Simultaneous Resection of Multiple Metastatic Brain Tumors with Multiple Keyhole Craniotomies

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■ BACKGROUND: **The proper management of symptomatic patients with 2 or more brain metastases is not entirely clear, and the surgical outcomes of these patients undergoing multiple simultaneous craniotomies have not been well described. In this article, we describe patient outcomes after simultaneously resecting metastatic lesions through multiple keyhole craniotomies.**

■ METHODS: **We conducted a retrospective review of data obtained for all patients undergoing resection of multiple brain metastases in one operation between 2014 and 2016. We describe a technique for resecting multiple metastatic lesions and share the patient outcomes of this operation.**

■ RESULTS: **Twenty patients with 46 tumor resections were included in the study. The primary site of metastases for the majority of patients was lung, followed by melanoma, renal, breast, colon, and testes. Nine of 20 (45%) patients had 2 preoperative intracranial lesions, and 11 (55%) had three or more. Karnofsky performance scales were calculated for 14 patients: postoperatively 10 of 14 (71%) scores improved, 2 of 14 (14%) worsened, and 2 of 14 (14%) remained unchanged. After surgery, 9 of 14 (64%) patients were weaned off steroids by 2-month follow-up. The overall median survival time from date of surgery was 10.8 months.**

■ CONCLUSIONS: **We present patient outcomes after simultaneously resecting metastatic brain tumors through multiple keyhole craniotomies in symptomatic patients. Our results suggest comparable outcomes and similar surgical risk compared with those undergoing resection of a single brain metastasis. Resection of multiple brain metastases may improve Karnofsky Performance Scale scores in the early postoperative period and allow patients to be weaned from steroids.**

INTRODUCTION

Recent data suggest that aggressive surgical treatment of metastatic brain tumors prolongs survival, even in the presence of systemic disease.[1-4] These findings are important to consider as authors have demonstrated that physicians do a poor job of prospectively estimating survival in cancer patients, often underestimating life expectancy as well.[5] With expanding treatments for primary and metastatic tumors, it is now common for those with multiple brain metastases (BM) to live longer than 6 months.[6-8]

Resection of multiple nonadjacent metastatic lesions has generally been avoided for fear that multiple large craniotomies are too morbid for patients with minimal life expectancy.[9] We argue that recent advancements have altered the treatment paradigm in two ways: (1) minimally invasive neurosurgery has allowed for less surgical morbidity and decreased patient recovery time and (2) improved adjuvant cancer treatments have increased life expectancies, establishing the necessity for quality of life considerations.[10-12] We believe the combination of these two factors prompts reassessment of the role of surgery in the treatment of multiple cerebral metastases. Alternative treatments

Key words
- Brain
- Craniotomy
- Keyhole
- Metastases
- Minimally invasive
- Multiple
- Resection

Abbreviations and Acronyms
BM: Brain metastases
KPS: Karnofsky Performance Scale
SRS: Stereotactic radiosurgery
WBRT: Whole brain radiotherapy

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are especially relevant considering the side effects of steroids as a long-term maintenance therapy.

Although the idea of performing multiple craniotomies in patients with brain metastases is not entirely new,[6,7] our report provides surgical outcomes in a patient population with a greater number of brain metastases and offers a full description of the surgical technique. Our results suggest that the majority of patients who undergo resection of multiple symptomatic tumors experience improved KPS scores, achieve steroid independence, and demonstrate acceptable postoperative morbidity outcomes.

METHODS

Patient Population

We conducted a retrospective review of data on all patients undergoing multiple craniotomies in a single operation for metastatic tumors between 2014 and 2016. Twenty patients met the following criteria: 18 patients had 2 craniotomies, 1 patient had 3 craniotomies, and 1 patient had 4 craniotomies. The total number of craniotomies correlated to the number of metastases removed, except in 1 patient who had 2 craniotomies for removal of 3 tumors. Forty-six tumor resections were included for review. Clinical records, hospital charts, operative notes, and imaging studies were reviewed through the last available follow-up or time of death. Tumor number and tumor volume were calculated independently by the authors C.B. and A.S. using preoperative and postoperative contrast-enhanced magnetic resonance imaging (MRI). Contrast-enhanced computed tomography of the brain was used in 1 patient who did not have an MRI.[13] This study was performed after obtaining patient consent and with the approval of our institutional review board.

