Clinical Study

Brain metastases in patients with ovarian carcinoma: prognostic factors and outcome

Zvi R. Cohen¹, Dima Suki², Jeffrey S. Weinberg², Eric Marmor⁴, Frederick F. Lang², David M. Gershenson³ and Raymond Sawaya¹

¹Department of Neurosurgery, Chaim Sheba Medical Center, Tel Aviv and Sackler School of Medicine, Tel Aviv, Israel; ²The Brain Tumor Center; ³Gynecologic Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA; ⁴Jewish General Hospital Hampstead, Quebec, Canada

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Summary

Between January 1975 and April 2001, 8,225 patients with ovarian cancer were seen at The University of Texas M. D. Anderson Cancer Center. Brain metastases developed in 72 of these patients (0.9%). The medical records of these patients were reviewed to assess the incidence of these metastases and their correlates of survival, as well as to describe the various treatment modalities used against them and their respective outcomes. The mean age of patients at the time of brain metastasis diagnosis was 53.7 years. The median interval between the diagnosis of the primary cancer and brain metastasis was 1.84 years. Neurological deficit, headache, and seizure were the most common symptoms. The brain was the only site of metastasis in 43% of patients. Multiple metastases were seen in 65% of them, although this may be a slight underestimate, as brain metastases in 17% of patients were evaluated prior to the magnetic resonance imaging era. The median survival time after the diagnosis of brain metastases was 6.27 months (95% CI, 4.48–8.06 months). The combination of surgical resection and whole-brain radiation therapy (WBRT) resulted in a longer survival time (median, 23.07 months) than did WBRT alone (median, 5.33 months) or surgery alone (median, 6.90 months) (p < 0.01 in both instances, multivariate Cox proportional hazards model analysis). The prognosis for patients with brain metastases from ovarian cancer appears to be poor. The existence of systemic dissemination at the time of brain metastasis was associated with a worse survival trend. The only significant predictor of survival in our series was the treatment modality. In particular, the resection of brain metastasis from ovarian cancer followed by WBRT appeared to be superior to resection alone or WBRT alone.

Introduction

Ovarian cancer is the fifth most common cancer among women in the United States and the leading cause of death from gynecologic cancer. Most patients present with advanced disease, resulting in poor prognosis (5-year survival rate of approximately 29% (American Cancer Society, 2002)) [1]. Brain metastasis from ovarian carcinoma is rare, with a reported incidence of 0.29–5% [2,3]. This incidence seems to be increasing [4,5], probably owing to more effective treatment of the primary cancer and the resulting survival prolongation. Published series of patients with brain metastasis from ovarian cancer described in the literature are relatively small [2,6,7]. Randomized treatment evaluations specific to this histology are not possible due to the small number of patients. Several meta-analyses of up to 194 patients have been conducted in an effort to formulate therapeutic treatment guidelines [3,8,9]. A common drawback of all these meta-analyses, however, is that the patients come from more than 1 treatment center, each with its own approach to treatment, which makes it difficult to draw firm conclusions about treatment outcome and prognostic factors. We reviewed a relatively large series of patients with brain metastases from ovarian cancer at a single institution. The review included an assessment of the incidence of brain metastasis, correlates of survival, and a description of the treatment modalities and their outcomes.
Materials and methods

The institutional database at The University of Texas M. D. Anderson Cancer Center (M. D. Anderson) was searched for all patients with a histological diagnosis of ovarian cancer from January 1, 1975, to April 30, 2001. We identified 8,225 consecutive patients with ovarian cancer. The distribution of the histological characteristics of the tumors in these patients is summarized in Table 1. Of these patients, 72 (0.9%) had brain metastasis and formed the basis of this study. The medical records of these patients were reviewed, and data were collected regarding patient demographic and clinical characteristics including patient age, surgical stage and histological grade of the ovarian tumor, treatment modalities used for the primary cancer, and metastasis to other organs at the time brain metastasis occurred. In addition, reports describing the brain tumor imaging characteristics, or the actual magnetic resonance (MR) or computed tomography images themselves, were reviewed, and data were collected regarding the number of lesions, their size, their location, and the extent of resection, where applicable. The vital status of the patients at the time of the review and the cause of death, if applicable, were noted. The patients’ medical records did not distinguish between death caused by brain metastases and death from systemic ovarian cancer.

Statistical methods

Frequencies and descriptive statistics of demographic and clinical variables were obtained. The chi-square test and Fisher exact test were used for categorical variables, and Student’s t-test and the Mann–Whitney test were used to compare continuous and ordinal variables, as appropriate. Kaplan–Meier estimates of overall survival were obtained, and the survival curves were compared using the log-rank test. Univariate and multivariate predictors of survival were determined using the Cox proportional hazards model. Rate ratios and their 95% confidence intervals were computed. A p value of ≤0.05 was considered significant.

Results

Patient characteristics

The patient characteristics as related to the primary tumor are presented in Table 2. The mean age of patients at the time of diagnosis of the primary cancer was 50.4 years. Surgical staging was performed according to the International Federation of Gynecology and Obstetrics (FIGO) system (Table 3). In most of the patients (81%), the ovarian cancer was classified as FIGO stage 3 or 4 at the time of presentation. Most of the patients (83%) presented with high-grade ovarian tumors. The clinical characteristics of the patients at the time of diagnosis of brain metastasis and the characteristics of the brain metastases are presented in Table 4. The median interval from diagnosis of the primary ovarian cancer to the development of brain metastases was 1.84 years (or 22 months; range, 0.00–18.85 years). Most of the patients (65%) presented with multiple brain metastases; 35% had a single brain metastasis in the following location: frontal lobe (11%), parietal lobe (10%), occipital lobe (3%), temporal lobe (3%), and cerebellum (8%). Three patients (4%) had leptomeningeal dissemination (LMD) of the ovarian cancer in addition to parenchymal tumors. At the time of diagnosis of brain metastasis, 57% of the patients had metastases in other organs.

Of note, among patients with grades 1 and 2 ovarian tumors, the median interval to the development of brain metastasis was 4.73 years (range, 0.33–10.59 years) compared with only 1.50 years (range, 0.00–18.85 years) in those with grade 3 tumors (p = 0.03). Factors such as surgical disease stage, tumor histological type, and cisplatin/paclitaxel-based chemotherapy were not significantly related to the length of this interval. None of these factors was significantly related to the observed number of brain metastases (single versus multiple). There was no association between the number of brain metastases and the presence of systemic noncerebral metastases (70% vs. 58% with multiple brain metastases in patients with and without noncerebral systemic metastasis, respectively; p = 0.26).

Table 1. Tumor histology of 8,225 patients with ovarian cancer seen between January 1975 and April 2001

<table>
<thead>
<tr>
<th>Histologies</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelial</td>
<td>6,833</td>
<td>83.2</td>
</tr>
<tr>
<td>Germ cell</td>
<td>895</td>
<td>10.9</td>
</tr>
<tr>
<td>Sex cord</td>
<td>276</td>
<td>3.4</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>37</td>
<td>0.5</td>
</tr>
<tr>
<td>Other</td>
<td>166</td>
<td>2.0</td>
</tr>
<tr>
<td>Total</td>
<td>8,207</td>
<td>100.0</td>
</tr>
</tbody>
</table>

*Among patients for whom data were available.