Predicting the First Site of Relapse for Cancerous Tumors Using Protein Expression Profiles

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Metastases are the most common adult brain tumors, and brain metastasis is a marker of increased morbidity and early mortality for patients with solid tumors. A better understanding of which solid tumors are more likely to cause brain metastasis could help to tailor treatment paradigms and screening protocols for brain metastasis. Although certain solid tumors are more prone to brain metastasis than others, relevant patient-specific markers of increased risk of brain metastasis are not generally applied to current clinical practice. Delineation of such markers could facilitate individualization of cancer care.

Breast cancer is the second most common solid tumor that metastasizes to the brain. Brain metastases are associated with a particularly poor outcome relative to other metastasis sites in the setting of breast cancer. The treatment of breast cancer has been facilitated by the discovery of multiple protein markers that predict the biological behavior of the tumor. Comprehensive marker profiles are used to tailor chemotherapeutic protocols for specific patients. In molecular analysis, some of these markers have been shown to predict sites of distant metastasis, but the delineation between the first metastatic site and subsequent metastasis locations has not been well described in prior studies.

A recent study performed at the University of Helsinki examined a nationwide cohort of breast cancer patients with the goal of determining whether the initial site of solid organ metastasis correlates with the tumor's initial molecular profile. The authors examined a cohort of 2390 breast cancer patients from Finland's national registry over a 2-year period, a group which comprised 53% of all breast cancers treated in that country over that time interval. From this group, the authors selected those patients with available molecular profile data as well as those with a recorded first site of distant metastasis, which provided a cohort of 234 patients. Paraffin-embedded tissue samples were obtained in order to perform immunohistochemical studies on the specimens, which were divided into 5 subtypes: luminal A, luminal B, basal-like, HER2-enriched, and non-expressor type. These subtypes were determined based on expression of estrogen hormone receptor (ER), progesterone hormone receptor (PgR), human epidermal growth factor receptor 2 (Her2), cytokeratin 5 (CK5), and epidermal growth factor receptor (EGFR).

The authors demonstrated that these molecular profiles were indeed predictive of the initial site of tumoral relapse. Brain was rarely the first site of distant metastasis (3.4%), and brain metastasis was more common in basal type and non-expressor type tumors, each of which are negative for both ER and PgR. Their findings are summarized in the Table.

TABLE Molecular Subt...

Although this study is most relevant to systemic therapy of breast cancer patients prior to solid
organ metastasis, it is also germane to neurosurgical oncology. The therapy of breast cancer is more advanced than the therapy of most other cancers in terms of our ability to use the molecular profile of the tumor to predict the tumor's biological behavior and tailor therapy. For example, in the setting of glioblastoma, O6-methylguanine methyltransferase (MGMT) promoter methylation status has been shown to predict increased sensitivity to alkylating agents; however, the treatment of choice for MGMT negative patients is still temozolomide, regardless of MGMT promoter status. Improvement of our understanding of the tumor molecular profile could facilitate the development of new therapies.

In the setting of other solid organ tumors, the application of such a molecular profile is more obvious. Care of tumors such as melanoma or non-small cell lung carcinoma, which commonly relapse in the brain first, would benefit from molecular predictors of increased brain metastasis risk. Screening protocols as well as chemotherapeutic protocols could potentially be affected. As the understanding of the molecular profiles of these other solid organ tumors continues to expand, patient-specific therapy for these patients can continue to follow the lead that has been demarcated in breast cancer therapy.

REFERENCES


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