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Secondary Neoplastic Brain Tumors: A 10-Year Single-Center Experience

İkincil Neoplastik Beyin Tümörleri: 10 Yıllık Tek Merkez Deneyimi

Ufuk TEMTEK[1]
[1]Department of Neurosurgery, University of Health Sciences, Erzurum City Hospital, Erzurum, Türkiye

Muhammet ELVEREN[2]
[1]Department of Neurosurgery, University of Health Sciences, Erzurum City Hospital, Erzurum, Türkiye

ABSTRACT

Objective: Brain metastases (BMs) are the most common intracranial tumors in adults and represent a major cause of morbidity and mortality in patients with systemic malignancies. This study aimed to evaluate the clinical characteristics, surgical management, and outcomes of patients who underwent surgery for brain metastases over a 10-year period and to assess the impact of intraoperative technologies on surgical outcomes.

Methods: This retrospective study included patients who underwent surgery for intracranial tumors between 2013 and 2023. Among 513 operated patients, 114 with histopathologically confirmed brain metastases were analyzed. Demographic characteristics, primary tumor origin, diagnostic modalities, lesion number and location, treatment strategies, and postoperative outcomes were evaluated. The impact of intraoperative neuronavigation and intraoperative ultrasound on surgical outcomes and reoperation rates was also analyzed.

Results: Of the 513 patients, 114 (22.2%) were diagnosed with brain metastases. The mean age was 59.1 years (range, 31–85), and the male-to-female ratio was 56.2% to 43.8%. The most common primary tumors were lung (52.6%), breast (19.2%), and gastrointestinal cancers (8.8%). Metastases were predominantly infratentorial (57.9%), and solitary lesions were observed in 52.6% of cases. Intraoperative neuronavigation was used in 68.4% of cases, and neuronavigation combined with intraoperative ultrasound was used in 24.5%. Reoperation rates were significantly lower in cases where intraoperative imaging modalities were utilized compared to those without additional intraoperative tools (P<.001). Postoperative adjuvant therapy was administered in 75.4% of patients, with a recurrence rate of 12.7%. The median survival time was 22 months.

Conclusion: Brain metastases remain a major clinical challenge requiring individualized treatment strategies. Surgical resection plays a critical role in selected patients by providing rapid relief of mass effect and improving neurological outcomes. The use of intraoperative technologies, particularly neuronavigation and intraoperative ultrasound, significantly contributes to improved surgical precision and reduced reoperation rates. Appropriate patient selection, meticulous preoperative planning, and the integration of advanced intraoperative tools may improve survival and quality of life in patients with brain metastases.

Keywords: Brain metastasis, neurosurgery, neuronavigation, intraoperative ultrasound, surgical outcomes

ÖZ

Amaç: Beyin metastazları (BM), yetişkinlerde en sık görülen intrakraniyal tümörler olup, sistemik maligniteleri olan hastalarda önemli bir morbidite ve mortalite nedenidir. Bu çalışmanın amacı, 10 yıllık süreçte beyin metastazı nedeniyle opere edilen hastaların klinik özelliklerini, cerrahi tedavi sonuçlarını değerlendirmek ve intraoperatif teknolojilerin cerrahi sonuçlar üzerindeki etkisini incelemektir.

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Sorumlu Yazar/Corresponding author: Ufuk TEMTEK
E-mail: ufuktemtek@gmail.com
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Yöntemler: Bu retrospektif çalışmada, 2013–2023 yılları arasında intrakraniyal tümör nedeniyle opere edilen hastalar incelendi. Toplam 513 hasta arasından histopatolojik olarak beyin metastazı tanısı doğrulanan 114 hasta analiz edildi. Demografik özellikler, primer tümör kökeni, tanı yöntemleri, lezyon sayısı ve lokalizasyonu, tedavi stratejileri ve postoperatif sonuçlar değerlendirildi. Ayrıca intraoperatif nöronavigasyon ve intraoperatif ultrason kullanımının cerrahi sonuçlar ve reoperasyon oranları üzerindeki etkisi analiz edildi.

