pISSN 1598-2998, eISSN 2005-9256

https://doi.org/10.4143/crt.2024.138 Cancer Res Treat. 2024;56(4):1105-1112

Original Article

Dural Metastasis in Breast Cancer: MRI-Based Morphological Subtypes and Their Clinical Implications

Sung Jun Ahn[1], **Bio Joo**[1], **Mina Park**[1], **Hun Ho Park**[2], **Sang Hyun Suh**[1], **Sung Gwe Ahn**[3,4], **Jihwan Yoo**[2]

[1]Department of Radiology, [2]Department of Neurosurgery, Brain Tumor Center, [3]Department of Surgery, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, [4]Institute for Breast Cancer Precision Medicine, Yonsei University College of Medicine, Seoul, Korea

Purpose This study aimed to investigate the clinical factors associated with breast cancer (BRCA) dural metastases (DMs), their impact on prognosis compared to brain parenchymal metastases (BPMs) alone, and differences between DM subtypes, aiming to inform clinical decisions.

Materials and Methods We retrospectively analyzed 119 patients with BRCA with brain metastasis, including 91 patients with BPM alone and 28 patients with DM. Univariate and multivariate analyses were performed to compare the clinical characteristics between the two groups and within subtypes of DM. Overall survival after DM (OSDM) and the interval from DM to leptomeningeal carcinomatosis (LMC) were compared using Kaplan-Meier analysis.

Results DM was notably linked with extracranial metastasis, luminal-like BRCA subtype (p=0.033), and skull metastases (p < 0.001). Multiple logistic regression revealed a strong association of DM with extracranial and skull metastases, but not with subtype or hormone receptor status. Patients with DM did not show survival differences compared with patients with BPM alone. In the subgroup analysis, nodular-type DM correlated with human epidermal growth factor receptor 2 status (p=0.044), whereas diffuse-type DM was significantly associated with a higher prevalence of the luminal-like subtype (p=0.048) and the presence of skull metastasis (p=0.002). Patients with diffuse DM did not exhibit a significant difference in OSDM but had a notably shorter interval from DM to LMC compared to those with nodular DM (p=0.049).

Conclusion While the impact of DM on the overall prognosis of patients with BRCA is minimal, our findings underscore distinct characteristics and prognostic outcomes within DM subgroups.

Key words Brain metastasis, Breast neoplasms, Dural metastasis, Hormone receptor–positive status, Metastasis, Prognosis, Retrospective studies

Introduction

Brain metastases (BMs) are the most common neurological complications affecting nearly 30% of patients with cancer [1]. The incidence of BM among breast cancer (BRCA) patients in Korea was estimated as 4.2 per 1,000 patient-years, which was the second-highest value, after lung cancer. The mean time interval between the primary cancer diagnosis and BM diagnosis was 30.9±21.8 months [2]. Additionally, the incidence of BRCA with BM is likely to have increased recently due to improved survival rates and advanced imaging techniques [3]. The clinical significance of BMs has been underscored by their increasing prevalence, attributed to advancements in therapeutic interventions and improved imaging techniques [4,5]. While brain parenchyma is the most frequently affected intracranial site, dural metastases (DMs) and leptomeningeal involvement can also occur. DMs are relatively rare, occurring in approximately 9% of patients with cancer at autopsy [6]. However, several case reports have described DMs in patients with BRCA that may mimic meningiomas, resulting in a diagnostic dilemma [7-9]. Moreover, BRCA is the primary tumor most frequently associated with DM, and its prevalence can be substantial [10]. Nevertheless, DM in BRCA has not been systematically studied. Specifically, the factors contributing to the development of DM remain poorly understood, and the impact of DM on the prognosis of patients with BRCA remains unclear. Moreover, DMs typically arise either through direct extension from skull bone metastases or via hematogenous spread [11]. Although these two subtypes may exhibit distinct character-

Correspondence: Jihwan Yoo
Department of Neurosurgery, Gangnam Severance Hospital, Yonsei University College of Medicine, 211 Eonju-ro, Gangnam-gu, Seoul 06273, Korea
Tel: 82-2-2019-3391 Fax: 82-2-2019-4966 E-mail: JHY8486@yuhs.ac

Co-correspondence: Sung Gwe Ahn
Department of Surgery, Gangnam Severance Hospital, Yonsei University College of Medicine, 211 Eonju-ro, Gangnam-gu, Seoul 06273, Korea
Tel: 82-2-2019-3370 Fax: 82-2-4462-5994 E-mail: asg2004@yuhs.ac

Received February 13, 2024 **Accepted** March 17, 2024
Published Online March 19, 2024

istics, comparative analyses thereof in patients with BRCA with DMs are notably lacking.

