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When Breast Cancer Spreads to the Brain: Diagnosis and Treatment Strategies

Dr. Chalasani:
After lung cancer, breast cancer is the second most common cause of brain metastases. In fact, brain metastases can affect up to 15 percent of patients with stage IV breast cancer, and the risk is typically highest for patients with the more aggressive subtypes. So how do we approach the management of these patients?

Welcome to *Project Oncology* on ReachMD. I'm Dr. Pavani Chalasani, and joining me today to talk about brain metastasis in metastatic breast cancer is Dr. Jose Pablo Leone. He serves as the Director of the Program for Breast Cancer in Men at Dana-Farber and is an Assistant Professor of Medicine at Harvard Medical School.

Dr. Leone, thanks for being here today.

Dr. Leone:
Thank you very much for having me, Dr. Chalasani.

Dr. Chalasani:
So to give us some background, Dr. Leone, can you tell us about the development of brain metastasis in patients with metastatic breast cancer, like the timeline on the presentation? Does it vary in the subtypes?

Dr. Leone:
Yes. So, as you were mentioning earlier, brain metastases do occur relatively frequently in metastatic breast cancer, unfortunately, and their presentation, the timeline, and also the rate of the presentation varies depending on tumor subtypes generally. So, for example, patients who have tumor subtypes of ER+/HER2- breast cancer tend to have brain metastases later in their course of their metastatic disease, whereas patients who have the subtypes of HER2+ breast cancer and triple-negative breast cancer tend to develop brain metastases earlier and at a higher rate in their course of their disease compared to those who have ER+/HER2- breast cancer.

Dr. Chalasani:
So what are the early signs and symptoms patients typically present with?

Dr. Leone:
So the symptoms can be broad. Some of the most common ones include new headaches or a significant change in headaches in patients who may have a history of having headaches frequently. That's one of the most common symptoms at presentation, but there are others that can also be seen. For example, patients can present with neurological deficits. That could be, for example, visual changes or motor or sensory deficits in a specific area of the body depending on the location of the lesion. There can also be the symptom of imbalance in patients who may have cerebellar metastasis, for example, or incoordination. So those are things to keep in mind. And then there are also the possibility of symptoms such as nausea and vomiting. Particularly, it can be suspicious when a patient presents with nausea and vomiting that is far out from their treatment. Treatment is not often thought to be the explanation when the nausea and the vomiting occurs so much later. That could potentially be a sign to suspect the possibility of brain metastasis well. Another one that can happen relatively commonly is seizures in patients who never had a history of seizures before, for example.

Dr. Chalasani:
So in follow-up of that, how do we confirm brain metastasis, more so, trying to get information on what is the role of biopsy for us and when we are talking about brain metastasis?

Dr. Leone:
So that is a very good question. Certainly, tissue diagnosis is the definitive confirmation of metastatic breast cancer in the brain. However, that is not always necessarily required. When a patient has confirmed metastatic breast cancer with distant metastases in other places, such as lung, liver, bones or other areas, that for whom we already have a tissue diagnosis of metastatic breast cancer and a patient presents with radiologic signs that are very compatible with brain metastases, oftentimes we can spare a biopsy to confirm that the lesions in the brain or the CNS are now coming from breast cancer. However, there are some unique scenarios where a tissue diagnosis may be very helpful and, in fact, encouraged, which are, for example, a situation where a patient presents with brain metastases and has no evidence of extracranial disease of any kind, including no evidence of prior breast cancer diagnosis. In that case, obviously, getting a biopsy of the brain metastasis can establish the diagnosis and also the source of the cancer cells.

Another scenario is when we see a discrepancy in the clinical outcome or discordance in the clinical outcome based on what we would expect and what we are seeing, and in scenarios like that, doing a biopsy can be helpful.

Dr. Chalasani:
So now, if we switch gears to treatment, Dr. Leone, can you tell us about the different currently available treatment options for us for patients with brain metastasis?

Dr. Leone:
Yes. So, broadly, treatments are divided into three categories. There is obviously the opportunity to do surgery. Another treatment modality is radiation therapy, and another treatment modality is systemic therapy, and each of those options have different possibilities that can be considered. So in the case of radiation therapy, for example, there is the possibility of using either whole-brain radiation in cases where there is multiple brain metastases or highly symptomatic disease in the brain, and there is also the possibility of using more directed techniques for radiation therapies, such as stereotactic radiation therapy or stereotactic radiosurgery. And in the case of systemic therapies, we have the options of traditional cytotoxic chemotherapies, and we also have the options of targeted therapies. In general, the treatment options that are best suited for patients will depend on the clinical presentation of those patients, the tumor subtypes, the volume of the disease, the number of lesions, the location of those lesions, and also the size of the lesions that we're considering for treatment.