Bulgular: Toplam 513 hasta arasında 114 (%22,2) hastada beyin metastazı saptandı. Ortalama yaş 59,1 (31–85) olup, erkek/kadın oranı %56,2/%43,8 idi. En sık primer tümörler akciğer (%52,6), meme (%19,2) ve gastrointestinal sistem (%8,8) kaynaklıydı. Metastazlar ağırlıklı olarak infratentoryal (%57,9) yerleşimli olup, vakaların %52,6'sında soliter lezyon saptandı. Olguların %68,4'ünde intraoperatif nöronavigasyon, %24,5'inde ise nöronavigasyon ile birlikte intraoperatif ultrason kullanıldı. İntraoperatif görüntüleme yöntemlerinin kullanıldığı vakalarda reoperasyon oranları, ek intraoperatif araç kullanılmayanlara kıyasla anlamlı derecede daha düşüktü (*P*<,001). Hastaların %75,4'üne adjuvan tedavi uygulanmış olup, nüks oranı %12,7 olarak bulundu. Medyan sağkalım süresi 22 aydı.

Sonuç: Beyin metastazları, bireyselleştirilmiş tedavi stratejileri gerektiren önemli bir klinik sorundur. Cerrahi rezeksiyon, kitle etkisini hızlı şekilde ortadan kaldırarak ve nörolojik sonuçları iyileştirerek seçilmiş hastalarda kritik bir rol oynamaktadır. Özellikle nöronavigasyon ve intraoperatif ultrason gibi intraoperatif teknolojilerin kullanımı cerrahi hassasiyeti artırmakta ve reoperasyon oranlarını anlamlı şekilde azaltmaktadır. Uygun hasta seçimi, titiz preoperatif planlama ve ileri intraoperatif tekniklerin kullanımı, hastaların sağkalımını ve yaşam kalitesini artırabilir.

Anahtar Kelimeler: Beyin metastazı, nöroşirürji, nöronavigasyon, intraoperatif ultrason, cerrahi sonuçlar

INTRODUCTION

Brain metastases (BM), which are common in patients with malignancies, have become an increasingly significant cause of morbidity and mortality due to advances in imaging techniques and prolonged patient survival.[1]

Determining the exact incidence of brain metastases in our country is challenging due to insufficient registry data; however, based on reports indicating that BM develops in approximately 10–40% of patients with solid tumors in the United States, an estimated 5,000–20,000 cases may occur annually.[2] Furthermore, advances in magnetic resonance imaging (MRI), its widespread availability, and improved control of primary tumors in modern oncological treatments have contributed to an apparent increase in BM incidence.[3]

In many countries, the incidence of BM is considered to be comparable to that of primary brain tumors.[1,4,5] However, due to the lack of reliable epidemiological data, this estimation remains uncertain in our country. Additionally, variability in clinical practice between centers and heterogeneity among patients represent important challenges in the management of BM.[6]

Historically, brain metastases were associated with poor prognosis, and whole-brain radiation therapy (WBRT) alone was considered the standard treatment, with a median survival of 3–6 months.[7] However, advances over the past decades have significantly changed the management of BM.[8] The addition of surgical resection in selected patients, the use of stereotactic radiosurgery (SRS) for limited lesions, and the development of targeted and immunotherapies have improved survival outcomes, preserved neurocognitive function, and enhanced quality of life.[9]

Despite these advances, the increasing number of available treatment modalities has made decision-making more complex. Therefore, evaluating real-world clinical outcomes is essential to optimize treatment strategies.

The aim of this study was to evaluate the clinical, radiological, and surgical outcomes of patients with brain metastases treated over a 10-year period and to assess the impact of intraoperative technologies on surgical outcomes within the context of contemporary treatment approaches.

METHODS

This retrospective study was conducted between March 2013 and September 2023 following approval from the Atatürk University Local Ethics Committee of the Medical Faculty (Approval No: B.30.2.ATA.0.01.00/324), which covered the entire study period, including retrospective data collection. In addition, the necessary institutional permissions were obtained for the use of hospital records and patient data.

A total of 513 patients who underwent surgery for intracranial tumors at our clinic during the study period were screened. Among these, 114 patients with histopathologically confirmed brain metastases were included in the study. Patients with primary brain tumors, non-neoplastic lesions, or incomplete clinical data were excluded.

The cases were analyzed in terms of demographic characteristics, primary tumor focus, diagnostic modalities, as well as the number, size, and location of lesions, treatment modalities, and clinical outcomes. Patients' hospital records and, where available, surgical images were reviewed. Additionally, the use of intraoperative tools such

as neuronavigation and ultrasound was evaluated to assess their impact on postoperative imaging findings and tumor resection rates.

All patients were followed up through clinical visits and radiological imaging. Survival time was calculated from the date of surgery to the last follow-up or death.