Therefore, our study aimed to address these knowledge gaps. We investigated the clinical factors associated with DM in BRCA, as well as its impact on prognosis when compared with patients with brain parenchymal metastases (BPMs) alone. Additionally, we explored the differences in clinical characteristics between the subtypes of DMs.

Materials and Methods

1. Participants

This retrospective study was approved by our institutional review board, which waived the requirement for informed consent. We retrospectively searched electronic medical records to identify patients with BRCA undergoing brain magnetic resonance imaging (MRI) for the evaluation of BMs between June 2011 and February 2022. We identified 123 patients with BRCA and BMs (Fig. 1). Four patients were excluded because leptomeningeal carcinomatosis (LMC) was the initial manifestation of BM. Of the remaining 119 patients with BMs, 28 patients had DMs. The remaining 91 patients had BPMs alone. For patients with DM, we further classified DMs as nodular type, demonstrating a rounded body growing inward from the dura, or diffuse type, growing along the dura, based on brain MRI (Fig. 2).

2. Clinical factors

The following clinical variables were reviewed as potential prognostic factors for overall survival (OS) and LMC: age at BRCA diagnosis, age at BM diagnosis, extracranial metastasis (ECM), number of BM, Karnofsky performance scale (KPS), presence of symptoms, TNM stage, graded prognostic assessment (GPA) grade at BM, biological subtypes (luminal-like, human epidermal growth factor receptor 2 [HER2]–positive, and triple-negative BRCA [TNBC]), presence of skull metastasis, and history of therapeutic agents (chemotherapy, HER2-targeted therapy, immunotherapy, and endocrine therapy). GPA grade was evaluated based on an updated graded prognostic assessment (Breast GPA) [12]. Immunohistochemistry was performed to evaluate estrogen receptor (ER), progesterone receptor (PR), and HER2 expression in the primary BRCA. Fluorescence *in situ* hybridization analysis of *HER2* amplification was performed for immunohistochemistry 2+ cases. Biological subtypes were defined as HER2-positive, TNBC (ER-, PR-, and HER2-negative) and luminal-like (ER- and/or PR-positive, HER2-negative) [13]. Clinical staging was performed according to the 8th edition of the TNM staging of BRCA by the American Joint Committee on Cancer (AJCC) [14].

3. Outcome assessment

The patients were followed up with MRI at intervals of 3 months after diagnosis of BM. The primary outcome was OS. OS after BM was calculated from the date of BM until death or last follow-up. The secondary outcome was LMC-free survival. LMC was diagnosed using the conservative definition of LMC (i.e., presence of malignant cells in cerebrospinal fluid (CSF) or typical leptomeningeal enhancement on MRI in the brain, spinal cord, or cauda equina). LMC-free survival was calculated from the date of DM until the occurrence of LMC in patients with DM.

4. MRI protocol

Routine MRI scans for the evaluation of the BMs were acquired using a Siemens 3T Vida (Siemens Healthineers, Erlangen, Germany) or GE 3T Discovery MR750 (GE Healthcare, Milwaukee, WI) scanner. Our BM MRI protocol consisted of T1-weighted image (T1WI), T2-weighted image, FLAIR, contrast-enhanced T1WI, and black-blood T1WI. Contrast-enhanced images were acquired after administering gadobutrol 0.2 mmol/kg (Gadovist, Bayer Schering Pharma, Berlin, Germany). The detailed MR parameters are provided in S1 Fig.

