More Than Hair Loss: Global Perspectives on the Clinical Diagnosis and Management of Alopecia Areata

CMEO Journal Club Transcript

Nekma Meah:

Hello, and welcome to this installment of the three-part Journal Club series titled "More Than Hair Loss: Understanding the Role the Immune System Plays in Developing Alopecia Areata and Its Treatment Implications." Today we will be discussing the Alopecia Areata Consensus of Experts, or ACE, study part II, results of an international expert opinion on the diagnosis and laboratory evaluation for alopecia areata. My name is Dr. Nekma Meah. I'm a consultant dermatologist with a special interest in alopecia and scalp disorders and I'm also the Secretary of the British Hair and Nail Society, and I have with me my colleague Dr. Dmitri Wall.

Dmitri Wall:

Hi, nice to meet you all. I'm also a consultant dermatologist with a special interest in hair disorders. I practice mainly in Dublin in Ireland, and I'm affiliated with University College Dublin there and I also have a second interest, which feeds into some of what we'll talk about, which is I'm a health care informatician. I specialize in the development and maintenance of patient registries.

Nekma Meah:

Fantastic. So, this activity is supported by an educational grant from Pfizer and brought to you by CME Outfitters, which is an award-winning, accredited provider for continuing education for clinicians worldwide.

Nekma Meah:

What we really started off with, how it all began, is that it really started back in 2019 when Dr. Wall and I were working as fellows in Melbourne under Professor Rodney Sinclair. The interesting thing was that we were from different countries and we realized we had different perspectives in treating alopecia areata and we wondered what these might be from a much more diverse group, from experts globally. And the ACE project, or the Alopecia Areata Consensus of Experts project, was really in the back of the Australian Alopecia Areata Consensus Paper, which outlined or summarized our thoughts on therapies in the pre-JAK era.

Dmitri Wall:

One of the challenges was coming up with a name, and it was Prof. Rod Sinclair who came up with the acronym Alopecia Consensus of Experts.

Nekma Meah:

He did. Yes.

Dmitri Wall:

It's a simple title. It took us a long time in that we identified 50 dermatologists from five continents, all of whom would've been considered recognized experts in the area of alopecia areata management and research. And then we conducted an e-Delphi process, which is a multi-step process, which we become familiar with through work that I've been involved with in the area of atopic dermatitis, the treatment work. And we took their process and adapted it for our purposes in alopecia areata. The first two rounds are online and it gives the participants the capacity to answer survey questions that we had thought about extensively, we had conducted preliminary reviews of those, and they would go through each set of questions and they would answer from their perspective. What you find over time is that you get to see those questions, but from the perspective of yourself and then from the perspective of the other participants, and then that's concluded with a final face-to-face meeting to resolve some of the questions where consensus hadn't been achieved. And we did that in Barcelona, in Sitges, or near Barcelona in Sitges, in Spain, at the World Congress of Hair Research.

Nekma Meah:

I suppose, Dr. Wall, one of the questions that we ought to really address is why was the e-Delphi process so important for ACE? Why was it selected for ACE? I mean, how we could have perhaps done it is asked all the experts, which was really hard work, but why did we select the e-Delphi process for ACE?

Dmitri Wall:

Well, I think at the time we were fellows and one of the really difficult things is when you're sitting in a room with one expert, when you're sitting in a room full of multiple experts and they're all the people you've read about in the various different papers, you tend to follow their leads. And even if you have an interesting perspective, it's very hard to raise that as somebody who's quite junior. So, the e-Delphi process, or the Delphi process, really helped us in that regard. It's designed to minimize influence or bias, and it facilitates all of that group coming together to gain consensus. It allows you to include that diversity. It allows people to say what they feel within the confines of the questionnaires, and how it does that is by presenting the patients in round two with the summary data of round one. And what you essentially do is you get to review your questions and you might have decided that you don't really agree with the point being raised, but what you might see is that as a population everybody else is very strongly in favor of it.

Nekma Meah:

Yes.

Dmitri Wall:

And from a very simple perspective, it may help you realize that you've actually misinterpreted the question, or it could be that you realize that you're a little bit of an outlier, but for some people, when they think about it, they might find that actually they can bring their thoughts more in line with the general group, and that's the whole point. We want people to gain consensus. The e-Delphi process recognizes that there will be a difference of opinion and you can't necessarily resolve it in all cases, but at least it allows that to progress. And our concept of agreement was 66% agreement or equivalent disagreement to enable us to say that there was consensus on a particular point for ACE. For example, if 60% of the participants disagree that blood tests were necessary in all patients with alopecia areata in round two, round two would then come in and it would show you that it's close to gaining consensus. And for some people, that was just enough to tweak it over the 66% at which we said that there was a majority consensus.

Nekma Meah:

If you look at the questionnaire itself and how it was designed, we know that there was an initial, quite extensive literature review on alopecia areata. And the preliminary questionnaire was designed by a core group of dermatologists. And in this particular component, or ACE II, 148 questions were addressed, looking at epidemiology, etiopathogenesis, diagnosis, lab investigation, and prognostic indicators, and what we see is that just over half of these, so about 55%, we achieved consensus.

