Brain Metastases from Esophageal Cancer: Clinical Review of 26 Cases

Zhengbo Song, Baochai Lin, Lan Shao, Yiping Zhang

Key words
- Brain metastasis
- Esophageal carcinoma
- Prognostic factor

Abbreviations and Acronyms
KPS: Karnofsky Performance Status
RPA: Recursive partitioning analysis
RTOG: Radiation Therapy Oncology Group
WBRT: Whole-brain radiation therapy

Department of Chemotherapy, Zhejiang Cancer Hospital, and Key Laboratory Diagnosis and Treatment Technology on Thoracic Oncology, Zhejiang province, Hangzhou, People's Republic of China

To whom correspondence should be addressed: Yiping Zhang, M.D.
[E-mail: yipingzhang@yahoo.cn]

Citation: World Neurosurg. (2014) 81, 1:131-135.
http://dx.doi.org/10.1016/j.wneu.2013.02.058

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

1878-8750/$ - see front matter Published by Elsevier Inc.

OBJECTIVE: **To assess the frequency of brain metastasis in patients with primary esophageal cancer and to describe the clinical characteristics, diagnosis, and prognosis.**

METHODS: **Of 1612 patients with primary esophageal carcinoma treated at a single institution from 2000–2010, a retrospective analysis of the medical files of 26 consecutive patients with central nervous system involvement was carried out. The clinical history, imaging, and pathologic findings were analyzed.**

RESULTS: **Of the 26 patients, 12 initially presented with a single cerebral metastatic lesion, and 14 had multiple brain lesions. There were 4 patients with adenocarcinoma and 22 with squamous cell carcinoma. Treatments were as follows: 5 patients underwent surgery followed by whole-brain radiation, 5 underwent stereotactic radiosurgery, 13 received whole-brain radiation, and 3 received chemotherapy. The median survival was 4.2 months; 1-year survival rate was 5.8%.**

CONCLUSIONS: **In this retrospective study of 1612 patients with esophageal carcinoma at a single medical center, 1.61% (26 of 1612) of the patients had a diagnosis of brain metastasis. The prognosis is poor for patients with brain metastasis from esophageal carcinoma. A solitary brain lesion, surgical treatment, and a good Karnofsky Performance Status may indicate a good prognosis.**

INTRODUCTION

Esophageal carcinoma is one of the most common malignancies worldwide, and the prognosis for patients has been extremely poor. The median survival is <1 year, and the survival rate at 5 years is about 10% in Western countries (15); the survival is even worse in China (21). The lungs, liver, and bone are the most common sites of visceral metastases (14). Brain metastases are rare in clinical series and have been found occasionally in autopsy cases (1-3, 13, 16, 20). Previous reports cited the incidence of brain metastases to be approximately 1%–3% (8).

Because of the rarity of brain metastases from esophageal carcinoma, there are no established treatment guidelines. Previously, small numbers of patients with esophageal adenocarcinoma were reported, and the data were from Western populations. The 2 largest studies from Asia included 49 patients and showed different histology in esophageal carcinoma. Adenocarcinoma accounted for 18% of cases in the study by Yoshida (22); however, squamous cell carcinoma was most prevalent in the study by Ogawa et al. (13). We reviewed the clinical data of 26 patients with esophageal carcinoma with metastasis to the brain to understand better the clinical characteristics and to identify the natural history, frequency, and factors that influence the prognosis.

MATERIALS AND METHODS

We reviewed the medical records of patients with esophageal carcinoma treated at Zhejiang Cancer Hospital during the period 2000–2010. The pathologic and imaging findings for all patients were reviewed, and data were collected regarding patient characteristics, clinical presentation, treatment, and clinical course. In all patients, brain metastases were diagnosed with a combination of computed tomography scans and magnetic resonance imaging.

The Radiation Therapy Oncology Group (RTOG) recursive partitioning analysis (RPA) describes 3 classes to predict survival of patients with brain metastases (6): class 1, patients with a Karnofsky Performance Status (KPS) >70, age <65 years, with controlled primary disease and no evidence of extracranial metastases; class 3, patients with a KPS <70; and class 2, all remaining patients who do not fit into classes 1 or 3. We applied the RPA scoring system to our patients.

Statistical Analysis

Survival was calculated using the Kaplan-Meier method from the start of confirmed brain metastasis to date of death or last follow-up examination. Multivariate analysis was performed using the Cox regression model. A probability level of 0.05 was chosen for statistical significance. Statistical analysis was performed with the SPSS 16 software (SPSS Inc, Chicago, Illinois, USA). Confidence intervals were calculated at the 95% level. Follow-up extended through June 1, 2011.