5. Statistical analysis

We categorized patients with BRCA BMs into two groups: those with BPM alone and those with DM. Among the clinical variables of the two groups, continuous variables were statistically analyzed using t tests and categorical variables using chi-squared tests. Among these, variables that were statistically significant or meaningful were subjected to univariate logistic regression analysis for DM. A p-value threshold of 0.2 was set for multivariate logistic regression, and

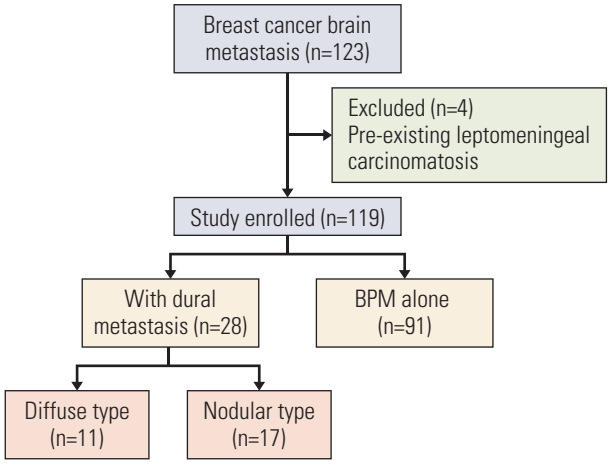

Fig. 1. Flow chart of patient enrollment. BPM, brain parenchymal metastasis.

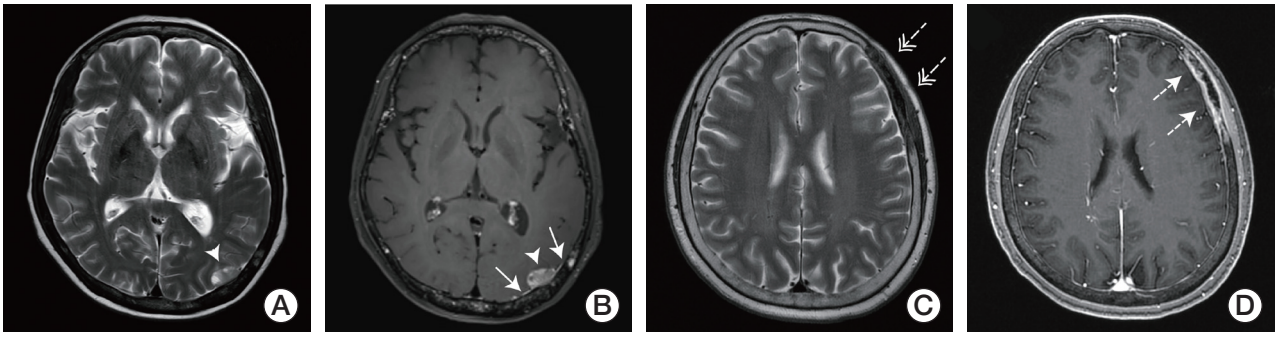

Fig. 2. Representative cases of nodular (A, B) and diffuse types of dural metastasis (C, D). (A) Nodular type of dural metastasis in left occipito-temporal region on T2-weighted image (T2WI) (arrowhead). (B) Dural tail was noted on contrast enhanced T1-weighted image (CE-T1WI) (arrows) accompanied by nodular dural metastasis (arrowhead). (C) Bone metastasis in left frontal bone on T2WI (double arrows). (D) Diffuse type of dural metastasis observed on CE-T1WI (dotted arrows).

backward elimination was performed to conduct a multivariate logistic regression test. Based on the results of univariate and multivariate logistic regression analyses, the odds ratios (OR) and 95% confidence intervals (CI) were calculated for each variable. Subsequently, we classified DM into diffuse type and nodular type based on radiological criteria and analyzed the relationship with clinical variables. Similarly, continuous variables were analyzed using t tests, and categorical variables were analyzed using chi-squared tests. We conducted Kaplan-Meier analysis to analyze the impact of DM on patient survival and the influence of radiological subtypes of DM on patient prognosis, including survival and LMC. All data analyses were performed using R ver. 3.5.3 (The R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set at $p < 0.05$.

Results

1. Clinical factors associated with DMs from BRCA

In total, 119 patients with BRCA and BMs were included in this study. Of these, 91 patients had BPMs alone, and 28 patients had DMs. The clinical and pathological variables are summarized in Table 1. DM was significantly associated with ECM (p=0.001) and the luminal-like subtype (p=0.019). Skull metastases were more frequently observed in patients with DMs than in those with BPMs alone (17/28 [60.7%] vs. 16/91 [17.6%], $p < 0.001$). Moreover, patients with DMs were more likely to receive hormone therapy (18/28 [64.3%] vs. 34/91 [37.4%], p=0.022). No significant differences were observed between the BPM alone and DM groups in terms of symptoms, age, KPS, TNM stage, ER status, PR status, hormone receptor (HR) status, history of chemotherapy, HER2-targeted therapy, or immunotherapy. Multivariate analysis showed that DM was independently associated with the presence of ECM (OR, 5.65; 95% CI, 1.42 to 37.84; p=0.030) and skull metastasis (OR, 4.40; 95% CI, 1.65 to 12.18; p=0.004) (Table 2).

