprotumumab by ophthalmology. After 4 weeks though, the blood sugars started increasing and she was sent back to endocrinology, and a hemoglobin A1c had increased from a baseline of 5.9 to a 7.2. Dr. Sistrunk, what would you start the patient on? Or what would you do at this point?

**Dr. Sistrunk:**

For the diabetes, you mean?

**Dr. Gupta:**

Yes.

**Dr. Sistrunk:**

I would get them to an endocrinologist that sees diabetes and I would get them to ophthalmology [inaudible]. Right, absolutely. They need to be managed better than I could do, so, yeah.

**Dr. Gupta:**

So, Dr. Sistrunk's practice is all almost all thyroid and parathyroid, I believe, so –

**Dr. Sistrunk:**

Correct.

**Dr. Gupta:**

And it's a wonderful practice. So, Dr. Desai, would you use metformin in this case?

**Dr. Desai:**

So, I guess, well, there's two things. So, first thing is are you going to stop this medication? Right? Is this enough for you to stop the medication? Or do you want to continue the medication? Because she's only had, I believe only one infusion, right, if you're getting it every 3 weeks? Yeah, actually, I would if this is her – she's only had one infusion, I would definitely do the basics of lifestyle changes, get her some education. I don't think there's any harm in starting metformin. If her A1c comes back down, you can always discontinue it. I also, my practice is also majority thyroid, so I might consider to be overly aggressive with the metformin when you could have done lifestyle changes.

**Dr. Khachikian:**

Dr. Gupta, by process of elimination, I could be a phone-a-friend for these two colleagues of mine. If you call me on the phone, I would say yes, I would. I would do a couple of different things. I would consider possibly getting a fructosamine level, because I think of fructosamine level would give you a better average 2-week blood sugar readings, so you have like a little bit of a better idea of what kind of numbers you're dealing with. Because 7.2 in and of itself doesn't seem too concerning. And maybe it's blood sugar readings around like 150s-160s. But if you calculate it fructosamine level and it's grossly elevated, it may give you a better indication maybe of where the numbers are. I don't think metformin, as long as you have some baseline labs and her renal function is adequate, is terrible. I would definitely use extended release, I would start with 500 mg twice a day and see how she tolerates it. Because even though we can go up to 1,000 mg twice a day, she may hate you, because you may cause her to have some GI issues.

The other thing I would do is see if we can get her a glucometer or, even better, if she came into my office and we were concerned about what's going on, I would consider putting a continuous glucose monitor on her just so that the burden from the sugars isn't adding to the burden of her eye disease already. I know – and then once you look at the CGM, even if you have like a day or two or three days of data, I feel much more comfortable about making changes.

One of the other things, you know, Dr. Desai, you had talked about, and I think this is something controversial that's kind of gone on and

endocrinologists feel a certain way and eye specialists feel a different way possibly, but I kind of equate this to a patient who has some sort of malignancy, where having abnormal glucose values isn't necessarily an indication or a contraindication to give them this particular medication. I feel that like we're talking about now, it's definitely an indication to take pause and see what we can do to get their numbers under better control. So, that's just my two cents on that.

**Dr. Desai:**

I would watch it very carefully because that's quite a large jump after like one treatment, so I was going back to what you said, probably on second thought, with that large jump in her glucose, it's probably significantly higher than what we're anticipating. But just to change that number so high in 4 weeks, she might need some.

**Dr. Khachikian:**

So, it's actually it's actually super interesting because when they give the teprotumumab, especially in some of the reports that they've like, one of the articles and stuff they've looked at, even in some of the cancer journals, it's the – there's a couple of different mechanisms behind it, but it seems to lead to insulin resistance. And for whatever reason, it's seen in patients who have impaired fasting glucose or certain ethnicities. I know that being at Stanford, you guys see a lot more like Asian and Hispanic people, or at least Dr. Kessler, had published some of that information. But what was I going to say? So, you'll see an elevation – you'll see an elevation of their glucose values. And then it's kind of surprising that after a third or fourth dose, their numbers actually come down. Yeah. Isn't that interesting? Like, it's like, oh, your body kind of adapts to that weird, like, you know, that stress. But I 100% agree with you, because you guys have had a couple of cases where patients have gone into DKA, which is really scary.

**Dr. Desai:**

And it looks like she was probably predisposed, because her A1c was a little bit high. So, she probably had some pre-diabetes. And her age, I think she was a little bit on the older side.

**Dr. Khachikian:**

I think the answer is yes to all those things. I think that we need to think critically like that. Because like, you know, you don't know this is a patient who just has a mild elevation or if this is a patient who's going to really, like you know, make you take pause about the next person you want to treat.

**Dr. Gupta:**

Those are some great points. And she did have improvement of her blood sugars over the course of her eight treatments. She had improvement of her eye symptoms with some improvement of dry eyes, but she still needed a lubricant. And here, you can see her about a year post. She has maintained a lot of the improvement that was seen in the teprotumumab, and she was removed from most of the hypoglycemics and just maintained on metformin.

**Dr. Desai:**

So, what did you start her on besides the metformin?

**Dr. Gupta:**

She actually got a DPP-4 inhibitor.

**Dr. Desai:**

Oh, that's smart.

**Dr. Desai:**

And I know you talked about the selenium last time, but I think also important for this particular case. So, lubricants also help a lot. It's easy, over-the-counter, I hey don't know if there's a specific brand that anybody uses. But they do seem to help a lot.

**Dr. Sistrunk:**

I usually tell people about Refresh or Refresh PM, and you know, you can pull it up easily on Amazon or show them what it looks like so they can go look for it.

**Dr. Gupta:**

So, ointment and an eye mask I think help a lot too, using an ointment at night or no fan, no ceiling fan.