RESULTS

Patient Characteristics

Examination of the medical records and imaging findings of 1612 patients with esophageal carcinoma identified 26

patients (1.61%) with documented brain metastases. Among the 1612 patients, 1560 had squamous cell carcinoma, 33 had adenocarcinoma, and 19 had other histology. Table 1 summarizes the clinical characteristics of the 26 patients with brain metastases. The median age of the 26 patients at the initial diagnosis was 62 years (range, 28–72 years). The median time from the diagnosis of esophageal carcinoma to the diagnosis of brain metastasis was 10.2 months (range, 0.0–39.2 months). Of the 26 patients, 25 were men. Histology showed squamous cell carcinoma in 22 patients and adenocarcinoma in 4 patients. Among the 22 patients with squamous cell carcinoma, 3 had a basaloid squamous cell carcinoma. Most patients (18 patients; 69.2%) experienced symptoms directly related to the brain metastasis; the remaining 8 patients were asymptomatic. In 19 patients (73.1%), KPS was ≥70; KPS was <70 in 26.9%. Of the 26 patients, 12 initially presented with a single cerebral metastatic lesion, and 14 had multiple brain lesions.

Table 1. Demographic Characteristics of the Study Population

	Number
Gender	
Male	25
Female	1
Age	
Range (years)	28–72
Median	
<65	21
≥65	5
Staging	
I and II	7
III and IV	19
KPS	
≥70	19
<70	7
Histology grade	
Squamous cell carcinoma	22
Adenocarcinoma	4
Extracranial systemic metastasis	
Yes	18
No	8
Number of brain metastases	
1	12
>1	14
Treatment modality	
Surgery + radiation therapy	5
Chemotherapy	3
Radiation therapy	18
RPA class	
I	3
II	15
III	8
Symptoms	
Yes	18
No	8

KPS, Karnofsky Performance Status; RPA, recursive partitioning analysis.

Brain Tumor Treatment

Surgical resection followed by whole-brain radiation therapy (WBRT) was performed in 5 patients. Among the 5 patients with surgical treatment, KPS ≥70 was present in 4 patients; 3 patients were asymptomatic. All of the surgical patients initially presented with <3 cerebral metastatic lesions (3 patients with a single cerebral metastatic lesion and 2 patients with 2 lesions). In 18 patients, treatment was with radiation therapy. Among the patients receiving radiation therapy, 13 patients received WBRT alone (dose range, 25–45 Gy), and 5 underwent stereotactic radiosurgery. Corticosteroids in individualized doses were given during radiotherapy. Chemotherapy was given to 3 patients; 2 received a regimen of cisplatin and paclitaxel, and the third patient received docetaxel treatment.

Survival and Prognostic Factors

The overall median survival was 4.2 months (95% confidence interval, 3.2–5.2 months) (Figure 1). The 1-year survival rate was 5.8%. Median survivals with respect to treatment modality were as follows: 7.0 months for patients in the surgery group, 4.0 months for patients in the radiation therapy group, and 1.8 months for patients in the chemotherapy group.

In univariate analysis, surgery, the presence of a single lesion, KPS, RTOG RPA class, and extracranial disease status each had a statistically significant impact on survival (Table 2). No significant differences in survival were seen with regard to other factors. In the multivariate analysis, treatment modality, RTOG RPA, and KPS were statistically significant prognostic factors for survival (Table 3).

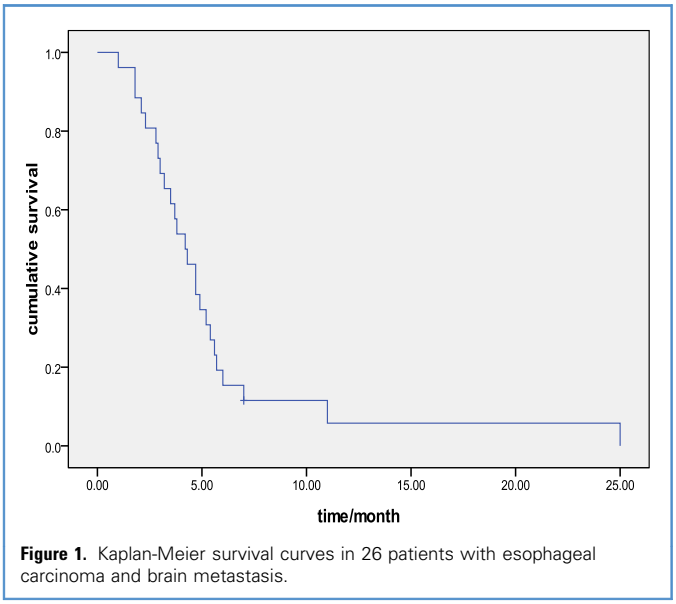

Figure 1. Kaplan-Meier survival curves in 26 patients with esophageal carcinoma and brain metastasis.