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Recognizing ARIA Before Symptoms Appear

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Episode 3

Dr. Weisman:
Hi, I'm Dr. Weisman. Here with me today is Dr. Cabral.

ARIA remains one of the most important safety considerations associated with anti-amyloid therapies. What should every treating physician know?

Dr. Cabral:
Great question. So ARIA, amyloid-related imaging abnormality, as we know, is the most concerning side effect that can happen with these anti-amyloid therapies, right? And so this is a profound change in our field, where we've all along had these symptomatic treatments with modest benefit, and clinicians kind of just prescribed them and didn't worry about them and moved on. But now we really need a lot of oversight, and it's because of this potential safety issue.

So what is this, and why does this happen? So what we think the reason that ARIA occurs is because amyloid can build up around the blood vessels in the brain, and especially in people who have Alzheimer's and APOE4 carriers, right? And so if they're having the amyloid removed so effectively by these medications, this can lead to fluid shifts and blood leaking out, which appears as microhemorrhages, other blood products, and edema and effusion. So we have the ARIA-E, is that edema side of things, and the H is the hemorrhage, right? And so we also think there may be some direct neuroinflammatory effect from these medications contributing to that.

And so this is crucial that clinicians understand this, but also that they understand that developing ARIA does not mean a death sentence. Okay? We've learned this is very manageable, right? And so typically, when people experience ARIA with these treatments, it's asymptomatic, and so the way we catch it is with set scheduled MRI. So each of the medications has their own schedule that they've determined is the best time to catch this ARIA from occurring when it occurs. And so the first 6 months are the highest-risk time for ARIA to occur.

We know that the biggest risk factors for ARIA are being an APOE4/4 homozygote. Right? So if you have an individual who is a homozygote, they're not excluded in our country, though, in some countries, they don't allow this, right, because of increased risk of ARIA. But I personally, and I think you also, are of the opinion of that approach is overly paternalistic, and someone should be able to

have the choice, to know their increased risk and decide for themselves if it fits in with their life and they're willing to take that on. And so that's a conversation that needs to happen.

We also want to note risk factors are baseline microhemorrhages. So any blood in the brain with that baseline MRI increases the risk of having ARIA, so we need to know about that, certainly. And so it's important to get the APOE testing done.

Now, like I said, mostly, usually, it's asymptomatic, and so we have to do a really high-quality MRI in the sequence. And so it needs to include T2 FLAIR, it needs to include T2 gradient echo and SWI, susceptibility-weighted imaging, to catch the hemorrhages. And so you get used to doing these things and catching these things, and the radiologists catch them too and communicate them with you.

And then if someone does have ARIA, so we have a well-established pathway to treat this, to manage it, it's usually mild and asymptomatic, and we can continue in that case. If it is symptomatic or it is more extensive in the brain, that's another conversation. But in the real world, people seem to be doing really well even when they do develop ARIA, and sometimes we can treat through it.

And so we have to have that shared decision-making between the patient, the treatment partner, and the clinician, right? And then things usually do go pretty well.

Dr. Weisman:
Yeah, I mean, I love the confidence. I would just echo that because it's so important to show that bravery in front of the patient. So when patients ask me, “What happens when I develop ARIA?” And we have just gone over their personal risk based on their APOE, and you know let's just say it's like 1 in 10. They know that they're going to be the 1 in 10. They know it in their bones. And so they’re like, “When this happens to me, what is going to happen?” And I say the most likely thing that’s going to happen is your phone is going to ring and we're going to tell you because we're going to be monitoring it. And that just fills them with like, "Oh, okay. Ah, they have me in the corner." I’m there for them. My team is there for them, so it’s all good.

Dr. Cabral:
Yeah, we have their back.

Dr. Weisman:
Well, that's been a great micro discussion. Our time's up. Thanks for listening.

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