2. Overall patient survival

The median OS after the detection of BMs was 33 months. However, there was no significant difference between the OS in patients with BPM alone and those with DM (p=0.62) (Fig. 3). Additionally, we conducted survival analysis by dividing the groups into synchronous brain metastasis (n=10) and metachronous metastasis (n=109) based on the timing of BRCA diagnosis and BM diagnosis and did not reach statistical significance (p=0.28) (S1 Fig.).

3. Nodular vs. diffuse type of DM

In the detailed subgroup analysis, we scrutinized clinical and pathological factors, contrasting nodular (n=17) and diffuse (n=11) types of DMs (Table 3). The nodular type of DM exhibited a higher prevalence of HER2-positive subtype (41.2%, 7/17) compared to the diffuse type, where it was notably absent (0%, 0/11). Conversely, the luminal-like subtype was more commonly associated with the diffuse type (72.7%, 8/11) than with the nodular type (41.2%, 7/17, p=0.048). Additionally, the presence of skull metastases was observed with a significantly higher frequency in the diffuse type (100%, 11/11) than in the nodular type (35.3%, 6/17, p=0.002).

4. Impact of DM subtypes on prognostic outcomes

The median OS for patients with DM was 34.5 months (Fig. 4A). Dissecting this further by subtype, patients with the nodular subtype had a median OS of 40.2 months, which was notably longer than those with diffuse type (12.9 months). Despite these differences, the variation in OS between the DM subtypes did not achieve statistical significance (p=0.30).

Table 1. Demographics of patients with BRCA brain metastasis

	BPM alone (n=91)	DM (n=28)	p-value
Age at BRCA diagnosis	49.7±10.9	47.5±10.2	0.349
Age at BM diagnosis	53.5±10.5	54.1±9.2	0.805
Initial TNM stage			
Stage 0	2 (2.2)	0	0.353
Stage I	5 (5.5)	3 (10.7)	
Stage II	24 (26.4)	6 (21.4)	
Stage III	38 (41.8)	8 (28.6)	
Stage IV	22 (24.2)	11 (39.3)	< 0.001
Extracranial metastasis	50 (54.9)	26 (92.9)	0.001
No. of BM	11.6±19.0	3.5±6.4	0.001
Presence of symptom	78 (85.7)	20 (74.1)	0.261
KPS			
90-100	23 (25.3)	6 (21.4)	0.913
70-80	55 (60.4)	18 (64.3)	
< 70	13 (14.3)	4 (14.3)	
Subtype			
Luminal-like	23 (25.3)	15 (53.6)	0.019
HER2+	38 (41.8)	7 (25.0)	
TNBC	30 (33.0)	6 (21.4)	
ER status	43 (47.3)	18 (64.3)	0.174
PR status	25 (27.5)	13 (46.4)	0.099
HR status	43 (47.3)	18 (64.3)	0.174
HER2 status	38 (41.8)	7 (25.0)	0.169
GPA grade			
3.5-4.0	7 (7.7)	0	0.258
2.5-3.0	29 (31.9)	6 (21.4)	
1.5-2.0	40 (44.0)	16 (57.1)	
0.0-1.0	15 (16.5)	6 (21.4)	
Chemotherapy before BM	83 (92.2)	22 (78.6)	0.095
HER2-target therapy before BM	33 (36.3)	8 (28.6)	0.602
Immunotherapy before BM	2 (2.2)	1 (3.6)	> 0.99
Hormone therapy before BM	34 (37.4)	18 (64.3)	0.022

Values are presented as mean±SD or number (%). BRCA, breast cancer; BPM, brain parenchymal metastasis; BM, brain metastasis; DM, dural metastasis; ER, estrogen receptor; GPA, graded prognostic assessment; HER+, human epidermal receptor 2–positive subtype; HR, hormone receptor; KPS, Karnofsky performance scale; PR, progesterone receptor; SD, standard deviation; TNBC, triple-negative breast cancer.

Conversely, a stark contrast was observed in the LMC-free survival between the subtypes (Fig. 4B). For diffuse type, the median LMC-free survival was significantly shorter than that of nodular type (p=0.049).

