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Journal Club: Height Improvement After Treatment

Dr. Peter Lio:
Hello and welcome to Atopic Dermatitis Journal Club. I'm Dr. Peter Lio, and today I'm here with Dr. Amy Paller, and we are excited to be discussing some new data that suggests that children with moderate to severe atopic dermatitis, when they're treated with dupilumab, they actually can show an improvement in growth. Dr. Paller, what is your take on this situation and what do you think is going on here?

Dr. Amy Paller:
Well, thanks for asking, Peter. I'm really excited about some of this new data. Of course, we've been watching for the last few years to see how dupilumab in prepubertal patients really can improve their clinical appearance and also their quality of life. Of course, these children are just miserable with their tremendous itch, their reduced sleep. It just permeates their lives terribly and also the lives of the family in terms of how disruptive atopic dermatitis is.

And we've seen this absolutely turned around by the use of dupilumab. And of course, now we have also for those who are 12 and above a variety of other drugs that we can choose from, which similarly are really helping with the lives of these children and their families. The concept of doing more is one that's now being explored and can be with dupilumab because of its availability in these younger children and also the fact that it's now been around for a few years and we're able to track children.

So I would say that the concept of growth is one that's always on the minds of families, and certainly as children get older on their minds as well, particularly when they're quite short. And that's the case with many of the children who have atopic dermatitis that is moderate to severe. We think about the fact that these children may be hypermetabolic and that they're constantly struggling with this inflammation on their skin.

We couple that with the fact that they're not sleeping well and we know that sleep can have a dramatic impact on linear growth. And we also know that many of these children have been using a lot of even oral corticosteroids, and we all know the effects on growth of being on systemic corticosteroids. So it's been interesting to think about the potential relationship between having the atopic dermatitis and poor growth.

In fact, there have been a few papers in the past that have tried to look at growth in terms of weight and height in children and have suggested that the height is reduced in children with atopic dermatitis. We've been able to use data from a new 10-year longitudinal study of children under the age of 12 who have moderate to severe atopic dermatitis that is severe enough and unresponsive enough to topical steroids to move on potentially to a systemic drug.

Some of these children are just staying with topical steroids. Some of these children have moved to methotrexate or cyclosporine, and many of these children have also moved to dupilumab. This is called the PDSTAT trial. And what's come out a year ago at the American Academy of Dermatology was that in a study of more than 1,200 of these children with moderate to severe atopic dermatitis, the percent that were below the 50th percentile for height was increased.

And this was particularly true of male children for some reason in whom 72% of those who were five to less than 12 years of age were below the 50th percentile for height. And in females, it was a slightly increased with 53%. Interestingly, this study also showed a little increase in weight of these children with atopic dermatitis. Not as significant as we were just talking about for height, but still slightly increased, and that gave them quite an increase in their BMI values.

Now, you could hypothesize why that is, maybe because children with atopic dermatitis, because they have trouble with sports and

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sweating and many of the activities that we consider exercise and help with weight control are reduced, but perhaps there are some other reasons metabolically that we're not aware of.

Dr. Peter Lio:
I love that. It's really neat to think about all the different mechanisms you've pointed out that are potentially at play here, the disease itself consuming metabolic fuel and diverting resources from growth, the issue with impact on sleep for these patients, dietary alterations people are doing. So all of those pieces. Then you have the other side, what medicines are they using that potentially could be contributing?

Of course, systemic corticosteroids, but I even wonder, overuse of topical steroids, they may be absorbing enough to have even a small effect on their growth. So if we fix all of those, it's not surprising in a way to see that the growth is actually improved. Now, my question for you is have you been able to use this for patients maybe and families who are treatment hesitant?

Because sometimes if families are nervous just about treating the atopic dermatitis, they say, "Maybe we can wait. It's not that big of a deal." I find it really helpful to say, "This is bigger than just the skin. This is affecting many aspects of life," and that's been really helpful to bring this up. Have you found the same sort of thing?

Dr. Amy Paller:
Well, let me talk a little bit about what was shown in the studies with the dupilumab then. And this is really hot off the press data. And I should say that this follows information that looked at some of the laboratory values in the studies of those who were in that prepubertal age, six to 11. That's an age where we see that growth spurt starting. So the very important age in terms of height development.

In fact, it became obvious that alkaline phosphatase, which many people in the world of adult dermatology might look at as a bad thing if it's increased, was increased in children who were on dupilumab. And when this was probed further in terms of looking at other biomarkers of bone health, because we in the pediatric world know that alkaline phosphatase goes up as children are growing. It was found that other bone biomarkers similarly were improved on the dupilumab.

And that has now been studied extensively and suggested that maybe this improvement in bone health seen on the dupilumab and in the clinical trials seen when those who were on placebo switched over at 16 weeks to dupilumab that maybe this could correlate with improvement in height over time. And I should say that this improvement in the bone health biomarkers was seen by 16 weeks on the drug.

Biomarkers, of course, can be seen earlier than you might see clinical change. So the newer studies that have come out have actually shown that there is evidence of the improved growth. If you look at those children in the studies of the dupilumab, indeed there was overrepresentation of children below the 50th percentile in height and some overrepresentation also of those who were a little bit above the 50th percentile in weight as noted in the PDSTAT trial as well.

When these children were followed out, a significant proportion of those children below the 30th percentile achieved that increase in percentile improvement in height by at least 5% who were on the dupilumab even over that relatively short period of time. So in the children who were on the placebo, that was seen with 11%. And in those who were on the dupilumab, that was seen in about 32%.

So a statistically significant growth just during that short period when we look at those who were less than or equal to the 30th percentile and achieved that five or more percentile increase in height. That's very exciting. I want to answer your question about how this information about the increase in linear growth contributes to our discussion with families about should they or should they not move on to a systemic therapy.

Of course, we only have that information for one systemic therapy right now, and that's dupilumab. But I think we can add this to our list of benefits when we talk to families who are worried about starting their children on a systemic medication and perhaps also concerned about the requirement for an injection. We can talk about the reduction in infection.

We can talk about some early evidence that it not just improves the allergic disorders that they may also have, but maybe even if we start early enough, it reduces the risk of developing other atopic disorders like asthma, food allergies, even allergic rhinitis. That's all being looked at right now. Now we can add to that list that their growth may improve, and this is something that has been of great concern for many of our families.

Dr. Peter Lio:
Well, thank you so much. This was wonderful. Really an exciting time in the world of atopic dermatitis, and I feel really lucky that we get to discuss this. Thank you all for joining us, and we look forward to seeing everybody soon.

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