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Optimizing Treatment Selection for HER2+ Breast Cancer Patients with Brain Metastases

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Sammons:
Welcome to CME on ReachMD. I'm Dr. Sarah Sammons, and joining me today is my colleague and friend Dr. Carey Anders.

I'll start our discussion with a case. We have a 32-year-old female who is initially diagnosed in her late 20s with metastatic breast cancer to the bone. Her biopsy showed that the receptors were estrogen-positive, progesterone-positive, and HER2-positive, so triple-positive. She was treated with first-line CLEOPATRA, and then she was transitioned to endocrine therapy and trastuzumab pertuzumab.

She was maintained on this for 3 years, at which time she had a brain MRI performed due to subtle changes in handwriting and some word-finding difficulty. And this showed evidence of CNS metastasis in the left parietal lobe and the right cerebellum. She had SRS, so stereotactic radiation to both lesions, the right cerebellum and the left parietal lobe. And then, she was continued on her systemic therapy, her HP, and her endocrine therapy. Her extracranial disease was all stable. Just sclerotic bone lesions that looked treated.

1 year later, we're checking her brain MRIs every 3 months like clockwork. We see that she has growth in the right cerebellar lesion that is concerning for progression. She has a brain biopsy that shows metastatic adenocarcinoma. It is ER 5% now, so lower, PR 0, and it is still HER2-positive. So, we have a progressive, radiated brain metastasis while on HP.

Carey, what are your thoughts about this? I can't think of a better expert to ask.

Dr. Anders:
Thank you, Sarah. So, this is an increasingly common scenario in our practice. I think there're a couple aspects of this case that are very clinically relevant. I think one is the young age of the patient. We do see patients present at very young ages with brain metastasis from HER2-positive and triple-negative breast cancer, but, of course, in this case, with regards to HER2-positivity.

The other thing that is key in this case is the extracranial disease is largely stable, and the challenge that we're facing is largely the CNS progression.

The other component of this case that is a common clinical conundrum is the progression of a lesion after radiosurgery, and this is debated on tumor boards every week across the world. Is what we're seeing related to radiation therapy necrosis, or is it truly a progression event? And I think that's what led to, very likely, the brain biopsy in this scenario. Do we need to treat this patient related to radiation therapy necrosis or progressive disease? And here, in fact, we do have evidence of progressive disease.

Another interesting component is that you're seeing down-regulation of the estrogen receptor, and we've seen about a 20% discordance in receptors when you look at primary breast cancers versus their intracranial match specimen. And largely, what we'll see is down-regulation of the estrogen receptor or gain of HER2. In this setting, the HER2 has remained consistent throughout the patient's

trajectory, which is more common.

So, I think there really are many components of this case that represent the clinical challenges in the setting of brain metastasis and how we move forward. And how we gain information to take best care of the patient.

Dr. Sammons:
Yeah, I completely agree. And so, now, here we are. We've done the biopsy, we've shown its progression, her extracranial disease is stable. You're going to talk to your radiation oncologist, but repeat radiation is pretty morbid. That comes with side effects. It comes with a increased risk of radiation necrosis.

Dr. Anders:
Absolutely. Absolutely.

Dr. Sammons:
And so if we could give her a systemic therapy that could take care of this, something with intracranial efficacy to spare her the morbidity of having repeat brain radiation, which is quite morbid, that would be my preference.

What would you be thinking about?

Dr. Anders:
I completely agree. I would certainly discuss this case with our radiation oncologist and determine whether or not they believed additional radiation therapy would be necessary or safe. They might consider fractionating to decrease toxicity. But I think the other thing to consider in our patients with HER2-positive breast cancer with brain metastasis, you know our patients are living for years. I have patients in my practice 5, 8, 10 years out from their first intracranial event. And so, it's really important to be thinking about how can we mitigate the late effects.

Dr. Sammons:
Would you think about resection?

Dr. Anders:
Absolutely. And then re-irradiating the cavity, for sure.

Dr. Sammons:
I think we would phone our friends in neurosurgery. Phone our friends in radiation. See what our local options are. And then in terms of systemic options, what would you think about?

Dr. Anders:
So, I think now the patient has had a second intracranial event while on backbone dual antibody therapy with endocrine therapy, and so I would start thinking about the fact that we needed to make a shift in systemic therapy. And here, I would really be thinking about likely T-DXd or trastuzumab deruxtecan, the antibody-drug conjugate with a TOPO 1 payload, given that it has historically the highest intracranial response rate of all of our agents.

Another reasonable option would be the HER2CLIMB regimen with capecitabine, the brain-permeable HER2 tyrosine kinase inhibitor tucatinib, and trastuzumab. But I think in most scenarios, I would reach for T-DXd in the second-line.

Dr. Sammons:
I agree, Carey. Thank you so much. I gave you a tough case here today.

Dr. Anders:
I appreciate it.

Dr. Sammons:
Thank you everyone for joining us. And we hope that the discussion will be useful in your practice.

Announcer:
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