Discussion

While DM frequently occurs in BRCA, there have been limited investigations specifically focusing on DM in patients with BRCA. We found that DM is significantly associated with skull metastasis and the luminal-like subtype of BRCA. In addition, morphologically different subgroups of DM exhibited distinct clinical characteristics and prognosis, especially in terms of LMC. The nodular type was predominantly associated with HER2-positive BRCA and was likely to occur through hematogenous spread. In contrast, the diffuse type was more commonly associated with luminal-like subtype of BRCA and appeared to result from direct extension of skull metastasis. Importantly, the diffuse type of DM had a worse prognosis compared to the nodular type in terms of LMC. These findings shed light on the underlying pathophysiology of BRCA DM and hold clinical relevance, as they allow for the stratification of patient prognosis based on

Table 2. Multiple logistic regression analysis for dural metastasis

	Univariate analysis			Multivariate analysis		
	OR	95% CI	p-value	OR	95% CI	p-value
Age	1.01	0.96-1.05	0.804			
ECM (yes vs. no)	10.66	2.94-68.63	0.002	5.65	1.42-37.84	0.030
Subtype						
Luminal-like	Ref			Ref		
HER2+ or TNBC	0.29	0.12-0.70	0.006	0.74	0.09-6.07	0.774
HR status (yes vs. no)	2.01	0.85-4.97	0.118	0.57	0.08-3.47	0.546
HER2 status (yes vs. no)	0.46	0.17-1.16	0.115	1.18	0.22-5.92	0.838
Hormone therapy before BM (yes vs. no)	3.02	1.27-7.52	0.014	2.07	0.78-5.66	0.147
Skull metastasis (yes vs. no)	7.24	2.91-18.94	< 0.001	4.40	1.65-12.18	0.004

BM, brain metastasis; CI, confidence interval; ECM, extracranial metastasis; HER+, human epidermal receptor 2–positive subtype; HR, hormone receptor; OR, odds ratio; TNBC, triple-negative breast cancer.

DM subtypes. This stratification facilitates the implementation of more aggressive treatment strategies for patients with the diffuse type of DM.

The direct extension of skull bone metastases is one of the pathways to DMs, which potentially explains why DMs are significantly associated with skull metastasis. Interestingly, our results also demonstrated that DMs were significantly associated with the luminal-like subtype and skull metastasis. Luminal-like BRCA shows a predilection for bone metastasis compared to HR-negative tumors, which have a proclivity to develop visceral metastasis [15,16]. High concordance for ER status between primary BRCA and bone metastasis indirectly implies that ER may promote bone metastasis [17,18]. Physiologically, bone metabolism is a well-balanced process maintained by osteoblasts and osteoclasts under the regulation of sex hormones and cytokines [19]. Thus, sex hormone receptors such as ER and PR and their downstream receptor signaling may play a vital role in BRCA bone metastasis. In particular, diffuse type DM is likely to result from the direct extension of skull metastases. In our subgroup analysis, skull metastases were more frequently observed in patients with diffuse-type DMs than in those with nodular type. Moreover, the proximity of skull metastases to diffuse type DM, and the simultaneous occurrence thereof may support our hypothesis that diffuse type DM may originate from direction extension of skull metastasis.

Nodular type DM is significantly associated with HER2-positive subtype, BPMs, and HER2-targeted therapy. Accumulating evidence has revealed that HER2-positive BRCA is a predictive factor for BMs [20,21]. As an oncogene itself, and through its interaction with other receptors, such as epidermal growth factor receptor (EGFR) and HER3, HER2 contributes to the brain metastatic potential of this subtype [22,23]. Taken together, these results suggest that nodular-type DM may have a hematogenous origin. Furthermore, it may be a result of exophytic growth of brain metastatic foci, which requires further investigation.

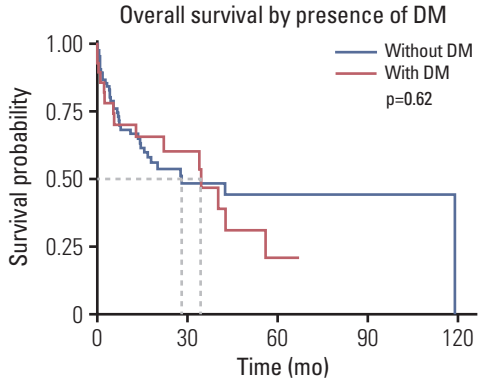

Fig. 3. Overall survival after brain metastasis (with BPM alone vs. with DM). BPM, brain parenchymal metastasis; DM, dural metastasis.