**Dr. Sistrunk:**

Right. The PM is the gooey one, and I'll usually tell them make sure that you're not planning to watch TV through that. Yeah.

**Dr. Desai:**

Do you guys ever have anyone tape their eyes shut? I guess this one wasn't that severe, but you could also do that for the proptosis.

**Dr. Sistrunk:**

With the paper tape, certainly, yeah.

**Dr. Khachikian:**

So, would you believe that some of the oculoplastics have told me that Glad Press and Seal, they've actually done studies with it, it helps more than anything else. So, and then with the scotch tape, like you don't have any damage to the tissue around the eyes though. I just tell them to wrap up it – no, I don't tell them to do that. But it is something you can do.

**Dr. Sistrunk:**

You know, you can also use that for your ultrasound probe if you're doing a biopsy on somebody who's latex allergic.

**Dr. Khachikian:**

Oh, is that true? Okay.

**Dr. Gupta:**

That's what I use.

**Dr. Sistrunk:**

I learned that from - Dev Abraham taught me that.

**Dr. Khachikian:**

Do you use Glad Press and Seal when you do all of them? Or for when –

**Dr. Sistrunk:**

Press and Seal, you could. I use – no, just for ones that are latex allergic, and just clean it with alcohol.

**Dr. Gupta:**

Great. So, we're ready for Case 3, and Dr. Sistrunk, I do that too. I use the Glad Press and Seal for my cases too, so we have a latex-free lab.

Okay, so Case 3. This is a 52-year-old female with a history of iron deficiency from heavy menses. So, she started to develop periorbital swelling of the left eye. And she had labs drawn by her PCP that showed hypothyroidism and she was started on levothyroxine. So, she had a history of losing weight early in college, told she was hyperthyroid. She was briefly on methimazole for 1 year, diagnosed with hypothyroidism 20 years later. She's a nonsmoker. She has a sister who has hypothyroidism and vitiligo. And she was recently divorced but has not been wanting to date because she felt self-conscious about her eye. And this is what you – these are the symptoms and signs that she's seeing. She had some watery eyes, pain on movement of her eyes, lid swelling, headaches, and the Hertel measurements showed a left eye that was 2 mm, more proptotic than the right eye.

Alright, so Dr. Khachikian, do you see anything unusual in this picture?

**Dr. Khachikian:**

So, she definitely has lid lag/lid retraction in her left eye. She almost looks like she has like an opacification over her corneas. Does anybody see that?

**Dr. Desai:**

It looks like it's on the top on the left one. And then on the bottom on the right.

**Dr. Sistrunk:**

Some on the bottom on the right.

**Dr. Khachikian:**

Yeah, yeah. And then she has some conjunctival injection. She definitely, you know, all the other things that you had already mentioned. So, I also again, if you look at this picture, and you look at the light reflex, you notice that they're not symmetric. So, this would again suggest that maybe she has some double vision.

**Dr. Desai:**

And then actually her eyebrows with her hypothyroidism, she has really sparse eyebrows. And you can see where she's had some hair loss from her eyebrows.

**Dr. Sistrunk:**

So, the hyperpigmentation below the eyes bothers me. And it may just be the angle of the light there. But I, you know, some of the – with the asymmetry and the appearance, and maybe it's just because of the very close-hand picture, I would probably want to scan this lady's

head to make certain that we're not missing anything else that could be going on, such as an infiltrative process, that could cause this type of appearance as well, even though she does have a history of hyperthyroidism, history of hypothyroidism following, we assume she had Graves'. It has been 20 years, and I think that we would do her justice to make certain that we're not missing something else that could be causing this unusual physical finding.

**Dr. Khachikian:**

So, Dr. Gupta, I have a question. Why was it important that she has iron deficiency? What am I missing? Oh, okay.

**Dr. Gupta:**

Just a minute. But Dr. Sistrunk, I do agree with you on the imaging. Question for you. Do you start with a CT or an MRI? Or what do you prefer? And why?

**Dr. Sistrunk:**

I think probably a CT would be sufficient. And I think it would be you know, cost and easy access. And so, I think I'd probably start with the CT.

**Dr. Gupta:**

Dr. Khachikian, what do you think?

**Dr. Khachikian:**

I agree with that 100%. I would do a CT without contrast is what I like to – I don't order them routinely, but when I do, that's what I like to order.

**Dr. Gupta:**

Alright, so she did not have anything on CT that was concerning for a tumor. But it was consistent with signs for thyroid eye disease that was more unilateral. And she was started on teprotumumab after she had normal hearing studies. However, she had irregular cycles during treatment and already had a baseline of iron deficiency from the heavy cycles.

Dr. Desai, what would you do in the middle of treatment if you had a patient who had developed irregular cycles with even heavier bleeding? Would you stop the teprotumumab? Would you send the patient to OB? What do you think you would do?

**Dr. Desai:**

Can you just remind me what her age is again? Sorry.

**Dr. Gupta:**

She – that's a good question. She was 52.

**Dr. Desai:**

Yeah, so I wouldn't necessarily stop the medication. She's on the older side. So, I would definitely refer to OB to make sure she doesn't have fibroids or other issues that might be causing excessive bleeding. But I wouldn't necessarily stop the teprotumumab just for the iron deficiency anemia. You could also kind of do a workup to make sure that she doesn't have any sort of IBD, because this medication has been known to cause IBD flares. So, you could consider a colonoscopy if you weren't sure that the anemia was directly related to the irregular, heavy menses.

**Dr. Gupta:**

Dr. Khachikian, would you do anything differently?

**Dr. Khachikian:**

In a 52-year-old?

**Dr. Gupta:**

Yes.

