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Using a Biologic in a Patient with Atopic Dermatitis and HSV Keratitis

Announcer:
Welcome to CME on ReachMD. This activity entitled: Using a Biologic in a Patient with Atopic Dermatitis and HSV Keratitis is provided by RMEI Medical Education, LLC and is supported by an independent educational grant from Sanofi Genzyme and Regeneron Pharmaceuticals. Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Leo:
Welcome to our second Clinical Consults in the series. I'm Dr. Peter Leo, and I'm joined once more by my colleagues Dr. Eric Simpson and Dr. Mark Boguniewicz.

We asked you to send your difficult atopic dermatitis cases for us to review and discuss collaboratively. Thank you for your participation.

Today's case is an 8-year-old girl with poor weight gain, dairy, wheat and peanut allergy. She also has a history of herpes simplex keratitis, frequent ear infections, mupirocin-resistant impetigo on the face and severe atopic dermatitis with 90% body surface area involved. She's already failed phototherapy and methotrexate, and she's been maintained on cyclosporine and mycophenolate mofetil, but she still has severe flares. The family thinks that cats cause some of these flares, and she is exposed intermittently to cats at a relative's home. She has no history of asthma but suffers from food allergy, anxiety, and sleep disturbance. Her peripheral eosinophilia and IgE usually total significantly elevated numbers. Her gastroenterological workup has been negative for celiac disease. Her severe atopic dermatitis is poorly controlled even on these 2 powerful immunosuppressants, and the question is really to consider dupilumab despite this history of herpes keratitis in the past. The question also notes that she has not had a flare of this for over a year while she's been on suppressive acyclovir, so really I think this comes down to the question of herpes keratitis and dupilumab.

Dr. Simpson, what do you think would be a safe option for this patient?

Dr. Simpson:
Sure. I just feel so bad for this young patient. We see these very severe patients, and it's just so difficult. It affects everything in their life. The first thing I think I would do would be maybe—and I know this isn't the topic for today—but verify the food allergy, so has the patient had multiple positive tests but no definite clinical reactions to the food. I would first try to clear that up, especially—and clarify that with the patient and an allergist like Dr. B here with us because with the poor weight gain, that makes me really just concerned that they may be overdoing it on the food restriction. When you have 90% body surface area also, you're often going to be low weight as well. But the first step I would do would be clarify that.

And then the second step, in terms of treatment options, I agree; she's run the gamut of therapies including double immunosuppressives, and so I'm glad that she's on acyclovir. That's a preventive from this herpes keratitis, which can cause permanent damage. So I think, actually, given the failure of traditional immunosuppressants, I think dupilumab would be a great off-label use. We don't know the efficacy and safety of dupilumab in this age range, but everything we've seen so far is that this would be a safe option for this patient.

The herpes keratitis doesn't concern me. In fact, when you look at the herpes—eczema herpeticum data of all of the trials combined, treatment with dupilumab actually reduces the risk of eczema herpeticum and does not appear to increase the risk of herpes simplex infections. Dupilumab does have a keratitis risk, which is extremely low. That's not a herpes keratitis. It's a completely different etiology, so I don't think that those... Just because the patient is getting ocular symptoms of one type doesn't mean that there's a risk of ocular symptoms of another type. We know the most frequent side effects with dupilumab are more of an allergic conjunctivitis or a

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conjunctivitis-type reaction with the eye, so I would not be concerned about the previous history of herpes keratitis. In fact, I think that's even more of a reason to treat the patient to get the skin under control, to get the child growing again and potentially even reduce the risk of herpes infections.

Dr. Boguniewicz:
So, if I could just add some comments as an allergist/immunologist—first of all, I really appreciate my dermatology colleague pointing towards the approach to the question of food allergies in these patients with severe atopic dermatitis because we know that's certainly what's on the minds of so many of our parents of these children and in our adult patients, what they think about. And it's really important to recognize that the basic concept that allergic sensitization—so having positive tests, as Dr. Simpson pointed out—is not the same as having clinically meaningful allergy, and so in our unit where we take on severe patients from around the country, typically our experience has been that if you have identified food allergy based on a positive in vitro test, then we put back roughly—and this is certainly an approximation—but 8 out of 10 foods that people may avoid or take out of their child's diet, and that's a huge issue because these difficult elimination diets really complicate life for our families. The problem is that, unless you can get their skin under control to then do the appropriate supervised challenges, this continues to be a problem for our patients.

As an immunologist I certainly support Dr. Simpson's approach to dupilumab because we know that correction of the immune dysregulation in our patients should lead to—and in fact, the clinical studies have shown fewer infections including viral infections, and in the studies that we recently completed in our 6-to-11-year-old patients with severe atopic dermatitis treated with dupilumab, we were very careful about having them evaluated by ophthalmologists for any ocular complaints, and we didn't see that safety signal, so we are very optimistic about using this biologic in that patient population if, in fact, it does get FDA approval.

Dr. Simpson:
That's great, and I really think that that summarizes this very tough case. This is really the kind of situation where you have to think about going off-label because they've really exhausted everything. And I would just say, personally, this is the type of case when I have these patients that I will think about sending to an inpatient program like where Dr. Boguniewicz practices for a week or 2 to let them get some support, because one can imagine the family is exhausted. If they're still having severe flares through this kind of level of immunosuppression, getting blood draws, monitoring, all of this stuff, they're going to need some extra support, especially until the dupilumab is on board and hopefully helping.

Dr. Boguniewicz:
And, in fact, in the case that you presented, you did mention anxiety and sleep disturbance, and so I would say that as important as addressing the question of are there food allergies, what's the infectious history, is addressing those very important and meaningful to the patient and family parameters of sleep and behavioral or mental health. And I'm sure that Dr. Simpson has studied that, in fact, in the trials with dupilumab and probably can comment further.

Dr. Simpson:
Yes, I agree, Mark. Up to 40% of the adult patients and even in the pediatric patient population there's a very high prevalence of anxiety and depression, and a lot of those symptoms can significantly improve with even just 4 months of treatment with dupilumab, and I would assume any beneficial treatment for that child would help those symptoms.

And I just wanted to make one more point regarding the eye symptoms. It's one of the most common side effects using dupilumab is dealing with this conjunctivitis, this irritation of the conjunctiva, kind of unclear reasons in this patient population. I don't know if you get this, Peter or Mark, patients say, "Oh, if I have…" If you have preexisting conjunctivitis, is that a reason not to put them on the drug? And I would say no. I don't think that's an increased risk of developing the side effect. In fact, there are some reports that even severe atopic keratoconjunctivitis can improve with dupilumab, so I don't let eye symptoms at baseline steer me away from the drug. I think it's still a very appropriate use in that patient population because up to 40, 50, or even 60% of these patients do have eye symptoms at baseline.

Dr. Leo:
I totally agree. In our case series we found that not a single patient who had presented to us with dupilumab-induced either keratoconjunctivitis, blepharitis or whatnot—none of them had preexisting eye disease. And I was tracking very closely people that had preexisting, usually allergic keratoconjunctivitis, and none of those patients seemed to have trouble, so certainly, I don't think they are necessarily excluded, but I'm totally with you that I don't think it's a reason to say, "No, I don't want to give you this drug."

Dr. Boguniewicz:
Agree.

Dr. Leo:
That was a wonderful question and wonderful discussion. Thank you. And thank you all for joining us today. Please don't forget to take

the posttest and complete the evaluation to receive your CME credit.

Announcer:
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