Outcome Assessment

Primary outcome assessments included overall patient survival, preoperative and postoperative Karnofsky Performance Scale (KPS) score, operative time, surgical complications, and steroid independence. Inpatient and outpatient medical records were reviewed for all patients to assess complications. Postoperative complications that persisted beyond 2 months after surgery were deemed permanent. KPS data were obtained from 14 patients during follow-up at our brain tumor clinic. All other data, including overall survival, were based on the entire cohort. Survival data were queried from the Social Security Death Index.

Adjuvant Therapy

A tumor board consisting of a radiation oncologist, a medical oncologist, and a neurosurgeon (M.E.S.) determined optimal postoperative adjuvant therapy for each patient. Regarding radiation treatment modalities, stereotactic radiosurgery (SRS) was performed when tenable. As discussed later, many patients included in this study had a high number of BM and therefore were treated with whole brain radiotherapy (WBRT).

Surgical Technique

Describing a comprehensive algorithmic approach to each possible clinical scenario is beyond the scope of this report. However, there are general principles that guide operability: (1) tumors larger than 2 cm in diameter, (2) tumors with substantial edema or mass effect, or (3) tumors that produce a neurologic deficit regardless of size.

In general, preoperative contrast-enhanced MRI containing image guidance sequences is obtained. A diffusion tensor imaging sequence is also included for deeper tumors; this is used to perform white matter tractography as described previously.[14] Frameless stereotactic navigation is used to plan each craniotomy in such a way as to incorporate working along the long axis of the tumor while avoiding major white matter tracts when possible.

Regarding craniotomy size and thus incision length, the philosophical approach of the keyhole principle is applied.[15] Although "modified" craniotomies have been described previously,[16,17] we believe certain principles make our method unique. First, for cortical-based tumors, the craniotomy is tailored to expose only the tumor surface. Second, the maximum craniotomy size for tumors deep to the cortical surface is approximately 2–2.5 cm. In our experience, deeply seated tumors are easily accessible through a 2-cm craniotomy, whereas larger or more superficial tumors greater than 2 cm in diameter may require a slightly larger craniotomy. An example of an incision outline and flap size is illustrated in Figure 1. Multiple craniotomy incisions are included in the operative field when possible. An illustrative case of multiple keyhole craniotomies and preoperative and postoperative imaging is shown in Figure 2.

Statistical Analysis

Categorical data are reported as frequencies and percentages, and continuous variables are reported as means with standard error. The Mann–Whitney U test was used when making comparisons between two independent groups with continuous and ordinal values. Survival is displayed using a Kaplan–Meier plot. The log-rank test was used to compare survival in 2 groups.

RESULTS

Patient Population

Twenty patients were treated in 1 operation for metastatic lesions with multiple craniotomies. In total, 46 tumors were resected. Characteristics of these patients are noted in Table 1. Eleven patients (55%) were men and 9 patients (45%) were women. In 12 patients (60%), the primary malignancy originated in the lungs, in 3 patients (15%) from melanoma and in 2 patients (10%) in the kidneys. Other primary sites included breast, colon, and testes.

Twenty-five (45%) of the BM were left sided and 21 (46%) right sided. Two BM were found in 9 patients (45%), 3–5 BM were found in 5 patients (25%), and 6 or more BM were found in 6 patients (30%). Tumor locations are shown in Table 2. The most common location of resected BM were in the parietal lobe (n = 18; 39%). Tumor location relationship between tumors resected within the same hemisphere is presented in Table 3. For tumors resected in opposite hemispheres, the data are described in Table 4.

Operative Data and Surgical Complications

Operative data are presented in Table 2. Eighteen patients (90%) underwent 2 craniotomies. The other 2 patients (10%) had 3 and