Our survival analysis demonstrated that DM did not influence the OS of patients with BM. However, prognosis of patients with DM have rarely been reported. A previous study compared the clinical presentation of patients with DM alone with that of patients with BM/LMC, reporting that the median OS was 12 months for patients with DM and 7 months for those with BM/LMC [24]. Based on a previous report and our results, DM is not significantly associated with patient survival. DM lies outside the blood-brain and blood-CSF barriers, and is more easily exposed to chemotherapy than BM and LMC [25,26]. We hypothesize that systemic chemotherapy and molecular targeted drugs may have effectively controlled DM in the patients in our cohort. However, the prognosis of patients with diffuse type DM was relatively poor compared to that of patients with nodular type (median overall survival after DM of 12.9 vs. 40.2 months),

Table 3. Subgroup analysis of dural metastasis according to morphological classification

	Nodular (n=17)	Diffuse (n=11)	p-value
Age at BRCA diagnosis (yr)	46.9±11.3	48.5±8.7	0.698
Age at BM diagnosis (yr)	52.9±9.8	55.8±8.2	0.428
No. of BMs	4.9±7.7	1.3±2.5	0.084
KPS			
90-100	2 (11.8)	4 (36.4)	0.215
70-80	13 (76.5)	5 (45.5)	
< 70	2 (11.8)	2 (18.2)	
Presence of skull metastasis	6 (35.3)	11 (100)	0.002
ECM	16 (94.1)	10 (90.9)	> 0.99
HR status	11 (64.7)	7 (63.6)	> 0.99
HER2 status	7 (41.2)	0	0.044
Subtype			
luminal-like	7 (41.2)	8 (72.7)	0.048
HER2+	7 (41.2)	0	
TNBC	3 (17.6)	3 (27.3)	
GPA group			
2.5-3.0	6 (35.3)	0	0.085
1.5-2.0	8 (47.1)	8 (72.7)	
0.0-1.0	3 (17.6)	3 (27.3)	
Chemotherapy before BM	15 (88.2)	7 (63.6)	0.281
HER2-target therapy before BM	7 (41.2)	1 (9.1)	0.159
Immunotherapy before BM	1 (5.9)	0	> 0.99
Hormone therapy before BM	11 (64.7)	7 (63.6)	> 0.99

Values are presented as mean±SD or number (%). BRCA, breast cancer; BM, brain metastasis; ECM, extracranial metastasis; GPA, graded prognostic assessment; HER+, human epidermal receptor 2–positive subtype; HR, hormone receptor; KPS, Karnofsky performance scale; SD, standard deviation; TNBC, triple-negative breast cancer.

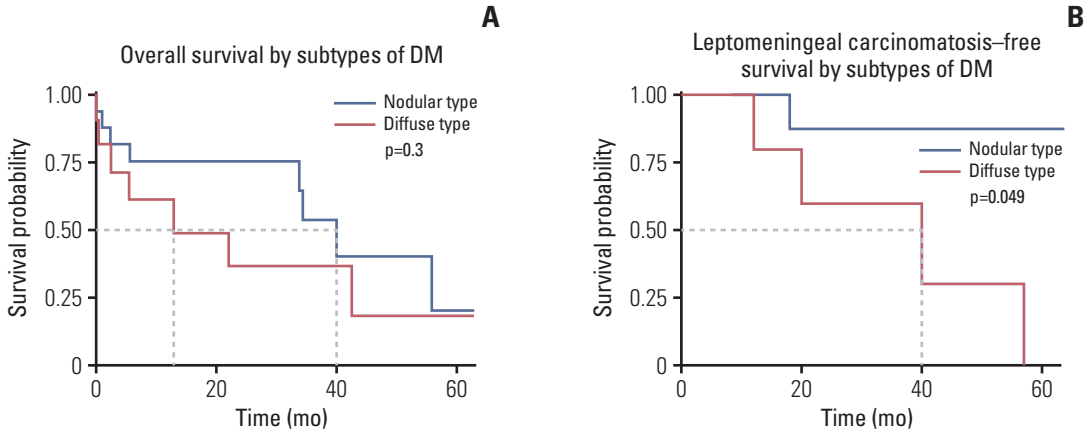

Fig. 4. Prognostic analysis between subtypes of dural metastasis (DM). (A) Overall survival between subtypes of DM. (B) Leptomeningeal carcinomatosis–free survival between subtypes of DM.