**Dr. Khachikian:**

I would do some baseline labs, I'd get an hCG level to make sure that she is not pregnant. I mean, 52 is a little bit old, but I would also get like an estrogen. So, now, I would get an estrogen level just to see, you know, she is making it. You could consider getting LH and FSH, just to kind of give you just the baseline idea of like, what is this from? And is she having frequent bowel movements? Is she having blood from her rectum? Or is it just cycles? Because it is something that I'm seeing more and more commonly in patients who I'm treating, they will oftentimes say that they, after their third or fourth dose, will have a lack of menstrual cycles. And sometimes they don't come back till around 5-ish months after they've had their – after they finished the course of treatment. So, that's what I would do.



**Dr. Desai:**

Sorry, I would add one other thing. You could check her for celiac disease too, because it's another autoimmune condition.

**Dr. Gupta:**

Or sickle cell. I mean, she's, I mean, I don't know.

**Dr. Desai:**

What did you do? You just left it alone, you're like, here's some iron.

**Dr. Gupta:**

Here's some iron. Well, while the audience is voting right now. Yeah, I – she did get a screening from OB/GYN to check for fibroids which she did have, but also was started on iron. The iron deficiency is common in thyroid disease and also is exacerbated by fibroids. So, she needed iron. The colonoscopy was also done just to rule out any issues there and to make sure that she didn't have any inflammatory bowel disease and/or cancer.

And I find like most of my patients really tolerate using either fortified iron water where you just boil the water in an iron skillet for about 30 minutes and then you can put that in ice cube trays or you can use something that's like a Lucky Iron Fish that can go into the cooking or you can use simple Flintstone vitamins for children that it's non-constipating. And I think the patients have a lot of benefit from that in iron deficiency in thyroid.

**Dr. Desai:**

Did you say you didn't stop the medicine, right?

**Dr. Gupta:**

Did not.

Okay, so we're ready for Case #4. And Case #4 is a 58-year-old nurse who had fatigue and she was complaining of a very rapid heart rate. Her primary care physician sent her to cardiology. Cardiologist checked the TSH and was found to be pretty much nonexistent, then what was referred to endocrinology.

So, Dr. Sistrunk, what do you see in this picture?

**Dr. Sistrunk:**

So, I captured by looking and seeing the amount of stare that she has, she has significant stare. She has bilateral temporal wasting, so she's probably been hyperthyroid for a while. We do see a mild degree of periorbital edema, but I do not see anything that would suggest any significant inflammation about the eyes. The lower eyelids, I do not see much edema. I would ask her if she is noticing anything? Is she having photophobia? Is she having any diplopia? Is she having any other symptomatology related to the eyes as the first – on the first visit, to see where she is with that? I can't see her thyroid, but I assume that she's quite thyrotoxic with the appearance of the temporal wasting in the stare.

**Dr. Gupta:**

And Dr. Desai, what do you see?

**Dr. Desai:**

I think there's a little asymmetrical lid retraction with the right side being a little bit worse than the left side, and you can see the sclera more on the right side than the left side. I also think that there's more swelling on the right side in general compared to the left side appears –

**Dr. Gupta:**

Alright. So, she did have a family history of celiac disease in a grandparent. And then cardiology started around atenolol 25 mg a day for the heart rate. She's a nonsmoker, and she had no weight loss. She had some increased pain in the left eye and some occasional lower lid swelling. The right eye had some proptosis greater than the left eye. So, the right eye had was greater than the left eye. And her thyroid stimulating immunoglobulins are 10 times the upper limit of normal. She was started on methimazole 20 mg twice a day and then had some selenium supplementation.

**Dr. Desai:**

Oh, wow. A huge difference.

**Dr. Gupta:**

So, going back one, to this point here, at what point during the treatment, do you go ahead and refer to oculoplastics or ophthalmology?

**Dr. Desai:**

I like to do it early on. We have Dr. Kossler here, she's wonderful. And, well, we have a lot of ophthalmologists. But she particularly focuses on TED, and they're pretty accommodating for the patients. I don't necessarily think this patient would have had an urgent referral, but I like to have them see ophthalmology kind of early on rather than wait till things get worse.

**Dr. Gupta:**

Dr. Khachikian, you're in South Dakota where it's a little bit harder to find specialists fast. At what point do you get your ophthalmology and oculoplastics teams involved?

**Dr. Khachikian:**

I think just like Dr. Desai, I like to do it pretty early in somebody who I'm concerned about. She definitely has a little bit of asymmetry. And I think the fact that she has pain on the left side is a little bit concerning to me. Oftentimes, when you see proptosis, or you see a lot of conjunctival injection, you – a little bit maybe it's false, but maybe a little bit more reassured that it's in the anterior part of the eye. When someone's having pain, I always wonder what's going on behind the eye. That's worrisome. So, I don't think there's anything wrong with getting them involved early. And I have a pretty good relationship with my oculoplastics here. So, even if they see them, and then there's not much intervention they're going to do, at least they're involved, so if something changes in regards to the patient's clinical status, you can always, you know, get them in a little bit earlier.

**Dr. Gupta:**

Dr. Sistrunk, what about you?

**Dr. Sistrunk:**

You know, so I guess if they express any concern whatsoever that I immediately pick up on, I offer referral at that time. I think starting the selenium is reasonable. And I think that in her, you know, we would as we talk about choices for options for treatment for Graves' disease, I think I would want to talk to her about our hope would be the methimazole may help with some of the inflammation that may have an impact with the eye disease and the concerns about radioactive iodine, if that were considered.

**Dr. Gupta:**

Great. So, she went to ophthalmology pretty much immediately and had audiology baseline testing, and she was started on teprotumumab. And this is the before and after the eight doses of the teprotumumab. What do you see in the second photo, Dr. Khachikian?

