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### Options for an Infant with Atopic Dermatitis

Narrator:

Welcome to CME on ReachMD. This activity entitled: Options for an Infant with Atopic Dermatitis 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:

Today will feature the last of our Clinical Consult series. We would like to thank all of you for submitting your cases for discussion. I'm Dr. Peter Leo, and I'm again joined by Dr. Eric Simpson and Dr. Mark Boguniewicz.

Today's patient is a 6-month-old baby with severe atopic dermatitis and sleep disturbance. He is not controlled on topical corticosteroids, topical calcineurin inhibitors or emollients. The question asker has explained that they have tried multiple short courses of oral steroids in the past that gives temporary improvement but not sustained.

So, the first part of the question I'd like to ask Dr. Boguniewicz. What emerging treatment options do we have for this very young age group?

Dr. Boguniewicz:

Peter, this is, unfortunately, all too often a common scenario that we face, and I think that we really need to consider before we talk about newer emerging treatments to take a step back. And one of the things that you might think about is, in an infant with an eczematous rash, is it possible that we are treating something other than atopic dermatitis? We recognize atopic dermatitis as such a common chronic inflammatory skin condition in this population, but yet there are those rare immunodeficiencies, in fact, that can present with a very much atopic dermatitis picture, and so we need to consider that in a patient who truly doesn't respond.

Here I think the history was somewhat reassuring in that you mentioned that the patient did respond to systemic steroids even though we really don't want to go down that path of recurrent use of systemic steroids, but we would document that the patient has a steroid-responsive dermatitis. After that I would say my approach would be to put the patient in a controlled setting and see what the response to more conventional, meaning topical, treatment would be, often combining a lower mid-potency topical steroid with wet wrap therapy for 4 or 5 days. And then, if that patient truly was not responsive to that, I would think about even a skin biopsy and looking further into the differential.

But to answer the question that you posed on emerging treatments, with topical calcineurin inhibitors I would just say historically we had hoped to get approval down to 3 months of age, and studies were done in that age range, and this patient apparently has failed off-label use of topical calcineurin inhibitors. Studies with a topical PDE4, phosphodiesterase-4 inhibitor ointment have been completed down to 3 months of age, but we await—or at least I'm not aware of the results yet from those trials. As Dr. Simpson has mentioned in a previous case, he's participated in trials with dupilumab, a systemic biologic therapy down to 6 months of age.

I don't know if, Eric, you want to share any of your experience there and talk about this patient.

Dr. Simpson:

Sure. I mean, I think it's a very rare situation that this happens, and I completely agree with you, Mark, that I would take a step back and confirm the diagnosis, consider other alternatives: is the patient having failure to thrive? have there been pneumonias? are there concerns for immunodeficiency syndrome? and work with our genetic and allergy colleagues to figure that out.

Assuming this is severe atopic dermatitis—I often talk to my residents when I hear a case like this—the devil is in the details, and the details are what's most important about good outcomes in patients like this, and so I would really want to know did the patient ever clear on topical steroids. So, if used once a day or twice a day, medium potency like you said or even high potency for a week full body, is that patient clear and then the disease just starts returning and that's their impression of something not working?

So the majority of these kids that have this story, I find that if you can induce clearance with medium-potency topical steroids usually at this age range for maybe 1–2 weeks, I like to employ either pimecrolimus cream, which we do have safety data down to 3 months—this is all off-label, but we do have some safety data in that age range—or even tacrolimus ointment, either .03 or .01, and use that in a proactive fashion to normal skin. And this hasn't been studied on a daily basis—it's been usually intermittent—but for these severe kids like this where I'm thinking they are going to need cyclosporin or they received oral steroids that could potentially even amplify the disease at times, I'll do daily full-body pimecrolimus cream or tacrolimus ointment to normal skin and then do that in a tapered-off fashion because they are so severe, and so sometimes you can avoid systemic therapy if you get very aggressive about proactive treatment with nonsteroidal approaches, and that could be pimecrolimus cream, tacrolimus ointment, or the new drug, crisaborole, a new nonsteroidal.

