Breast cancer intracranial metastases case series

2018

Wang et al., identified 134 consecutive patients diagnosed with operable breast cancer and then who developed brain metastases (BM) at the Sun Yat-sen University Cancer Center from 2000 to 2015, and analyzed the therapeutic methods for primary breast cancer and BM to evaluate whether they were associated with longer survival after the development of BM. The median age at breast cancer diagnosis was 47 years (range 21-73 years).

The median survival after BM was 16.2 months (range 12.1-20.3 months), and the survival rates were 62% and 37% at 1 and 2 years, respectively. Multivariate analysis showed that craniotomy ($p = 0.034$) and targeted therapy ($p < 0.001$) for BCBM were positively correlated with survival after diagnosis of BM; radiotherapy ($p = 0.024$) after surgery for primary breast cancer was beneficial to BM.

Surgical resection and targeted therapy are effective treatment for BCBM. Radiotherapy after surgery for the management of primary breast cancer is necessary in patients with brain progression later [1].

2016

Crozier et al., conducted a retrospective review of 196 patients who received brain radiation for BCBM between 2009-2013 at Mayo Clinic. Primary tumor characteristics were collected, including simplified molecular subtype. Other characteristics included patient's ECOG, number of brain lesions at BCBM diagnosis, and treatment received, including neurosurgery, whole-brain radiation therapy (WBRT), and stereotactic radiosurgery (SRS). The primary endpoint was OS from time of BCBM diagnosis.

Single-variable analysis revealed patients with HER2+ breast cancer had improved OS (HR = 0.6, p = 0.008). Compared to patients with 1-3 brain lesions, the risk of death in patients with leptomeningeal disease was 2.5-fold higher (p = 0.003). Worsening ECOG status was associated with worsening OS. Patients who received SRS and WBRT had improved OS (HR = 0.37, $p < 0.001$) compared to patients receiving WBRT alone.

Patients with the best OS had an ECOG of 0, HER2+ disease, and 1-3 brain lesions. The best OS was associated with the combination of neurosurgery and radiation therapy. A comprehensive treatment plan including neurosurgical evaluation and radiation therapy should be considered for patients with BCBM [2].

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65 patients were seen between January 2012 and January 2015. At the time of presentation to the BCBM clinic, most patients (74%) had multiple (≥2) brain metastases and had received prior systemic (77%) and whole brain radiation therapy and/or central nervous system stereotactic radiosurgery (65%) in the metastatic setting. Seventy-eight percent returned for a follow-up visit; 32% were enrolled in a clinical trial. Median time from diagnosis of brain metastasis to death was 2.11 years (95% confidence interval [CI] 1.31-2.47) for all patients, 1.15 years (95% CI 0.4-2.43) for triple-

negative breast cancer, 1.31 years (95% CI 0.51-2.52) for hormone receptor-positive/HER2- breast cancer, and 3.03 years (95% CI lower limit 1.94, upper limit not estimable) for HER2+ breast cancer (p = .0037).

Patients with BCBM have unique and complex needs that require input from several oncologic disciplines. The development of the UNC-CH multidisciplinary BCBM clinic is a model that can be adapted at other centers to provide coordinated care for patients with a challenging and complex disease.

Patients with breast cancer brain metastases often require unique multidisciplinary care to meet the numerous and uncommon challenges associated with their conditions. Here, the development and characteristics of a clinic designed specifically to provide for the multidisciplinary needs of patients with breast cancer brain metastases are described. This clinic may serve as a model for other institutions interested in creating specialty clinics with similar objectives [3].

2015

274 patients received whole brain radiotherapy for BC BM (01/2000-12/2011). The primary objective was to determine factors influencing overall survival (OS). All information relevant to primary BC, disease recurrence, treatment, outcome and cause of death (either neurological (NP) or systemic progression (SP)) were collected. Univariate (UV) and multivariate (MV) Cox regression analysis were used. RESULTS: One hundred and forty four patients (53%) were ER positive, 104 (38%) HER2 positive and 57 (21%) TN. Median age at BM was 53 (27-81) years and median OS from BM diagnosis 7.3 (5.7-8.9) months. On MV analysis, Her2 status, RPA score, surgery, stereotactic radiotherapy, and absence of TN disease were independent prognostic factor for OS. NP was the cause of death in 69.2% of HER2 positive patients and 17.3% had SP. Of the TN patients, 29.8% had NP and 54.4% SP (p < 0.001). CONCLUSION: A consistent OS advantage is noted for HER2 positive BM cases and inclusion of BC subtype in the breast GPA score should improve the prognostic factors' sensitivity. The unique presentations, response to treatment and causes of death for HER2 positive patients means more aggressive focal therapy should be considered and studied in the context of clinical trials. For TN BM patients with poor performance status, best supportive care may be appropriate [4].