Postoperative records were reviewed, and the contribution of postoperative radiotherapy to patient outcomes was evaluated.

Statistical Analysis

Statistical analyses were performed using SPSS software (version 25.0; IBM Corp., Armonk, NY, USA). Categorical variables were expressed as frequencies and percentages. Comparisons between groups were performed using the Chi-square test or Fisher's exact test, as appropriate. A *P*-value of <.05 was considered statistically significant.

RESULTS

In this study, a total of 513 patients who underwent surgery for intracranial tumors were retrospectively analyzed. Of these, 114 cases (22.2%) were histopathologically diagnosed as metastases. The mean age was 59.1 years (range: 31–85), and the male-to-female ratio was 64 (56.2%) to 50 (43.8%) (Table 1).

Preoperatively, metastasis was suspected in 70 cases (61.4%). The most common primary tumor sites were the lungs (52.6%), breast (19.2%), and gastrointestinal tract (8.8%) (Table 1). Among patients with a known primary tumor, 50 (43.8%) had received chemotherapy and/or radiotherapy. The mean interval between primary tumor diagnosis and detection of brain metastases was 24 months.

Metastatic lesions were diagnosed using MRI in 102 cases (89.4%) and PET in 12 cases (10.5%). Lesions were predominantly located in the infratentorial region (57.9%), and 52.6% of cases had solitary metastases. The distribution of metastases according to location and number is presented in Table 2.

All 114 patients underwent surgical treatment. Reoperation was required in 28 cases (24.5%). When analyzed according to intraoperative techniques, reoperation rates were significantly higher in patients operated without additional intraoperative tools (61.1%) compared to those in whom neuronavigation alone (10.0%) or neuronavigation combined with intraoperative ultrasound (3.6%) was used. This difference was statistically significant (Chi-square test, *P*<.001) (Table 3).

Hydrocephalus was present in 12 patients (10.5%), and peritumoral edema was observed in 106 patients (92.9%). Extracranial metastases were detected in 72 cases (63.1%). Postoperative adjuvant therapy (radiotherapy and/or chemotherapy) was administered in 86 patients (75.4%), with a recurrence rate of 12.7% (11/86). The surgical mortality rate (within 30 days) was 24.5%, and the median survival time was 22 months.

Table 1. Distribution of primary tumor sites by gender

Primer Site	Male (n=64)	Famale (n=50)	Total (n=113)
Lung (AC)	50	10	60
Breast	-	22	22
Thyroid	-	4	4
Malignant melanoma	2	2	4
Bladder	2	-	2
Stomach	6	-	6
RCC	2	2	4
Colon	-	6	6
Ovary	-	6	6
Cervix	-	2	2
Esophagus	2	-	2
Total	64	50	114

Table 2. Distribution of metastases by location and number

Location	Single	Multiple	Total
Infratentorial	34	32	66
Supratentorial	26	22	48
Total	60	54	114

Table 3. Relationship between reoperation and intraoperative technologies

Group	Total (n)	Reoperation (n, %)
No additional tools	36	22 (61.1)
Neuronavigation only	50	5 (10.0)
Neuronavigation + intraoperative USG	28	1 (3.6)
Total	114	28 (24.5)

A statistically significant difference was observed between groups (Chi-square test, *P*<.001).

DISCUSSION

The incidence of brain metastases has increased recently due to advances in cancer treatments, prolonged patient survival, and improvements in screening protocols.[10] Brain metastases require aggressive treatment because they not only cause epileptic seizures, paralysis, and speech disorders but can also affect the patient's survival.[11] Brain metastases present with different clinical manifestations in each patient. Therefore, developing an effective treatment plan is crucial, and the plan must be tailored to the individual patient. Clinical variables such as patient age, performance status, number and size of BMs, neurological

symptoms, extracranial metastases, and genetic alterations should be considered.[12] To treat brain metastases, treatments include surgical resection, stereotactic radiosurgery (SRS), and whole-brain radiation therapy (WBRT), as well as systemic therapies involving immunotherapeutic agents.[5,13]

Brain metastases (BMs) are the most common cause of intracranial neoplasms in adults with invasive cancer.[14] In our study, the pathological diagnosis of brain metastases was confirmed in 22.2% of patients who underwent surgery for an intracranial mass. The incidence of BMs has been reported to range from 20% to 45% in cancer patients.[15] BMs can present as solitary or multiple lesions. Most BMs are solitary, and in 20% of diagnoses, two or fewer lesions are present; however, in 30% of cases, three or more lesions are found. Lung and melanoma primarily lead to multiple BMs, while breast, renal, and colon cancers typically present as solitary lesions.[15] This data is further supported by the fact that 35 (58.3%) of the 60 patients with lung cancer in our study had multiple BMs, 3 out of 4 (75%) patients with malignant melanoma had multiple metastases, and 15 out of 22 patients with breast cancer had a single BM.

