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Clinical Conundrums in ARIA: How to Manage Asymptomatic ARIA

Announcer:
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Dr. Bateman:
Welcome to Clinical Conundrums: Navigating Case Scenarios in Your Own Practice Setting, where we will cover quick and challenging cases related to amyloid-related imaging abnormalities, or ARIA, management. I'm Dr. Trey Bateman, and here with me today are doctors Jerry Barakos and Joy Snider. Let's dive into our case.

Dr. Snider:
Our first case is Michael, who's a 70-year-old gentleman who's on donanemab and underwent routine MRI monitoring. His imaging revealed findings consistent with ARIA. However, he remains asymptomatic.

Dr. Bateman:
Let's explore how to approach asymptomatic ARIA cases and to determine the best path forward. First, Jerry, can you walk us through how you would classify the type and severity of ARIA seen in this image?

Dr. Barakos:
Yes. So the idea is, when grading ARIA-E, we use a relatively simple approach in which we measure the entire area of abnormality and simply use a rule of 5s. If it's 1 to 5 cm in diameter or extent, that would be mild. If it's between 5 and 10, it would be moderate. And if it's more than 10, it's severe. So pretty easy to remember, nothing too nuanced. There just rules of 5; 1, 5, and 10.

However, applying this is critical to do it properly. When you measure the area, and this is the single most important thing I can say, and many people who are in the business doing this work still do not appreciate this. And the pearl here is the following: you do not simply measure the area of hyperintensity, not at all. That typically will vastly underestimate the magnitude and extent of the pathology, and so you can wind up calling some significant abnormality mild and the patient may get dosed through, which can be catastrophic. So what do you do? You must measure from normal parenchyma to normal parenchyma, which includes the area of hyperintensity. Because it turns out that much of the ARIA-E that we're dealing with consists of gyral swelling and sulcal effacement without hyperintensity. It's on the margin of these areas of hyperintensity.

So the case illustrated in this fashion is clearly more than 5 centimeters. It may not look it, but when you compare it to the prior baseline scan, and you measure all the way till you finally get to a normal sulcus, you will exceed 5 centimeters. And additionally, we're not just looking in one plane. Oftentimes you'll see disease starting, let's say, in the low temporal/occipital area, and it'll be heading north towards the parietal/occipital peak, or the parietal convexity. So you want to triangulate and measure the full longitudinal extent of the area of abnormal parenchyma. So long story short, we have this example here that will show up, this appearance by severity. The mild is less than 5 cm. This moderate case, the hyperintensity itself may seem to be less than 5 cm, but when you compare it to baseline,

there's no normal sulcus in that right temporal lobe. So you really have to measure the full extent, and that gets us greater than 5 cm. So it actually worked out to about 6 or 7, so between 5 and 10. So that's moderate. And then finally, this last example, the severe example, well, there's not a normal sulcus in that entire hemisphere. That is a massive, extensive, severe example. But making the point it's greater than 10 cm that will be considered severe.

Dr. Snider:
So Jerry, thanks for that great discussion, and you raised some excellent points. I think for me, what is striking is not only your point about measuring to normal brain, but also that it takes about a hemisphere's worth of abnormality to get to be the severe ARIA area. So really a lot of what we see is going to be moderate ARIA.

And then the key question is going to be, is it symptomatic or not? In this case, the gentleman was asymptomatic, and we would certainly reassess that by talking to him and his family. But in the case that the person is asymptomatic but has moderate ARIA, our proposal would be to stop dosing, to reassess in 4 to 8 weeks and to see if the ARIA resolves. As we've talked about in other cases, sometimes we see ARIA on one scan, and then it actually gets worse and becomes symptomatic. So it is important, when you see moderate ARIA, to really push strongly to suspend dosing for at least a dose and reassess.

If we reassess and the ARIA is resolved, we might go ahead and dose again. One of the other considerations we weren't given in this case is where the patient is in the course of dosing. Again, for donanemab and lecanemab, most ARIA happens early on. So if it's early on, we are going to be suspicious and concerned. If it's later on, we're really going to scratch our heads, because that's pretty uncommon. But for this case, asymptomatic, moderate ARIA would stop dosing, reassess. If the ARIA resolves in 4 to 8, 12 weeks, then we could resume dosing.

Thank you both for this insightful discussion. To our viewers, be sure to explore our other episodes for more in-depth insight into the nuances of ARIA management. Thank you for joining us.

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