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140 consecutive patients who underwent craniotomy for BCBM (either for diagnostic purpose or with therapeutic intent) at the University of Texas MD Anderson Cancer Center between 2002 and 2009.

Most patients had invasive ductal histology (91%), grade 3 tumors (67%), and positive axillary lymph node (64%). Of the tumors, 56% were ER-negative, 62% were PR-negative, 44% were HER2-positive, and 28% were triple negative (TN). Brain metastasis (BM) was solitary in 51% of patients. Median interval from breast cancer diagnosis to BM was 46 months; median survival after BM was 14.1 months. In the univariate analysis, younger age, solitary brain metastasis, and ER or PR positivity in the breast tumors were associated with longer survival. There was a statistical trend toward increased survival in HER2-positive patients compared with HER2-negative patients (18 vs. 11 months). In the multivariate analysis, predictors for longer survival included younger age, solitary brain lesion, and HER2 positivity in the breast cancer. Biomarkers were evaluated in paired primary and brain tumors in 35 patients for ER status, 34 for PR status, and 36 for HER2 status. Discordant rates were 28% for ER, 20% for PR, and 3% for HER2. CONCLUSION: Compared with unselected breast cancer patients at the same institution, patients with breast cancer who had brain metastases had a higher proportion of

hormone receptor-negative, HER2-positive, and TN tumors. Younger age, solitary brain lesion, and HER2 expression were independent predictors of better survival in patients with BCBM. HER2 status was highly concordant between the paired primary and brain tumors, whereas changes of ER and PR status occurred in a substantial proportion of the patients. These findings are important for making effective treatment decisions for patients with BCBM [5)].

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131 patients who received SRS for breast cancer BM between 2001 and 2013. Survival was estimated by the Kaplan-Meier method. Effects of tumor biology, number and location of lesions, and number of SRS sessions on survival were evaluated by Cox proportional hazards regression. Of the 122 patients with subtypes available, 41 patients (31%) were classified as estrogen receptor positive/HER2 negative (ER(+)HER2(-)); 30 patients (23%), ER(+)HER2(+); 23 patients (18%), ER(-)HER2(+); and 28 patients (21%), ER(-)HER2(-) (or triple negative breast cancer, TNBC). Median age at first SRS was 50 years. Median overall survival for ER(+)HER2(-), ER(+)HER2(+), ER(-)HER2(+), and TNBC was 16, 26, 23, and 7 months, respectively ($p < 0.001$ for difference between groups). Patients with TNBC had the shortest time to retreatment with WBRT or SRS or death with hazard ratio of 3.12 ($p < 0.001$) compared to ER(+)HER2(-). In all subtypes other than TNBC, SRS can provide meaningful control of BM even in the setting of multiple lesions and may be worth repeating for new lesions that develop metachronously. For patients with TNBC, prognosis is guarded following SRS, and there is an urgent need to develop more effective treatment strategies [6)].

Stokes et al., retrospectively compared 35 patients with breast cancer brain metastases who received WBRT and SRS to 30 patients who only received SRS. All patients had evaluable imaging at a median of one year after their initial management. The development of white matter T2 prolongation as detected by T2 or FLAIR imaging was graded: grade 1 = little or no white matter T2 hyperintensity; grade 2 = limited periventricular hyperintensity; and grade 3 = diffuse white matter hyperintensity. After WBRT plus SRS, patients demonstrated a significantly higher incidence of WMC ($p < 0.0001$). After one year, 71.5 % of patients whose treatment included WBRT demonstrated WMC (42.9 % grade 2; 28.6 % grade 3). Only one patient receiving only SRS developed WMC. In long-term survivors of breast cancer, the risk of WMC was significantly reduced when SRS alone was used for management. Further prospective studies are necessary to determine how these findings correlate with neurocognitive toxicity. WBRT usage as initial management of limited brain disease should be replaced by SRS alone to reduce the risk of delayed white matter toxicity [7)].

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