**Dr. Khachikian:**

You know, I was noting isn't it almost interesting that she has so much more erythema of the upper eyelids. I don't know if we just weren't seeing it previously. Like, these are the people who we wonder if they had like a few more doses of teprotumumab, like it would do a little bit better? I noticed that, you know, that stare that we talked about is definitely better. I noticed that the proptosis looks better, though it's a little bit still more manifested in the right eye than in the left eye. That's kind of what I'm seeing when I'm looking at her.

**Dr. Sistrunk:**

To me, it seems like the periorbital edema maybe even a little worse in the lower eyelids.

**Dr. Gupta:**

So, the eyebrows. Dr. Desai, can you comment on her eyebrows?

**Dr. Desai:**

Oh, her eyebrows actually disappeared. She had much fuller eyebrows prior to treatment than after treatment.

**Dr. Sistrunk:**

What's her TSH here?

**Dr. Desai:**

Maybe she became severely hypothyroid and they all fell out.

**Dr. Sistrunk:**

With the edema at the lower eyelid. I can see that.

**Dr. Gupta:**

Yeah, the thyroid actually normalized. But the methimazole dose got tapered down all the way to 5. At what point do you guys take patients off the methimazole?

**Dr. Sistrunk:**

I usually check antibodies to see where they are. And, you know, I usually will keep up with which antibodies were positive previously and try to get the same antibodies in the same methodology in the same lab, which is nearly impossible, to compare how much did the antibodies drop and did they respond. And, you know, oftentimes will tell them, you know, once we've gotten, you're down to 5, 2.5 mg per day and antibodies are negative, we'll stop it and see where they are a couple of months down the road.

**Dr. Desai:**

I agree. I usually do it for about 2 years; you have to do it for the minimum of 18 months. But I usually find it easier to do it at the 2-year mark. If the antibodies are positive, then it's a pretty big discussion about whether we want to continue it because you can continue it longer, versus doing a trial off of it with positive antibodies. And just, you know, reminding the patient that they might have a recurrence, so get regular testing, especially if the antibodies are positive and you're going to stop it. So, I would check it 1 month, 3 months, 6 months. Obviously, if the antibodies are negative, you have a much better chance of remission, so you can offer the patient we can continue the medication for another 6 months and recheck antibodies, or we can do the trial off. And then if it recurs, then we'd have to leave you on it longer. You can come back to it too.

**Dr. Gupta:**

Alright, we're getting an audience question about selenium and how do you guys measure. Do you measure selenium? Or do you just start selenium? And for how long do you use the selenium? Dr. Khachikian?

**Dr. Khachikian:**

So, I do not measure selenium levels. I just encourage my patients to start selenium 200 once a day, one Brazil nut a day, or 100 twice a day is totally fine. Sometimes they're noticing that their multivitamins have them. And if they're multivitamin has a good dose, then that's what I do.

**Dr. Desai:**

I agree. I don't think you need to check selenium levels. It's pretty safe. As long as you're not taking like 10 pills a day. I wouldn't necessarily say more is better but it's pretty safe at the 100 twice a day or 200 once a day dose.

**Dr. Gupta:**

You can develop selenosis at 400, so definitely try to make sure that they're not getting more than those two Brazil nuts a day because you are getting selenium and some other foods as well and other vitamins. And I have them toast the Brazil nuts because actually tastes way better. Having thyroid issues myself, I take the Brazil nuts.

**Dr. Khachikian:**

Dr. Gupta, why am I not surprised by that? She's like I have this delicious recipe that's a selenium cookie and I just make 300 of them every weekend along with all the other things I do. And that's what I give to my thyroid patients in a goodie bag. And thank you. I'm going to start doing that.

**Dr. Gupta:**

Well, I was lucky to be gifted some Brazil nuts from Dr. Leo Rangel, who's a thyroid surgeon in Rio that when he had come up to the states last, and they were already toasted and I thought, oh my gosh, these tastes so much better.

**Dr. Khachikian:**

Panel, any questions? No? That's fine. One vote for Dr. K.

**Dr. Gupta:**

But you can actually die of selenosis. And it's sitting right next to arsenic on the periodic table, so you have to be really careful about that.

**Dr. Desai:**

And it takes a long time to go down too, I found that out in a patient who took a lot of selenium, took like months to go down.

**Dr. Khachikian:**

I'm going to have to look that up. I have no – like, what did manifestations of that look like?

**Dr. Gupta:**

Selenosis? Selenosis definitely is something that I think everybody needs to be worried about because it can lead to hair loss, a garlic odor in your breath, GI disorders, irritability, fatigue, some neurologic damage, and nail fragility, and then it can lead to pulmonary edema, liver cirrhosis, and then death.

**Dr. Sistrunk:**

You know, one of the things that I think about, and I actually looked this up, our Department of Environmental Quality for our state has soil sampling. And you can look at the map of Mississippi and see where the highest selenium levels are. And they pretty much follow the Mississippi River. And I'm very curious at times of could that potentially be why, despite being in a thyroid-only practice, I don't see a massive amount of Graves' eye disease. Because I really don't, you know. I see a lot less than I would anticipate.

**Dr. Gupta:**

I'm upstream from you. And I do see a good bit of thyroid eye disease. Our water's coming in from the aquifers though. So, that is interesting.

Alright. Let's go to Case #5. Alright, Case #5 is very interesting. And she's a 55-year-old female who had a recent diagnosis of MS. And she had some vision problems, difficulty looking up and down and to the sides, and double vision or the diplopia. She could no longer drive by herself, had a lot of heat and intolerance, and increased bowel movements. Dr. Desai, can you talk a little bit about what you're seeing in this photo?

