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Alopecia Areata Pathophysiology: What Clinicians Need to Know

Announcer:
You're listening to *DermConsult* on ReachMD, and this episode is sponsored by Lilly. Here's your host, Dr. Charles Turck.

Dr. Turck:
Welcome to *DermConsult* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss the pathophysiology of alopecia areata is Dr. Natasha Mesinkovska, who's an Associate Professor and Vice Chair for Clinical Research in the Dermatology School of Medicine at the University of California, Irvine. Dr. Mesinkovska, welcome to the program.

Dr. Mesinkovska:
Thank you for having me.

Dr. Turck:
So, let's just dive right in, Dr. Mesinkovska. Can you tell us about the key drivers of disease pathogenesis in alopecia areata?

Dr. Mesinkovska:
Alopecia areata is an autoimmune condition. And it is a complex interplay between two major factors. One is the genetics that one possesses, and the other a group of factors or triggers throughout one's life that ultimately lead to loss of immune privilege at the hair follicle. What does loss of immune privilege mean? The hair follicle actually is a very protected unit that has a way to shield itself from immune response. This is something that's also found in the level of the brain, the eye, and the liver. And how is this maintained? Through physical barrier from the lymphatics in the skin through antigen sequestration. And really, it almost has its own little immune guardians to keep it away from the immune system. But once the interferon gamma activities in play from triggers in life that we don't know, we think that collapse of immune privilege is gone. And that initiates the attack on the hair follicle and leads to loss of hair.

Dr. Turck:
So, zeroing in on that role of immune privilege, what else do we need to know about the mechanisms behind it?

Dr. Mesinkovska:
So, for a very long time, we've made significant advances in understanding the genetics, particularly through the work from Columbia University, Dr. Angela Christiano, and these genome-wide studies to understand what are the other autoimmune conditions that one possesses to kind of zero in on what are the genetics.

And interesting to these genome-wide studies, we found different regions that were at play. So, it wasn't just that the T-cell function regulators can be affected. Also, natural killer cells can be affected along with certain molecules at the level of hair follicle, even melanin, filaggrin, and autophagy things. So, the genetics has been dissected little by little, but the question was really, what are the other things? What are the triggers that we've had the privilege of learning more particularly in the last couple of years?

Dr. Turck:
And what else can you tell us about the mechanisms that lead to a collapse of that immune privilege?

Dr. Mesinkovska:
So, upon alopecia areata initiation from whatever that trigger may be, there is stimulated cytotoxic T-cell pathway that eventually leads to hypersecretion of interferon gamma. That induces expression of MHC class 1 cells at the level of hair follicle, and then there's this immunologic recognition of these autoantigens, and that leads to loss of the hair.

Dr. Turck:

For those just tuning in, you're listening to *DermConsult* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Natasha Mesinkovska about the pathophysiology of alopecia areata.

So now that we have a better understanding of the underlying pathophysiology, I'd like us to switch gears and focus on how that impacts what we see in practice. Dr. Mesinkovska, what do we need to know about the clinical presentation of alopecia areata?

Dr. Mesinkovska:
So, patients with alopecia areata tend to be typically young. It's a condition that can start early in childhood, as early as age 2, but honestly, there are patients that walk in with their first episode at age 70. The average age of a person is early 30s. So, what does that mean? That means that these patients are relatively healthy. But one thing is to understand just the toll that the condition has on their life. And that is they can start with a couple of patches of hair loss on the scalp, on the body, in the beard area, eyelashes, and eyebrows, but the thing is that the condition can be pretty quick, or it can happen little by little. But it's really that loss of control and the unpredictability of the condition that takes its toll on a person.

The hair loss can start with a couple of spots, and for some people that's where they stay. And that can be honestly in about 20 to 30 percent of patients. So about 20 percent of patients may only have one episode, and that's it. However, another 20 percent will progress to have a little bit of a longer course. And it will have more than one patch and more than two patches where they will need a little bit of treatment. And then people kind of divide in several groups. Some wax and wane, meaning they'll get a patch here, they'll be fine for a couple of years, and then they may get it again. And we think less than 12 percent ultimately will progress to what we now refer to as alopecia totalis and universalis, meaning they lose complete scalp hair, they lose eyebrows, eyelashes, and body hair.

Dr. Turck:
And when it comes to prognosis, how can that vary from patient to patient?

Dr. Mesinkovska:
There are several factors that can predict the severity of disease so that we know we have to maybe be a little bit more concerned and more vigilant. What are those? Early onset of conditions, so the earlier you get it, the more severe it tends to be, maybe because you just have many more years to kind of wax and wane.

The other thing is if there's a family history, patients tend to have more of a severe condition. If there are severe allergies and maybe some other autoimmune diseases such as thyroid, this has been a factor that predicts more of a severe disease.

Dr. Turck:
Now we've certainly covered a lot of ground today. So, before we close, Dr. Mesinkovska, are there any final thoughts you'd like to share with our listeners?

Dr. Mesinkovska:
The importance of the JAK/STAT kinase pathway is something that has actually allowed us to now have the first and only approved medications out there on the market, and that's the family of JAK inhibitors, which are becoming more important in treating particularly chronic skin conditions and then autoimmune arthritis.

With these JAK inhibitors, which are pills, unlike some of the biologics that we've had that work very well, this gives us a little bit of an improvement because it’s a pill, so people don't have to inject themselves. And what these medications do is they block the activation of these proinflammatory pathways, and as such, have been able to reverse the hair loss even in patients that have had complete hair loss for many years, even patients that had disease for 20 years or episodes that lasted as long as 8 or 9 years.

So, it's been a very exciting time in the field of alopecia areata because as we're learning more about the pathogenesis, we are able to offer more targeted treatments.

Dr. Turck:
Well with those final thoughts in mind, I want to thank my guest, Dr. Natasha Mesinkovska, for joining me to help us better understand the pathophysiology of alopecia areata. Dr. Mesinkovska, it was great having you on the program.

Dr. Mesinkovska:
Thank you so much for having me.

Announcer:
This episode of *DermConsult* was sponsored by Lilly. To access other episodes in this series, visit ReachMD dot com slash Derm Consult, where you can Be Part of the Knowledge. Thanks for listening!