although this difference was not statistically significant. The worse prognosis of patients with diffuse type DM can be partially explained by the shorter time interval from DM to LMC. Additionally, LMC developed more frequently after diagnosis in patients with diffuse type DM (4/11, 36.3%) than in those with nodular type DM (1/17, 5.8%). LMC is a devastating complication with a good prognosis. Although several studies have suggested that the mechanical spread

of tumor cells to the CSF space could contribute to the development of LMC, the exact underlying mechanism remains unclear [27,28]. Further studies with larger sample sizes are necessary to confirm our findings on whether diffuse type DM serves as a precursor to LMC in BRCA.

This study had some limitations. First, this was a retrospective, single-center study with a small number of patients with DMs, which was not sufficient to draw a solid conclusion. Therefore, a prospective multi-center study is required to improve the generalizability of our results. Second, the presence of DM was not pathologically confirmed. Thus, although equivocal cases were not included in our study, it is possible that extra-axial tumors and reactive dural thickening were misdiagnosed as DMs.

Our study identified MRI-based morphological subtypes of BRCA DM that could potentially affect treatment outcomes in patients with BRCA and BM.

Electronic Supplementary Material

Supplementary materials are available at Cancer Research and Treatment website (https://www.e-crt.org).

Ethical Statement

This retrospective study was approved by Gangnam Severance Hospital institutional review board (No. 3-2024-0019), which waived the requirement for informed consent based on the minimal risk of this electronic linkage-based research.

Author Contributions

Conceived and designed the analysis: Ahn SG, Yoo J.
Collected the data: Ahn SJ, Joo B, Park M, Yoo J.
Contributed data or analysis tools: Ahn SJ, Park HH, Suh SH.
Performed the analysis: Yoo J.
Wrote the paper: Ahn SJ, Ahn SG, Yoo J.

ORCID iDs

Sung Jun Ahn : https://orcid.org/0000-0003-0075-2432
Sung Gwe Ahn : https://orcid.org/0000-0002-8778-9686
Jihwan Yoo : https://orcid.org/0000-0001-8746-1245

Conflicts of Interest

Conflict of interest relevant to this article was not reported.

Acknowledgments

This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (RS-2023-00246346) to JY, National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (No. 2020R1F1A1056512) and a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number : HI20C2125) to SJA.

References

1. Scoccianti S, Ricardi U. Treatment of brain metastases: review of phase III randomized controlled trials. Radiother Oncol. 2012;102:168-79.
2. Kim T, Song C, Han JH, Kim IA, Kim YJ, Kim SH, et al. Epidemiology of intracranial metastases in Korea: a national cohort investigation. Cancer Res Treat. 2018;50:164-74.
3. Arnold M, Morgan E, Rumgay H, Mafra A, Singh D, Laversanne M, et al. Current and future burden of breast cancer: global statistics for 2020 and 2040. Breast. 2022;66:15-23.
4. Fox BD, Cheung VJ, Patel AJ, Suki D, Rao G. Epidemiology of metastatic brain tumors. Neurosurg Clin N Am. 2011;22:1-6.
5. Hatiboglu MA, Akdur K, Sawaya R. Neurosurgical management of patients with brain metastasis. Neurosurg Rev. 2020;43:483-95.
6. Laigle-Donadey F, Taillibert S, Mokhtari K, Hildebrand J, Delattre JY. Dural metastases. J Neurooncol. 2005;75:57-61.
7. Agarwal B, Das P, Nasim M. Dural metastatic cancer from primary breast carcinoma. Int J Neurosci. 2010;120:442-6.
8. Seki S, Kamide T, Tamase A, Mori K, Yanagimoto K, Nomura M. Intraparenchymal hemorrhage from dural metastasis of breast cancer mimicking meningioma. Neuroradiol J. 2016;29:179-82.
9. Richiello A, Sparano L, Del Basso De Caro ML, Russo G. Dural metastasis mimicking falx meningioma: case report. J Neurosurg Sci. 2003;47:167-71.
10. Nayak L, Abrey LE, Iwamoto FM. Intracranial dural metastases. Cancer. 2009;115:1947-53.
11. Coleman RE. Metastatic bone disease: clinical features, pathophysiology and treatment strategies. Cancer Treat Rev. 2001;27:165-76.
12. Sperduto PW, Mesko S, Li J, Cagney D, Aizer A, Lin NU, et al. Beyond an updated graded prognostic assessment (Breast GPA): a prognostic index and trends in treatment and survival in breast cancer brain metastases from 1985 to today. Int J Radiat Oncol Biol Phys. 2020;107:334-43.
13. Riecke K, Muller V, Neunhoffer T, Park-Simon TW, Weide R, Polasik A, et al. Long-term survival of breast cancer patients with brain metastases: subanalysis of the BMBC registry. ESMO Open. 2023;8:101213.
14. Giuliano AE, Edge SB, Hortobagyi GN. Eighth edition of the AJCC cancer staging manual: breast cancer. Ann Surg Oncol. 2018;25:1783-5.