**Dr. Desai:**

Sure. She actually has a lot of stare, and then it looks like her right side might have more proptosis than her left side. She has significant lid retraction on her right side compared to her left side which almost has like a ptosis appearance. She has a little bit of orbital swelling. I think this photo is kind of hard to see if she has a lot of chemosis or conjunctival injection. And then she has – her lower eyelids are a little bit as swollen like periorbital swelling. Yeah, I think that would be most of it.

**Dr. Gupta:**

Dr. Khachikian, do you see anything in these photographs?

**Dr. Khachikian:**

I feel like she also has like alopecia. But it's interesting because she retains her eyebrows.

**Dr. Sistrunk:**

I think that's red hair.

**Dr. Khachikian:**

Okay, excellent. Because I was like, oh.

**Dr. Sistrunk:**

Yeah, it's red hair.

**Dr. Khachikian:**

Dr. Gupta, you were trying to trick us.

**Dr. Gupta:**

You know, I am. I am. She does have red hair.

**Dr. Khachikian:**

Okay, I take back what I said.

**Dr. Sistrunk:**

Selenium red.

**Dr. Gupta:**

Selenium red. So, she had TSH that was 0, she's TPO antibody positive, ANA positive, thyroid stimulating immunoglobulin positive, and she has a confirmed diagnosis of Graves' at this point. Now, so, she has Graves' and MS. She was started on methimazole 20 mg BID.

**Dr. Sistrunk:**

You know, I would be curious to know what were the manifestations that led to the diagnosis of MS to make certain that we're not overlapping symptoms that could be attributed to thyroid eye disease only?

**Dr. Gupta:**

Very, very good question, because as you know, MS can affect the eyes. She had the lid swelling, the chemosis, bulging of the right eye over the left eye, the eyes felt uneven. She had dryness of the eyes, spontaneous eye pain, restricted eye movements, a CAS score of 6-7. And so, CAS score, Dr. Khachikian, how often are you using the CAS score?

**Dr. Khachikian:**

I am using CAS score. I will document it as part of my routine exam; however, I mean, now that the data has been updated on using

teprotumumab, it doesn't matter whether somebody has acute disease or they have chronic disease, they used in people who have a CAS score of less than or equal to 1, and they noticed that it was equally efficacious. It has new FDA indication to use whether you have a CAS score as high as 7 or as low as 1. So, do I still use it in documentation? Yes, but I think I use it more for insurance reasons, so.

**Dr. Gupta:**

Great. So, ordered some imaging. And with the MS, we will – we have an issue with a neurologic issue. Can you tell me which modality would you use now? Would you get an MRI? Or would you still get a CT?

**Dr. Khachikian:**

Is this me?

**Dr. Gupta:**

Go ahead.

**Dr. Khachikian:**

In this patient, it may be better to get an MRI because I think you're going to want to see a little bit more clarity. So, in this particular patient, and I've never done it, but maybe an MRI is a little bit easier to get or will give you more information perhaps.

**Dr. Desai:**

Yeah, I agree with the MRI. It's going to give you more of your soft tissue, as opposed to the CT scan. But if you refer to oculoplastics, and they're considering surgery, they might get a CT scan prior to surgery. I don't know. Dr. Sistrunk, do you have a preference?

**Dr. Sistrunk:**

No. I think in this one, I'm still worried about the diagnosis of the making sure that we have two things going on. And so, you know, if an MRI would help confirm other lesions, sure, I'd be all for it, you know, in addition to the thyroid eye disease, which we know she has, but making sure that we're not missing anything else here.

**Dr. Khachikian:**

Because it's my understanding that if we get an MRI of the muscles, if she truly has thyroid eye disease, which she obviously looks like she does, the muscles will light up more so which may be a little bit easier to see.

**Dr. Gupta:**

And you can see the nerves better on the MRI, so you get that nerve impingement. So, I'd definitely in her case, get an MRI as well. So, she was referred to oculoplastics and was started on teprotumumab. She started to have blood pressure elevation, and she had no blood pressure problems before she was started on three medications. Still had no improvement and then was referred to cardiology. She finished the 24-week course of teprotumumab. She had some orbital decompression. And then a year later, she had cosmetic improvement, stable MS, but her blood pressure remained erratic. Dr. Desai, have you seen any cases like this before where the blood pressure remains elevated?

**Dr. Desai:**

Usually, the blood pressure will improve after you stop the medication but, I mean, some symptoms can last a while. I would say if it's been a year since we stopped the medication, it's unlikely to get better at this point. But yeah, her improvement is so significant. Is this picture with the orbital decompression surgery as well?

**Dr. Gupta:**

Yes.

**Dr. Desai:**

Okay. Because it looks like her prognosis is significantly improved. But she still looks like maybe she has a little bit of swelling, especially on the bottom eyelids it's still remaining. And she really dyed her hair, as you can see.

**Dr. Khachikian:**

I wasn't going to comment about the hair anymore because you know, stick to the facts. Doesn't she almost look like she has a little bit of swelling above her left eye this time? Like, the right eye so much better but the left eye maybe is a little bit more prominent. It's better, but –

**Dr. Desai:**

Maybe she just had more improvement on the right side than the left side.

**Dr. Gupta:**

Yeah. So, interestingly enough, the orbital decompression was on the left side not the right side.

**Dr. Sistrunk:**

Interesting. And I think it was the hyperthyroidism guidelines from 2000, not the most recent hyperthyroidism guidelines, but the one that Rebecca Bahn was the lead author on, there was a really nice table. It may have been in the second one as well but had the exophthalmometer measurements for different races. And that's something that really, you know, is important to have a good idea about that, because so many of our patients that we see of African American background, you will see some degree of exophthalmos just in the normal population, compared to, you know, their Caucasian age and age matched counterparts, you know. And so, I think that's, you know, something to consider with all of this as well.