Dr. Chalasani:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Pavani Chalasani, and I'm speaking with Dr. Jose Pablo Leone about brain metastasis in patients with metastatic breast cancer.

Now, Dr. Leone, we were just talking about the treatment options; how do you work with patients when you initially see them to figure out what is the best option for them?

Dr. Leone:
There are several things to consider and discuss with our patients when we meet them and they're facing a diagnosis of brain metastases. First is the history of their disease to find out where they are in their course of their treatment, their natural history of the breast cancer, and how many treatments they have received so far. Also, physical exams, including performance status and functional assessments of how our patients are doing, are very helpful in selecting between treatment options. And then characteristics specific to their tumors in terms of the tumor subtype, also the genomic profiling of their breast cancer, and then last but not least, a detailed discussion with the patient about the treatment options and the patient preference of their goals of care. And from all of that information, we discuss with our patients to make a treatment plan together that works to their best benefit based on their beliefs as well. And so the spectrum is very, very wide of the specific treatments that patients may need, and it can go from whole-brain radiation and palliation all the way to surgery with stereotactic radiation and systemic therapy options depending on the individual circumstances of each patient.

Dr. Chalasani:
So once their treatment begins, what challenges might arise? And how do you overcome them? So more in terms of the treatments and some of the side effects like radiation necrosis.

Dr. Leone:
So for radiation specifically, there are, I think, at least two very important considerations to keep in mind. One is the possibility of radiation necrosis, as you mentioned, Dr. Chalasani, particularly after treatment with stereotactic forms of radiation, such as stereotactic radiosurgery or stereotactic radiation therapy. So radiation necrosis is a common thing that we see in our practice, and it's problematic because it's not always very easy to diagnose by imaging findings, and it requires a very close discussion with our neuroradiologists and our radiation oncologist colleagues to try to arrive to the right diagnosis as much as possible, and it requires a lot of communication with the patient about times when we're required to monitor the findings and monitor with serial imaging versus intervening in those

scenarios.

Another potential complication from radiation is the cognitive dysfunction that can be seen with the use of whole-brain radiation after years of treatment, and that's particularly relevant for breast cancer because certain subtypes of breast cancers, such as HER2+ breast cancer, can have a very prolonged survival after the diagnosis of brain metastasis, and using whole-brain radiation early can lead to the occurrence of cognitive dysfunction later in the patient's life, and that can significantly impact the quality of life for our patients, so it is one thing to consider as we are thinking about the treatment options and sometimes try to delay whole-brain radiation to avoid this complication.

Dr. Chalasani:
So one topic that I just definitely wanted to touch base and get your insight is, they're rare, but the devastating complication we see with leptomeningeal carcinomatosis. So if you could just comment on the presentation and the challenges in the diagnosis.

Dr. Leone:
Yes. So, certainly, leptomeningeal disease is a devastating complication of metastatic breast cancer, and the diagnosis sometimes can be challenging. Normally, there are three elements to the diagnosis of leptomeningeal disease, or at least three, one being the radiologic findings on MRI. That can include the MRI of the brain and the whole spine. And sometimes it's unequivocal that there are findings on MRI that are very suspicious of leptomeningeal disease, and the imaging alone sometimes can help us, depending on how definitive the findings are, arrive at the diagnosis.

When leptomeningeal disease is suspected, lumbar punctures are generally recommended if they are deemed safe for the patient because it is a way to confirm the diagnosis in terms of cytology. And nowadays, we can also do more testing from these samples, including genomic analysis as well, which can give us insights into potential targeted therapies, so we try to do lumbar punctures when we suspect a new diagnosis of leptomeningeal disease. The challenge is that the sensitivity is very low for lumbar punctures, and we often have negative lumbar punctures or negative cytology in the lumbar puncture in a patient who has even unequivocal evidence of leptomeningeal disease on an MRI, so we have to interpret it in the context of the other evidence that is present. So there is the imaging piece, there is the lumbar puncture piece, and the third element is the symptoms. So symptoms from leptomeningeal disease can include worsening headaches with nausea or vomiting or headaches alone. It can also include vision changes. It can include very specific focal neurological deficits, such as cranial nerve deficits among others. And so when those symptoms arise, there is also the clinical suspicion for leptomeningeal disease as well.

Dr. Chalasani:
Well, with those final insights in mind, I want to thank my guest, Dr. Jose Pablo Leone, for discussing how we treat brain metastasis in patients with metastatic breast cancer. Dr. Leone, it was a pleasure speaking with you today.

Dr. Leone:
Thank you very much, Dr. Chalasani.

Dr. Chalasani:
For ReachMD, I'm Dr. Pavani Chalasani. To access this and other episodes in our series, visit *Project Oncology* at ReachMD.com, where you can Be a Part of the Knowledge. Thanks for listening.