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Prognostic Factors in Leptomeningeal Metastasis

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Abstract

Objective: To investigate prognostic factors this can be effective in survival of patients with Leptomeningeal Metastases (LM) from solid tumors.

Materials and Methods: Between 2005-2015, in the Radiation Oncology Department of Kayseri Education and Research Hospital, 16 patients with leptomeningeal metastasis from solid tumors were evaluated. Retrospective review of patient medical records was conducted to gather demographics, treatment patterns, and clinical outcomes.

Results: A 8 patients with breast cancer; 4 patients with lung cancer; 4 patients with prostate cancer were diagnosed as a primary cause of disease. The mean age at the time of diagnosis was 58.9. Of all patients, 87.5% had ECOG 2 and 3; 43.8% had comorbidity; 56.3% had two organ metastases; 43.8% had parenchymal brain metastases. The most frequent location for leptomeningeal metastasis was brain. All patients received palliative Radio Therapy (RT) and 18% of the patients received chemotherapy following RT. The median overall survival after LM was 9.4 month and 1 year overall survival was 40%. Factor affecting overall survival was age ≤65 years ($p = 0.046$), female gender ($p = 0.046$), comorbidity ($p = 0.039$) and radiotherapy fraction dose schedules ($p = 0.002$). According to univariate and multivariate analysis was a not significant factor affecting overall survival.

Conclusion: In this study, LM was seen mostly in breast cancers and lung cancer patients' survival was found shorter. Age, gender and accompanying comorbidity was found to be effective in prognosis.

Keywords: Leptomeningeal metastasis; Solid tumor; Radiotherapy; Prognostic factors

Introduction

While Leptomeningeal Metastasis (LM) is a neurological complication of several systemic tumors, it is also a result of tumor cell proliferation and spread in leptomeninx and/or in cerebrospinal fluid. Although the actual prevalence is not known, incidence rate for all solid tumors is around 5 to 8%. With increasing life expectancy, incidence rates increase. It is mostly seen in lung cancer, breast cancer, melanoma, leukemia and lymphoma. They are usually formed by hematogenous spread. Patients usually present with headache, nausea, vomiting, cranial nerve involvement and cognitive impairment. Diagnosis is made by cranial and spinal contrasted magnetic resonance imaging, and analysis of cerebrospinal fluid [1-3]. At the time of diagnosis systematic disease of the patients is usually either refractory to the treatment or at an advanced stage. Therefore, treatment is evaluated separately for each patient. There is small chance of cure with today's treatment regimens. In non-treated patients, the median time for survival is 4-6 weeks; in treated patients, it is usually 3-6 months. Mostly palliative intrathecal chemotherapy, systemic chemotherapy and radiotherapy are recommended [3-5]. Radiotherapy is given to local sites or neural network which are consistent with both imaging studies and clinical signs [2-4]. Clinical, pathological and demographic data have been found to provide useful information which are valuable in prognosis of LM from solid tumors according to the recent studies [3,4,6].

Materials and Methods

In this study, between 2005-2015, in the Radiation Oncology Department of Kayseri Education and Research Hospital, prognostic factors and survival were evaluated in patients with LM from solid tumors. A total of 16 patients (F/M, 1) were included. The mean age was 58.9 (43-82). Primary site of tumors were as follows: breast (8 cases); lung (4 cases) and prostate (4 cases). The most common pathology in breast cancer was invasive ductal carcinoma; it was adenocarcinoma in both prostate and lung. Of all patients, 87.5% had ECOG 2 and 3 at the time of admission, 43.8% had comorbidities (hypertension, type 2 diabetes mellitus, CAD, etc.), 56.3% had metastases in two organs. Site of LM was brain in 50%, brain and vertebrae in 43.8% and only vertebrae in 6.3%.

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Metastases were like nodules in the MRI or CT. The most common symptoms were nausea, vomiting and impaired vision. Patients with brain involvement (+/- parenchymal metastasis) or vertebral involvement received either 30 Gy (3 Gy/fraction) or 20 Gy (4 or 5 Gy/fraction) palliative RT. Boost or second series irradiation were not perfumed in any case. Eighteen percent of the patients received chemotherapy after RT. After LM metastasis, the median follow-up time was 9.7 months (range 1.2 to 40 months), overall survival was 9.4 months and 1 year survive was 40%. 68.8% of the patients died due to disease related or non-disease related causes. Factor affecting overall survival was 65 years and younger age ($p = 0.046$), female gender ($p = 0.046$), patients without comorbidities ($p = 0.039$) and radiotherapy dose fraction schedules ($p = 0.002$). The survival was found to be better in patients without parenchymal brain involvement, patients with only 1 metastatic organ presence and LM to the vertebrae but it wasn't statistically significant. According to univariate and multivariate analysis was a not significant factor affecting overall survival. LM occurrence was observed in order of frequency, in breast, lung and prostate cancer, in our study. Brain was the most common site for LM and vertebrae was the least. In lung cancer, survival was found to be shorter than in breast and prostate cancer. The median overall survival was 9.4 month and 1 year survival was 40%. In our study, patients older than 65 years of age, male and who had parenchymal brain involvement with multiple organ metastases, survival was less. Browner et al. [3] reported that LM was observed mostly in breast cancer, lung cancer and melanoma. In one study, 80 patients with LM from solid tumors were evaluated and LM was seen mostly in lung cancer (59%) followed by breast cancer (25%). They also reported the median survival 2.7 months and the 1 year survival 11.3% [6]. When the literature examined, the most common location for LM was reported to be brain and then vertebrae [1]. After LM occurrence, parenchymal brain metastasis are observed and the rate is 30 to 50% [4,5]. The median survival measured in lung cancer patients with LM is 4 months and in patients with either lung cancer or breast cancer, course of survival is slower (median survival of 7 to 12 months) [2]. Presence of such factors; parenchymal brain involvement with LM, age >55 to 60 years, low Karnofsky index (<60 to 70%), severe neurological deficits, extensive tumor involvement with little opportunity to response to systemic therapy have been reported to reduce KPS survival too much [3,4,6].

Results

In this study, patients with brain involvement received total cranial RT, patients with vertebrae involvement received RT to effected regions. None of the patients received second series RT or boost. In the statistical analysis, there was difference between different fractions schemes. In the literature, especially in patients with parenchymal brain involvement, Whole Brain Radio Therapy (WBRT, Usually a dose of 30 to 36 Gy in fractions of 3 Gy) has been recommended. Morris and colleagues reported no difference between WBRT-received and non-received group in terms of survival [4]. Gani et al. [5] indicated that WBRT was an effective treatment in patients with lung or breast cancer in the presence of chemotherapy intolerance or low overall performance. Although WBRT has no effect on survival in patients with cranial nerve involvement, better control of symptoms was reported. In another study, results univariate analysis of patients with high Karnofsky Performance Status (KPS) ($p = 0.001$) and receipt of chemotherapy ($p <0.001$) indicated better survival. Results of multivariate cox analyzes revealed that receipt of chemotherapy and a complete course of Whole Brain Radio Therapy (WBRT) (median dose 30 Gy in 10 fractions, range 24-40 Gy) were predictive of longer survival ($p = 0.013$ and 0.019, respectively) [3].

Conclusion

Our study showed that patients with LM from solid tumors have shorter survival. In lung cancer patients, whilst parenchyma involvement was frequent, in prostate cancer it wasn't observed. Age, gender and accompanying comorbidities were found to have impact on prognosis. However, in these patients, larger and comprehensive studies investigating prognostic factors are needed.

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