**Dr. Desai:**

And I'm assuming that her hyperthyroidism was treated, and that was not the cause of her blood pressure issues as well. Right?

**Dr. Gupta:**

Correct. So, she was treated successfully on the methimazole, does remain on 5 mg of methimazole because she still has some antibody elevation, but it's lower than where the baseline was. But I often find in many of these patients that you remove the methimazole, the antibodies are still elevated, you're going to get a rebound, and it can be about off where you're starting right back where you started. So, she is happy with the cosmetic effect of this, using the teprotumumab and the orbital decompression. However, she is really bothered by the blood pressure issue, and it is very difficult for her. Would you do anything else?

**Dr. Desai:**

Did she get a secondary workup for her hypertension? I would definitely look at, you know, the three medications, it's a pretty big jump. Yes, it could be a side effect, but maybe she had something predisposing as well, that can be treated either surgically or with different medications to kind of control her erratic blood pressure.

**Dr. Gupta:**

So, yes. A good, good answer. I think that we definitely always need to do a workup of secondary hypertension when we have three or more medications that are not doing the job. So, she had a negative workup for secondary causes of hypertension, including pheo and some of the other things that we do see in Cushing's. Do you think that any MS treatments would have been contributory to what she's going through with her eyes? Or would you keep neurology completely out of it? Dr. Khachikian?

**Dr. Khachikian:**

I mean, autoimmune diseases travel together. I mean, it's possible because she –could she have a little bit of like myasthenia? Is it just related to MS? I don't know if I'm an expert in MS, to be able to comment on that. I did want to go back and ask when she had the orbital decompression, they did the left eye. Is it because they saw nerve impingement on that side? Or?

**Dr. Gupta:**

Yes.

**Dr. Khachikian:**

Okay. And then the imaging, did it confirm MS?

**Dr. Gupta:**

Yes. Okay, we're getting another audience question about how well do the thyroid stimulating immunoglobulins or TRAb levels correlate with thyroid eye disease activity? And can we use them to predict when and if thyroid eye disease will be present in Graves' disease patients? And should we be trending these antibodies over time? Dr. Desai, do you want to tackle that one?

**Dr. Desai:**

Sure. Okay, so the Graves' antibodies, they do predispose you to having the eye disease as opposed to if you were completely antibody negative. Of course, you can have variations. Patients with high antibodies don't necessarily get the TED. Most of the TED is going to come within the first year, slightly before or following the diagnosis of the Graves' disease. I don't necessarily think that you need to keep following the antibody levels long term, especially if you get out from that 1-year mark, the chances of having TED like 20-30 years later, is pretty low. So, I wouldn't necessarily keep following them. But I think that every patient with Graves' disease, regardless of the antibodies, should have a really good eye exam at the time of diagnosis. And if you're going to consider radioactive iodine treatment, it's definitely something to consider because 15 to 20% of patients who get radioactive iodine do develop Graves' – sorry, the TED, and the TED can become significantly worse after the iodine treatment. But that doesn't necessarily mean that if they have positive antibodies, you shouldn't do the radioactive iodine treatment. But it's just something to consider.

**Dr. Sistrunk:**

Let me ask you a question, it's that one thing that I noticed with the people that I do treat with radioactive iodine, and I still treat a fair

share of people with radioactive iodine. My personal opinion, and there is maybe some research to back this up, but those people that you give a mutagenic dose of radioactive iodine, maybe 10-12 millicuries for hyperthyroidism versus a higher dose, I personally believe that we see more thyroid eye disease later developing in them, as opposed to those that get a higher dose of radioactive iodine. And so, I guess that if I'm going to treat somebody with radioactive iodine, my hope is to render them hypothyroid, but also minimize the complications. And so, I will give a higher dose, 25 millicuries of radioactive iodine, without any hesitation at all, with very little development of eye disease. Do you guys have any insight on that? Or have you seen any data to support a higher dose radioactive iodine with a less chance of eye disease?

**Dr. Khachikian:**

Dr. Sistrunk, I have a question for you.

**Dr. Sistrunk:**

Sure.

**Dr. Khachikian:**

So, if you saw a patient and in the office, and they had Graves' disease, and they, I mean, if they had significant proptosis, I suspect that you'd stay away from the radioactive iodine.

**Dr. Sistrunk:**

Absolutely.

**Dr. Khachikian:**

But if they had any ocular symptoms, whether it's like scratchy eyes, dry eyes, light sensitivity, and it was mild, like mild thyroid eye disease, would you still feel comfortable giving them radioactive iodine? Because –

**Dr. Sistrunk:**

I think if it was very mild, I would give them an oral dose of and a taper of steroids. And I would not hesitate to if that was in the clinical picture that would be of benefit to them.

**Dr. Khachikian:**

So, I guess I'll follow it up with this. I think it's now been like, 3 years or 4 years, but there was a quality of life study that came out for patients who received either surgery, medication, or radioactive iodine for Graves' disease. And they looked at these patients, and they went forward in time and notice that even like 5 years, 10 years out, patients who had the same thyroid labs, whether it was through any modality of treatment, patients who had received radioactive iodine had a lower quality of life. I used to use it earlier on in my career significantly, and now, I don't know if it's a selection bias, but like, anecdotally, I noticed it in my office. I mean, I still use it, especially the patient who I feel like isn't going to be compliant with methimazole. But I don't use it as much as I used to use it.

**Dr. Sistrunk:**

Right, and I don't either.

**Dr. Khachikian:**

I don't know if I just convinced myself? Yeah.