Nekma Meah:

The findings were summarized into specific categories, as you know, Dr. Wall.

Dmitri Wall:

That's right, Dr. Meah. So, for epidemiology, we saw that the experts agreed that ethnicity does not alter the natural history of alopecia areata or seem to influence the risk of poor response to therapy. Factors that would have been considered to increase the risk of developing alopecia areata were a family history of alopecia areata or organ-specific autoimmune disease. Other factors were genotype, a personal history of autoimmune disease, or atopic dermatitis. I think many people who treated patients with alopecia areata would be familiar with those, or you'd be suspicious that they would be involved, so that's no surprise.

Factors that influence the natural history or prognosis of alopecia areata included genotype, and a personal history of autoimmune disease or atopy. Factors that were felt to trigger initial disease and episodic relapses included genotype with an environmental trigger, a major traumatic life event, which is still a contentious issue. You see that it's still a question that although there was consensus on it, I think people would reflect on that. And then acute stress, which comes up all the time with patients, and they come in and they ask if it could have been triggered by stress. And we do see this. We see this in young children, for example, who've had a viral illness. And then in terms of factors that influenced this response to treatment, it was found that genotype can influence this.

Nekma Meah:

That's right. And I think a lot of the consensus for the epidemiology category, and we often capture this in our history-taking and when we see our patients with alopecia areata, so very much the consensus statements tie in with that.

Nekma Meah:

Now we want to move on to clinical features and see what was agreed by the expert group. There are certain features that we really need to look out for, as clinicians, that indicate disease activity for alopecia areata. The key thing is, you need to examine your patients and you need to use the dermatoscope, and be proficient in the use of a dermatoscope. So, signs of disease activity include exclamation mark hairs, that's what the expert group agreed on, black dots, a positive hair pull result, and anagen effluvium. If we look at figure 2, you'll see a patient with multiple patches of alopecia areata. You see that some of these have joined together or coalesced. You can also see black dots in figure 3, and presence of the black dots on its own is not representative of alopecia areata, as you know.

We can see it in other conditions such as trichotillomania or tinea capitis. Figure 1 is interesting because that's where you see this exclamation mark hair. These are recognized features of alopecia areata, as you know, and exclamation mark hairs are these short, broken hairs about 2-3 millimeters in length, slightly narrow towards the proximal end. They stand out quite rightly at the periphery of the patch, and they represent a weakened hair shaft. If you're looking for them, you're looking at the edge of an alopecia patch, and that's what was agreed upon. A positive pull test is performed really at the periphery of those patches that you can see. The exact process of how you conduct a pull test is debated but generally involves grasping about 20-50 hairs between your forefinger and thumb and applying gentle traction as you pull the hair along its entire length from the base to the distal tip. If you've got more than six hairs, then that will be consistent with a positive pull test. But it's important to then evaluate the hair that you've extracted with a dermatoscope again, and you can then confirm that, in fact, in alopecia areata, these hairs tend to be anagen hairs. That's where the consensus was for clinical features.

Dmitri Wall:

It is such an important feature, because often in difficult cases the dermatoscope gives you that eureka moment when you realize that when you see those exclamation mark hairs, it is alopecia areata. It's also really important to state that, with the pull test, if you get a positive once, that's sufficient. If you do it repeatedly for somebody who has very active alopecia areata, you quickly traumatize the patient because so many hairs come out.

Nekma Meah:

What about recording areata severity? Patients with single patches. Patients with multiple patches. We see that this is mentioned in the ACE paper.

Dmitri Wall:

Yes. So, when recording disease activity, while the objective area involved was considered to be important and the expert felt that the SALT score, as you might expect, is the most important component to record in clinical

trials and clinical practice. SALT 100 corresponds to complete hair loss or alopecia totalis. And a patient with SALT zero and corresponds to complete head of terminal hair. As you can see, I keep stressing terminal hair. It's something that you think is easy to do in photographs, but sometimes the best skull scores are done with a dermatoscope in hand, we can zoom in, because sometimes terminal hair is not quite there. And you are on the side of caution and include it if there isn't terminal hair there. The experts also agreed that quality of life, for example, the Dermatology Life Quality Index score, should be included in clinical trials, and scalp surface area could also be included in clinical trials. In reality, as novel therapies are emerging, there's a growing sense in the community and the literature that quality-of-life scores will play a crucial part in clinical practice to enable access to novel therapeutics. Though this wasn't, unfortunately, directly addressed in our project, I think it is still worth saying.

Nekma Meah:

In terms of the diagnosis of alopecia areata, I think the expert group agreed that this is primarily a clinical diagnosis, so you don't need to do lots of investigations. You can actually at the best time make the diagnosis that this is alopecia areata. Sometimes scalp biopsies are required and can be considered, but only when the diagnosis is unclear. So, if you have someone you initially felt had alopecia areata but then was not responding to conventional treatments or topical steroids or intralesional triamcinolone injection and was sort of recalcitrant to treatment, you may consider biopsy at that stage. There's also the case where you have diffuse alopecia. In that case, the differentials include telogen effluvium or even androgenetic alopecia and, again, scalp biopsy for diffuse alopecia areata then becomes indicated, or when you think actually this might represent a cicatricial alopecia and a biopsy is important. So, there are certain instances where you might need to biopsy, but primarily alopecia areata is a clinical diagnosis.