Dr. Leo:

I really like that. So the idea there is we want to get them clear, which presumably we can with the appropriate strains of corticosteroid, maybe even a mid-potency, something like triamcinolone, maybe with the addition of wet wrap therapy—let's get this cleared up—but then instead of just stopping at the end of 5 or 7 or maybe even 10 days of intense treatments, then we'd say, "No, we're not going to do nothing, but we're going to do a nonsteroidal," so the whole body application even if the skin looks good to maintain it. I think that's brilliant. Of course, this is all very off-label, and I feel like most people don't do it this way yet, but this really seems like the best way for these difficult cases, and I think they can turn everything around.

Dr. B, in the inpatient setting when you guys do your it's similar to that, is it not?

Dr. Boguniewicz:

It is, and I would say though it's really important to emphasize that, unlike our European colleagues who view a wet wrap therapy as something that they may do long-term, we really think of it as heroic rescue, so an acute intervention that most of our severe patients can be discontinued from after 4 or 5 days. Occasionally, we'll use it selectively like to resistant hand or foot eczema longer, but the downside of prolonging wet wrap therapy is that you risk the possibility of a folliculitis. Sometimes it's a sterile occlusion folliculitis, but in this day and age of MRSA, we always have concerns about overuse of wet wrap therapy.

And of course it makes life more difficult for our families. It's time-consuming. The way we would do the minimal wet wrap therapy would be a bedtime application to selectively the worst areas of eczema over a topical corticosteroid.

Again, because topical calcineurin inhibitors actually say not to use with occlusive dressings, we don't do it even though you could argue that it probably would be safe for short-term use, but we use wet wraps with topical steroids. Occasionally, you hear about people using them only with moisturizer, and to us that really doesn't make sense because we're using it when the eczema is really severe.

Dr. Leo:

That is great information. Now, the last question they wanted to address was: Is there anything that can be done right now to reduce the risk of developing food allergies or other types of allergies or asthma in the future? What do we think is the state-of-the-art? And, Dr. Simpson, you maybe should start us off since you kind of—you started this whole thing with the concept of prevention with moisturization.

Dr. Simpson:

Sure, yeah, and the idea of preventing allergy has been around for 5 decades at least, and it's just had varied approaches. Some are allergy avoidance and food restriction or food avoidance, dust mite avoidance, etc., etc., and nothing is really panning out. We've been interested in potentially protecting the barrier from birth, especially in high-risk neonates, and we've seen some positive responses in some of the clinical trials that have been performed both in the United States and in Asia. Some of the confirmatory studies are ongoing. Some of them have not been positive, so we still don't know the role of emollients early in life, if that can prevent atopic dermatitis, but the hypothesis is, if we can prevent atopic dermatitis, if we can control or reduce the barrier dysfunction early in life, we may be able to modify the whole atopic march and potentially reduce the IgE sensitization that could happen through the skin, and even in just reducing atopic dermatitis you might be able to prevent things like downstream events like allergic asthma or even food allergy. None of this has

been shown. These are endpoints that we're looking at right now in a big cohort of 1,200 babies, so we're going to know in a couple years, have a readout there.

I think a big question that still remains to be studied is whether early control of atopic dermatitis with any means, so once you develop atopic dermatitis, if you control that aggressively with the proactive approach or with systemics such as anti-IL-4/13 therapy, can that modify the allergic march or the risk of developing asthma, hay fever, food allergy? And again, these are very difficult, very expensive studies. You need to treat kids very early. And so that's a big important question that's yet to be answered.

Dr. Boguniewicz:

Yeah, such a complex and critical issue. Part of our frustration is that it's hard to identify really who are the at-risk patients to design the right trials, and so we have been frustrated with some of the early intervention trials. Nevertheless, we know that so much of that sensitization does occur through that damaged skin barrier. We know that patients who, for example, have mutations in filaggrin, which is the risk factor that's most strongly associated with development of atopic dermatitis, also is a risk factor for development of asthma and allergies, so we think that there's something to be done there in early intervention like Eric mentioned. It's just figuring out the timing and the right intervention.

Dr. Leo:

Well, that's fantastic and very, very comprehensive. I'd like to thank you for joining us today, and I want to just remind our participants to please take the posttest and complete the evaluation to receive the CME credit. Thank you for your attention.

Narrator:

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