**Dr. Sistrunk:**

Right. I don't either. I think everything is selective. And I think so much of what we do is patient driven to talk to them about the risk and benefits. And, you know, I see some people that are pretty sick with Graves'. And, you know, when somebody comes in and their free T4 is 5.5 and they're sick, and they are 50 years old, they want to feel better, you know. And they want to know that they're going to feel better and this is not going to come back again. And but I'll talk to him about it. And I do spend quite a bit of time talking about the risk of each of those treatments, because having caused agranulocytosis a few times in my career, it is not something you want to be on the wrong end, you know?

**Dr. Khachikian:**

No.

**Dr. Desai:**

Well, it's interesting. We actually I have a larger Asian population over here, so I generally rarely use radioactive iodine and partly it is patient preference.

Most of the patients gravitate towards methimazole. And then we actually have a couple of patients that have chosen surgery as their primary, ideally as their primary. Of course, we hold them over with methimazole until they get their surgery, but we have a few patients

that have chosen surgery as well.

**Dr. Sistrunk:**

You know, I will tell you, in my training, and this was around starting in 1998, I was working at Mayo as a trainee, I remember maybe once using antithyroid drugs in my whole fellowship, you know. And it was like, you know, it was very foreign, a foreign concept at that time. And I know that that has all changed by all of the information we have. But it's, you know, I think that, you know, I talk to patients about it and, you know, patients usually, you know, they will listen to what you have to say and, you know, I oftentimes do express the risk of developing thyroid eye disease, but I don't use that to the extent of 50% are going to develop it after getting the radioactive iodine.

**Dr. Desai:**

Interesting. I don't think Mayo changed that for a while, because I also trained there and we still use a considerable amount of radioactive iodine.

**Dr. Sistrunk:**

Right. Absolutely. Absolutely. And I think that, you know, you look at one of these things with the Clinical Activity Score or the Gorman index, I mean, that's a big part of that, you know, the history of, and also the success. And I think that you can't, you know, you can't argue with the success of some of these people that were so ill that got better within a month, you know.

**Dr. Gupta:**

That's great.

So, we're going to go to our final case in just a minute. And we are having a great time discussing thyroid eye disease from the endocrine perspective. It's very interesting that of all the contestants in these rounds, we've had several who trained at Mayo, so did not know that about some of you. Well, although I did know Dr. Sistrunk and Dr. Falahati were co-fellows.

Alright, so we're going to go ahead and move on to Case #6. And Case #6 is a 67-year-old female with a history of taking thyroid replacement for 20 years. She's been decreasing her dose multiple times with physician assistance there. The current TSH on no medications is 0.04. She does not smoke. Dr. Khachikian, what do you see in this photograph?

**Dr. Khachikian:**

So, when I am looking at this photograph, I'm noticing some eyelid erythema and some orbital edema, more so on the left than on the right. You can see some scleral or conjunctival injection. And there is a little chemosis on the right-hand side. You can definitely notice it in the left eye on the left side that you see a little bit of caruncle or plica inflammation. It looks like the left eye has a little bit of asymmetry and there's a little bit more proptosis than in the right. I think those are the things I'd start with.

**Dr. Gupta:**

Great. She was sent to the endocrinologist because the levels were dropping. And she had a positive TPO antibody, negative thyroid stimulating immunoglobulin. And we do have an audience question about thyroid eye disease, and can you have thyroid eye disease in patients who are hypothyroid? And the answer is yes, you can have – thyroid eye disease is a separate disease from Graves' disease and other autoimmune thyroid diseases. It can occur in up to 50% of Graves' disease. We do see a number of patients who have hypothyroidism or Hashimoto's who do have thyroid eye disease. And you do have patients who are euthyroid who do have thyroid eye disease. So, Dr. Sistrunk, is this what you're seeing in practice as well?

**Dr. Sistrunk:**

I would say so. I'm very keen to know what the free T4 in this patient is.

**Dr. Gupta:**

So, the free T4 on this patient actually was starting to trend upwards.

**Dr. Sistrunk:**

Okay, so was it 2 to 4? Or was it, you know, was it 1.8? Or any idea? If you don't know, that's fine too.

**Dr. Gupta:**

Cannot recall.

**Dr. Sistrunk:**

Alright. And the other thing too is I definitely would have checked the TSH, a TRAb antibody, TSH receptor antibody in this patient probably at the same time I did the TSI, TPO. I bet it would have been positive.

**Dr. Gupta:**

And I usually get an anti-thyroglobulin on these patients too.



**Dr. Sistrunk:**

Right, absolutely.

**Dr. Gupta:**

It actually wasn't my patient but was started on methimazole 30 mg in the morning. And then it was reduced to 5 mg over the next 4 months. And these are some of the manifestations, both eyes had pain, watering. The left eye had more watering than the right. And she had lid swelling in the morning. The optometrist gave her drops, the ophthalmologist who was involved measured the left eye to be 2 mm more proptotic than the right eye. And I definitely agree with imaging right here when you have asymmetry. She was started on the teprotumumab and finished a 24-week course, had no side effects. Dr. Desai, can you comment on the differences between the two pictures?

**Dr. Desai:**

So, her redness and conjunctival injection definitely improved. I think the chemosis also improved. Interestingly, I think she still has a significant amount of ptosis, which is almost covering the top of her eyes. And her bottom lower lids had edema previously which has subsequently resolved. I think that was mostly – I think she has improvement. I think there's a lot of improvement compared to \_\_\_\_\_. And maybe her proptosis is actually better, but I still think that the left side is a little bit more than the right side.

**Dr. Gupta:**

Dr. Khachikian, at what point when somebody has finished their course of teprotumumab, how much time would you allow between deciding whether or not somebody may need a second course of teprotumumab?