Nekma Meah:

The last section was on prognostic indicators. By poor prognosis, the group was referring to developing severe disease, so developing alopecia totalis, alopecia universalis, rather than a patient being refractory to treatment. The experts agree that prognosis is worse when alopecia areata persists beyond 5 years. He also said that hair loss, although it's a non-scarring condition, can become irreversible after 10 years, but that really shouldn't be a contraindication to a trial of therapy. We've seen, obviously, patients who've had long duration of disease lately who have responded to treatment.

Dmitri Wall:

Which is wonderful.

Nekma Meah:

Yes. And development of alopecia areata patches can be influenced by systemic factors, such as hormones and even certain pro-inflammatory cytokines. There are certain phenotypes that indicate poor prognosis, the ophiasis phenotype. The ophiasis phenotype is this band-like alopecia areata, which occurs along the hairline margin.

There are patients who have eyebrow, eyelash, and bodily hair loss, and that indicates poor prognosis. That was agreed upon by the expert group. Nail signs are important. The group felt that there are certain nail signs, such as nail pitting or even the extreme form of trachyonychia, that could also suggest a greater chance of progressing to alopecia totalis or alopecia universalis.

It's important to know that while there have been a number of areas where there was consensus, there were also areas where no consensus was achieved. I think, perhaps, the most interesting relates to whether early treatment in disease affects prognosis. There's obviously quite a lot of work at the moment with respect to some of the JAK inhibitors in that context.

Dmitri Wall:

I think it's also worth considering some of the limitations with the process.

Nekma Meah:

Yes.

Dmitri Wall:

There were a few. We really took a lot of trouble to try to make this a very collaborative and diverse group, and it did have wide international participation and involvement in both academic and clinical hair experts. But there was a low representation from Africa where only one person represented Africa, and in South America where we didn't have any, and Asia where there were only three.

Nekma Meah:

Yes.

Dmitri Wall:

One thing I think we definitely could have benefited from, I think you'll back me up on this Dr. Meah, is the involvement of the hair scientists in the initial design of the questionnaire to provide that additional perspective on alopecia areata pathogenesis.

Nekma Meah:

Yes.

Dmitri Wall:

Then one of the things that you realize is that at the final round meeting, when you do pack all of those experts into one room and you present them with even a relatively smaller group of questions, it's exceptionally difficult to get full interaction because there are a lot of questions. There are a lot of incredible opinions. It was actually something that was lovely to be part of. You could hear all of those years of experience just coming together, and with limited time it was very hard to represent all of that. You could have run another four or five studies just off that single interaction.

Nekma Meah:

Absolutely. I think what this really provides is such a useful framework for clinicians such as you and me, for researchers, for scientists, and patient organizations to identify where there are gaps in knowledge and where more research needs to be directed.

Dmitri Wall:

Also, one of the things, as I pointed to earlier, it raised a point that was close to my heart, which is this concept of an international alopecia areata registry. And what's so important about that is that at this time of major change in the treatment paradigm for alopecia areata, that kind of process will allow us to develop mechanisms of recording comparable, robust, real-world data, to better inform us on the prognostic significance of alopecia areata. And, in fact, that's something that we have progressed to doing. And you would think that after it was quite an extensive project, there was hundreds of hours put into this from both our sides, you think that we would've had enough, but we have progressed that. We're actually at the point of international pilot testing that registry in a couple of countries at this time.

Nekma Meah:

That's fantastic. And I think it's very important to say the data that would be captured there would not be necessary captured in clinical trials. I think that's very important, isn't it? And I think just leading on from that, we should step back and ask what further research is needed at this stage to improve alopecia areata clinical evaluation and patient care. What your thoughts?

Dmitri Wall:

This does feed into a project that we're currently working on. And it's looking at bringing in better measures of quality of life and patient assessment of disease impact. There's been some wonderful research that's been conducted recently that tells us all what we knew already, which is that the measures that we currently have need to be augmented, and it needs to bring in the patient voice. ACE in particular highlighted that there's a huge amount that we do not know. For example, we're still unaware of the trigger, the triggers of alopecia areata in genetically susceptible patients. And this is important because it won't just answer the questions that the patients keep asking us. It will also lead us down the path to more targeted therapies. And maybe it will provide us with a

means to identify which patients are likely to get a result from which medication and in whom, I suppose, ultimately we might be able to prevent the emergence of alopecia areata, which is an interesting debate in its own rights, whether we can stop it from developing. It's shown in research.

Nekma Meah:

Absolutely. And I think at this stage, we've probably come to the end of the Journal Club. I thank everyone for listening today. It's been a huge pleasure and delight to present to you. Thank you.

Dmitri Wall:

Thanks.

