Researchers uncover new risk factors for brain metastases in breast cancer patients

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Nearly one-fifth of all metastatic breast cancer patients develop brain metastases and have significantly shorter overall survival than patients who do not have brain involvement. One way to improve the affected patients' survival might be to prevent the brain metastases from arising in the first place. With that in mind, researchers have been working on a predictive model that accurately identifies these high risk patients. Now, Veeraiah Siripurapu, M.D., and colleagues from Fox Chase Cancer Center have verified several factors -- including high tumor grade, negative progesterone receptor status, and inflammatory breast cancer -- that are associated with an increased risk.

"If we can identify those patients who are predisposed to brain metastases, we may be able to mirror the model used in small cell lung cancer where prophylactic cranial irradiation has decreased the frequency of brain metastases and improved patient survival," says Siripurapu, a surgical oncology fellow at Fox Chase, who will present the new data at the 33rd Annual San Antonio Breast Cancer Symposium.

In this study, Siripurapu and colleagues identified 49 patients with brain metastases who were included in a prospectively-collected database of breast cancer patients. They compared these patients with control patients who had similar tumor size, nodal status, and estrogen receptor status at diagnosis but lacked brain tumors. The patients with brain metastases had a median overall survival of just 38.6 months compared with the group of control patients which had not reached a median overall survival with a mean follow-up of 100 months.

When the team compared the tumor characteristics of the two patient groups, they found that prior non-brain metastases, high nuclear tumor grade, progesterone receptor negativity, and inflammatory breast cancer were associated with an increased risk of brain metastases in a univariate analysis with high nuclear grade remaining significant in a multivariable analysis.

"The data are accumulating in the literature with regard to what tumor characteristics are associated with brain metastases, but there is no consensus on what should be included in a model to predict risk," Siripurapu says. "Factors such as age, tumor grade, lobular or mixed histology, estrogen receptor negativity, Her2/Neu status, and number of extra-cranial metastases have all been thrown into the mix, and some investigators have suggested recently that a predictive tool can be formulated. We agree with that."

"Looking at our case-control analysis – which is a novel approach for this question – we also found that high tumor grade was certainly a marked factor in risk. Progesterone receptor negativity and a diagnosis of inflammatory breast cancer may also be valuable additions to a predictive model." Siripurapu added.

Siripurapu cautions that it is too early to say how a predictive model might alter patient care.

"At a minimum, we might be able to use it to identify patients who should be followed more closely," he says. "Ultimately, we might be able to use in a preventive treatment strategy, but that would require having a model that has higher sensitivity and specificity than we can achieve right now."

Finally, while prophylactic cranial irradiation has improved overall survival in patients with small cell lung cancer, Siripurapu is cautious

that researchers would need to prove that this was also true for breast cancer patients before such an approach could be widely adopted. "The importance of piecing together a strong predictive model is that it would allow us to test the possibility in a randomized clinical trial."

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