**Dr. Khachikian:**

So, there actually is no downtime. I mean, it obviously takes time to get them off medication. But usually within 3 weeks, the medication is out of your system, which is why, like, if you look at the half-life, that's why they dose it every 3 weeks. Having said that, some experts will argue that you want to wait about 5 to 6 months before you give a second dose. And in my experience in patients who've done really well with treatment, if they have a resurgence of ocular symptoms, usually it's around 6 to 9 months. But there is no given time, there's no cases that have been done that said you have to wait a certain period.

**Dr. Desai:**

I agree. I think if the patient is getting worse and more symptomatic, you can consider doing it sooner than the 6 months. If they're stable, or it's very, very mild, you could consider stretching out a little bit more.

**Dr. Gupta:**

Great. Dr. Sistrunk, do you get a lot of cases where you see failure on the teprotumumab after a certain period of time? Or do most patients seem to hold in the cases that you've seen?

**Dr. Sistrunk:**

In the ones that I've seen, it seemed they have seemed pretty stable, but I guess that to play the devil's advocate here, if you had just waited 24 weeks in this lady, would we have had the same result without any intervention? You know, she still has a significant degree of periorbital edema and, you know, with the, you know, just the tincture of time with thyroid eye disease, you will see some improvement and so, you know, I question whether if you had just waited with no intervention, would we have seen the same picture on the other side 24 weeks later with no intervention.

**Dr. Gupta:**

So, this is interesting. I always start the selenium in these cases anyways and sometimes I have had a lot of response to just the methimazole and selenium by itself before we do have some improvement there. An audience question is how does selenium help with thyroid eye disease? Dr. Khachikian, do you want to help answer that one?

**Dr. Khachikian:**

Oh, I can take a stab at it. It is believed that selenium helps to stabilize the microarchitecture. And that's what it does in the thyroid, so I suspect that's what it does in the muscles in the back of the eye. But maybe Dr. Sistrunk would have more information about it. Phone a friend.

**Dr. Sistrunk:**

I'm thinking about the original paper and there was another drug, the comparison – oh, gosh, I'm drawing a blank on the other drug that was used. But they compared it to another drug that was a not a nonsteroidal, but I'm drawing a blank on which drug it was. And there was some improvement there. But it wasn't marked improvement. And there's always been question of, was it because the people who were studied in that particular study were in an selenium-deficient part of the world? And that's something that has always been brought

up as well. So, I don't have a strong idea about that. Yeah.

**Dr. Khachikian:**

You know, Dr. Gupta, one other thing I was going to bring up, and I think we've kind of skirted around a little bit is, we are doing a clinical picture and we're looking at all the physical exam findings, I think another factor that we really need to take into consideration is what this patient's quality of life is like. So, I don't disagree. We may notice a degree of clinical significance if we just treat with antithyroid medication. And the recommendations are you should have a free T3, free T4 that it's in the 50% within the upper or lower limit and the TSH – and/or a TSH that's normal. Because even back to the initial ATA guidelines, the thought is that when someone is either overtly hyperthyroid or significantly hypothyroid, that in and of itself can cause concern within people's eyes. So, you want to get rid of that. Right?

**Dr. Sistrunk:**

Stare, absolutely. Yeah, absolutely. Stare, because –

**Dr. Khachikian:**

So, I think – right. So, we want to make sure that we don't – I think the like even with the TSH above 7.5, I think it said in like the initial ATA of like 2016 guidelines that it can cause, in case reports, a change. But I'd also be curious to see like, apart from this, I mean, does she have light sensitivity? Is she not able to do certain things that she needs to do? Which I think now needs to take enough of a way that we consider whether we want to wait or we want to start treatment.

**Dr. Gupta:**

Alright. So, we're getting another audience question, how often might patients who are euthyroid present with positive thyroid antibody tests? And how is this possible? Dr. Desai?

**Dr. Desai:**

So, you can actually have antibodies to a lot of diseases, not just Graves' disease. And there may be some time lag before you actually get the clinical condition, because there's some question about whether there's an environmental trigger on top of just having the antibodies. So, I've definitely seen patients with antibodies that we've followed, and that don't necessarily get Graves' disease, but obviously, they're more highly likely to get Graves' disease, so I would follow them kind of carefully compared to somebody who was antibody negative. But you can definitely have people with antibodies and not guaranteed to have diseases. Even with Hashimoto's, tons of people, the population doesn't have positive antibodies, you just monitor their TSH, and then then if they're hypothyroid, then you treat it; we don't have to do anything preemptively.

**Dr. Gupta:**

I'm going to just tell you my personal experience with this. I actually was euthyroid for 10 years with positive antibodies, for positive TPO antibodies. And so yes, very possible. And I learned a lot about it firsthand.

I think it's interesting that we probably have a lot more thyroid disease out there. It is one of the most commonly diagnosed issues. And I think that thyroid eye disease is very important to note that we're probably missing a lot of thyroid eye disease cases with the old knowledge of saying it's just with Graves' disease. It's not a symptom of Graves' disease, it's its own disease, and it's a separate disease from autoimmune thyroid disease. It's an actual separate disease. And the pathophysiology to it is different as well.

So, I think they're calculating who we have as our champion. And we are ready to and now announce our champion from for the KOL Knockout – Endocrinology Edition. Our final champion is Dr. Desai.

**Dr. Sistrunk:**

Good job.

**Dr. Desai**

Thank you.

**Dr. Sistrunk:**

Congratulations.

**Dr. Khachikian:**

I think all of us talked about something today.

**Dr. Gupta:**

And thank you. This is a CME event provided by Evolve Medical Education. Thank you, Dr. Khachikian, Dr. Desai, and Dr. Sistrunk.

**Dr. Sistrunk:**

Thank you.

**Dr. Desai:**

Thank you.

**Dr. Khachikian:**

Thank you, guys.

**Dr. Sistrunk:**

Thank you for letting us participate.

**Announcer:**

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