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Clinical Investigation: Breast Cancer

Impact of Triple-Negative Phenotype on Prognosis of Patients With Breast Cancer Brain Metastases

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Summary

A retrospective analysis was conducted on a total of 103 breast cancer patients with brain metastases undergoing upfront or adjuvant stereotactic radiosurgery. Triple-negative phenotype in 24 patients represented a significant adverse prognostic factor with respect to overall survival, neurologic survival, and radiosurgical survival. Recursive partitioning analysis class also served as an important and independent prognostic factor.

Purpose: To elucidate survival times and identify potential prognostic factors in patients with triple-negative (TN) phenotype who harbored brain metastases arising from breast cancer and who underwent stereotactic radiosurgery (SRS).

Methods and Materials: A total of 103 breast cancer patients with brain metastases were treated with SRS and then studied retrospectively. Twenty-four patients (23.3%) were TN. Survival times were estimated using the Kaplan-Meier method, with a log−rank test computing the survival time difference between groups. Univariate and multivariate analyses to predict potential prognostic factors were performed using a Cox proportional hazard regression model.

Results: The presence of TN phenotype was associated with worse survival times, including overall survival after the diagnosis of primary breast cancer (43 months vs. 82 months), neurologic survival after the diagnosis of intracranial metastases, and radiosurgical survival after SRS, with median survival times being 13 months vs. 25 months and 6 months vs. 16 months, respectively ($p < 0.002$ in all three comparisons). On multivariate analysis, radiosurgical survival benefit was associated with non-TN status and lower recursive partitioning analysis class at the initial SRS.

Conclusion: The TN phenotype represents a significant adverse prognostic factor with respect to overall survival, neurologic survival, and radiosurgical survival in breast cancer patients with intracranial metastasis. Recursive partitioning analysis class also served as an important and independent prognostic factor.

Keywords: Triple-negative, Breast cancer, Brain metastases, Survival, Stereotactic radiosurgery

Introduction

Approximately 10%−16% of patients with breast cancer eventually develop clinically symptomatic intracranial metastases (1). Triple-negative (TN) breast cancer is characterized by negative hormone receptors and absence of human epidermal growth factor receptor 2 (HER2/neu) amplification or protein overexpression. It accounts for 15% (2) of all breast cancer and constitutes a distinct subtype of neoplasm. Owing to a lack of targeted treatment modalities, the prognosis of patients with TN breast cancer brain metastasis remains poor, with median survival of 3 months as compared with 11 months in non-TN breast cancer patients (3).

Stereotactic radiosurgery (SRS) has emerged as a valuable upfront or salvage treatment option in the management of brain metastasis (4). Mounting evidence indicates that patients with

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Table 1 Patient demographic and clinical features

Feature	Total	TN	Non-TN	p*
No. of patients	103	24	79	
Age at GKS (y)				.344†
Mean	51.5	49.5	50	
Median	49	48.5	52.06	
Range	30–92	33–74	30–92	
Race				.808‡
Caucasian	96 (93.2)	22 (91.6)	74 (93.7)	
African American	4 (3.9)	1 (4.2)	3 (3.8)	
Asian, Hispanic	3 (2.9)	1 (4.2)	2 (2.5)	
Stage at diagnosis of primary malignancy				.051‡
I	14 (13.6)	5 (20.8)	9 (11.4)	
II	26 (25.2)	10 (41.7)	16 (20.3)	
III	17 (16.5)	1 (4.2)	16 (20.3)	
IV	6 (5.8)	0	6 (7.6)	
Unknown	40 (38.8)	8 (33.3)	32 (40.5)	
ER status				N/A
Negative	46 (44.7)	24 (100)	22 (27.8)	
Positive	56 (54.4)	0	56 (70.9)	
Unknown	1 (1.0)	0	1 (1.3)	
PR status				N/A
Negative	64 (62.1)	24 (100)	40 (50.6)	
Positive	37 (35.9)	0	37 (46.8)	
Unknown	2 (1.9)	0	2 (2.5)	
HER2 status				N/A
Negative	61 (59.2)	24 (100)	37 (46.8)	
Positive	42 (40.8)	0	42 (53.2)	
First site of systemic metastases				
Brain	43 (41.7)	16 (66.7)	27 (34.2)	.026§,‖
Lung	24 (23.3)	11 (45.8)	13 (16.5)	.003§,‖
Bone	26 (25.2)	1 (4.2)	25 (31.6)	.007§,‖
Liver	18 (17.5)	3 (12.5)	15 (19.0)	.555‡
RPA class at GKS				.881‡
I	29 (28.2)	6 (25)	23 (29.1)	
II	72 (69.9)	18 (75)	54 (68.4)	
III	2 (1.9)	0	2 (2.5)	
GPA class at GKS				.981‡
0–1.0	4 (3.9)	1 (4.2)	3 (3.8)	
1.5–2.5	68 (66.0)	16 (66.7)	52 (65.8)	
3	22 (21.4)	5 (20.8)	17 (21.5)	
3.5–4.0	7 (6.8)	2 (8.3)	5 (6.3)	
Indeterminate	2 (1.9)	0	2 (2.5)	
KPS at GKS				.143‡
100	15 (14.6)	7 (29.2)	8 (10.1)	
90	39 (37.9)	7 (29.2)	32 (40.5)	
80	35 (34.0)	6 (25)	29 (36.7)	
70	12 (11.7)	4 (16.6)	8 (10.1)	
60	2 (1.9)	0	2 (2.5)	
No. of lesions at initial GKS				.570§
Single	35 (34.0)	7 (29.2)	28 (35.4)	
≥2	68 (66.0)	17 (70.8)	51 (64.6)	
Total volume (cm^3)				.692§
<5.6	45 (43.7)	9 (37.5)	36 (45.6)	
≥5.6	47 (45.6)	11 (45.8)	36 (45.6)	
Indeterminate	11 (10.7)	4 (16.7)	7 (8.9)	
Lesion location				.446‡
Supratentorial	60 (58.3)	16 (66.7)	44 (55.7)	
Infratentorial	17 (16.5)	5 (20.8)	12 (15.2)	

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