Breast cancer intracranial metastases

- Cesium-131 collagen tile brachytherapy for salvage of recurrent intracranial metastases
- Precision medicine approaches to CNS metastatic disease
- Brain metastases' radiologic phenotypes: correlation between tumor's consistency, extent of edema, histologic features and vascular territory affected
- Stereotactic radiosurgery for HER2-positive breast cancer brain metastases: prognostic factors and the evolving role of anti-HER2 therapies
- Gene signatures associated with brain-topical proliferative activity in breast cancer
- Re-resection of brain metastases - outcomes of an institutional cohort study and literature review
- Patritumab deruxtecan in leptomeningeal metastatic disease of solid tumors: the phase 2 TUXEDO-3 trial
- Cyst fluid ctDNA as a biomarker for genetic profiling and treatment monitoring in cystic brain metastases

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Intracranial metastases (IM) in breast cancer (BC) differs from intracranial metastases from other primaries for several reasons.

The first concerns the high incidences of IM and relapse in BC, which vary from 25 to 40% [1) 2)].

Brain metastases (BM) from primary breast cancer can arise despite use of systemic therapies that provide excellent extracranial disease control.

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see Li-Fraumeni syndrome

Epidemiology

Breast cancer intracranial metastases epidemiology.

Classification

Breast cancer intracranial metastases classification.

Etiology

Intracranial metastases etiology

RET expression was characterized in a cohort of patients with primary and brain metastatic tumors. RET functionality was assessed using pharmacological inhibition and gene silencing in patient-derived brain metastatic tumor explants and in vivo models, organoid models, and brain organotypic cultures. RNA sequencing was used to uncover novel brain metastatic relevant RET mechanisms of action.

Results: A statistically significant enrichment of RET in brain metastases was observed in estrogen receptor-positive breast cancer, where it played a role in promoting cancer cell adhesion, survival, and outgrowth in the brain. In vivo, RET overexpression enhanced brain metastatic competency in patient-derived models. At a mechanistic level, RET overexpression was found to enhance the activation of gene programs involved in cell adhesion, requiring EGFR cooperation to deliver a pro-brain metastatic phenotype.

The results illustrate, for the first time, the role of RET in regulating colonization and outgrowth of breast cancer intracranial metastases and provide data to support the use of RET inhibitors in the management strategy for patients with breast cancer brain metastases [3)]

Receptors

The status of estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor type 2 (HER2) may be altered in the time window between the emergence of the primary breast tumor and the development of metastases.

Diagnosis

CSF CEA: levels>1ng/ml are reported with a leptomeningeal spread of lung Ca (89%),breast cancer (60–67%), malignant melanoma (25–33%), and bladder Ca. May be normal even in CEA-secreting cerebral metastases if they don’t communicate with the subarachnoid space. Only carcinomatous meningitis from lung or breast cancer consistently elevates CSF CEA in the majority of patients.

Treatment

see Breast cancer intracranial metastases treatment.

Outcome

Predictors of long-term survival included HER2+ status (P = .041) and treatment with TT (P = .046). A limited number of patients (11%) died of central nervous system (CNS) causes. A predictor of CNS-related death was the development of leptomeningeal disease after SRS (P = .025), whereas predictors of non-CNS death included extracranial metastases at first SRS (P = .017), triple-negative breast cancer (P = .002), a Karnofsky Performance Status of <80 at first SRS (P = .002), and active systemic disease at last follow-up (P = .001). Only 13% of patients eventually needed whole-brain

radiotherapy. Among the long-term survivors, none died of CNS progression [4].

Brain metastases significantly affect morbidity and mortality rates for patients with metastatic breast cancer.

Poor penetration of systemic therapies into the CNS can create a reservoir for tumor growth in the brain despite excellent control of extracranial disease.

Delayed toxicity after whole brain radiation therapy (WBRT) is of increasing concern in patients who survive more than one year with breast cancer intracranial metastases.

Case series

see Breast cancer intracranial metastases case series

1)
Duchnowska R, Dziadziuszko R, Czartoryska-Arłukowicz B, Radecka B, Szostakiewicz B, Sosińska-Mielcarek K, et al. Risk factors for brain relapse in HER2-positive metastatic breast cancer patients. Breast Cancer Res Treat. 2009;117:297–303.
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