15. Pareek A, Singh OP, Yogi V, Ghori HU, Tiwari V, Redhu P. Bone metastases incidence and its correlation with hormonal and human epidermal growth factor receptor 2 neu receptors in breast cancer. J Cancer Res Ther. 2019;15:971-5.
16. Jiang X, Chen G, Sun L, Liu C, Zhang Y, Liu M, et al. Characteristics and survival in bone metastatic breast cancer patients with different hormone receptor status: a population-based cohort study. Front Oncol. 2022;12:977226.
17. Aurilio G, Monfardini L, Rizzo S, Sciandivasci A, Preda L, Bagnardi V, et al. Discordant hormone receptor and human epidermal growth factor receptor 2 status in bone metastases compared to primary breast cancer. Acta Oncol. 2013;52:1649-56.
18. Hilton JF, Amir E, Hopkins S, Nabavi M, DiPrimio G, Sheikh A, et al. Acquisition of metastatic tissue from patients with bone metastases from breast cancer. Breast Cancer Res Treat. 2011;129:761-5.
19. Hofbauer LC, Rachner TD, Coleman RE, Jakob F. Endocrine aspects of bone metastases. Lancet Diabetes Endocrinol. 2014; 2:500-12.
20. Zimmer AS, Van Swearingen AE, Anders CK. HER2-positive breast cancer brain metastasis: a new and exciting landscape. Cancer Rep (Hoboken). 2022;5:e1274.
21. Kyeong S, Cha YJ, Ahn SG, Suh SH, Son EJ, Ahn SJ. Subtypes of breast cancer show different spatial distributions of brain metastases. PLoS One. 2017;12:e0188542.
22. Palmieri D, Bronder JL, Herring JM, Yoneda T, Weil RJ, Stark AM, et al. Her-2 overexpression increases the metastatic outgrowth of breast cancer cells in the brain. Cancer Res. 2007; 67:4190-8.
23. Sirkisoon SR, Carpenter RL, Rimkus T, Miller L, Metheny-Barlow L, Lo HW. EGFR and HER2 signaling in breast cancer brain metastasis. Front Biosci (Elite Ed). 2016;8:245-63.
24. Sakaguchi M, Maebayashi T, Aizawa T, Ishibashi N. Whole-brain radiation therapy for breast cancer patients with dural metastasis without concomitant brain metastasis and leptomeningeal metastasis. Anticancer Res. 2018;38:6405-11.
25. Oechsle K, Lange-Brock V, Kruell A, Bokemeyer C, de Wit M. Prognostic factors and treatment options in patients with leptomeningeal metastases of different primary tumors: a retrospective analysis. J Cancer Res Clin Oncol. 2010;136:1729-35.
26. Boogerd W, van den Bent MJ, Koehler PJ, Heimans JJ, van der Sande JJ, Aaronson NK, et al. The relevance of intraventricular chemotherapy for leptomeningeal metastasis in breast cancer: a randomised study. Eur J Cancer. 2004;40:2726-33.
27. van der Ree TC, Dippel DW, Avezaat CJ, Sillevis Smitt PA, Vecht CJ, van den Bent MJ. Leptomeningeal metastasis after surgical resection of brain metastases. J Neurol Neurosurg Psychiatry. 1999;66:225-7.
28. Jung JM, Kim S, Joo J, Shin KH, Gwak HS, Lee SH. Incidence and risk factors for leptomeningeal carcinomatosis in breast cancer patients with parenchymal brain metastases. J Korean Neurosurg Soc. 2012;52:193-9.