Predicting prognosis plays a significant role in BM treatment. Surgical resection is generally recommended for patients with an expected survival of at least three months, and it is important to thoroughly assess the patient's clinical condition.[16] Gaspar et al. developed a prognostic prediction system based on the Karnofsky Performance Score (KPS), number of brain metastases, systemic disease status, presence of extracranial metastases (ECM), and genetic status.[17] In this study, patients with a KPS of 70 or higher, controlled systemic disease, <65 years of age, and no ECM were classified as Class I; those with a KPS <70 were classified as Class III, and the remaining patients as Class II.[12] This system easily classified patients using simple variables to predict prognosis; however, it was considered an outdated system because it was not disease-specific and did not reflect current systemic treatments. Sperduto et al.[12] retrospectively analyzed 3,940 patients newly diagnosed with BM and published specific prognostic assessment scores for each cancer type.[12,18–20] The most significant change in prognostic factors compared to the previous study was the inclusion of genetic alterations.[18] A distinct assessment system was developed for each cancer type by including mutations associated with prognostic factors: non-small cell lung cancer (epidermal growth factor receptor [EGFR] or anaplastic lymphoma kinase [ALK] alterations), breast cancer (estrogen receptor [ER], progesterone receptor [PR], human epidermal growth factor receptor 2 [HER2]), and melanoma (BRAF) mutations.[20–22] This prognostic prediction system is continuously updated as new information becomes available. Neurosurgeons must keep track of these changes when treating patients or designing clinical trials.

Treatment for brain metastases includes surgical resection, radiation therapy such as stereotactic radiosurgery (SRS) and whole-brain radiation therapy (WBRT), targeted therapy, and systemic treatments involving immunotherapeutic agents.[5,13] In our study, adjuvant (radio/chemo) therapy was administered in 86 of the 114 cases (75.4%). The recurrence rate in these patients was 12.7%.

The most important factors in determining the treatment method are the number of brain metastases and performance status. In cases of a single metastasis, if the tumor is accessible and the patient is in Class I or II, surgical treatment and adjuvant WBRT or adjuvant SRS are recommended.[16,23] In Class III cases, SRS or WBRT is recommended without surgical treatment.[16,24,25] If the tumor site is inaccessible, SRS is recommended for Class I or II, and WBRT is preferred for Class III.[16] In cases of multiple BMs, treatment methods are largely classified based on the number of BMs (n>4); surgical treatment is recommended if the tumor has caused mass effect and the lesion is accessible.[16,23] If the patient's performance status is poor and the BM does not cause mass effect, SRS or WBRT is recommended.[16]

Surgical treatment offers a significant advantage in tumors larger than 3–4 cm because it allows for the rapid removal of mass effect, may reduce the need for steroids, and can minimize radiation necrosis that may occur after radiation therapy.[26] However, SRS can be applied to relatively small tumors and provides treatment on an outpatient basis without requiring general anesthesia, thereby reducing hospital stay.[26] WBRT is effective in nearly all tumors, but the neurocognitive decline that may occur after treatment has recently reached a notable level.[27]

Although the role of surgical treatment in brain metastasis (BM) is limited, it appears to offer high survival rates in patients with good performance status and single or multiple lesions.[16] Furthermore, since performance status is one of the most important prognostic factors in patients with BM, the primary goal of surgical treatment is to achieve maximum safe resection without causing neurological deficits. To achieve this goal, various neurosurgical modalities such as neuronavigation, intraoperative ultrasound, motor evoked potentials (somatosensory, visual, and auditory EP), and subcortical stimulation (SCS) can be utilized.[28–33]

In our study, reoperation was required in 5 cases (10.0%) in which only neuronavigation was used and in 1 case (3.6%) in which both neuronavigation and intraoperative ultrasound were used. In contrast, the reoperation rate was markedly higher in cases where no additional intraoperative

tools were used (61.1%). This difference was statistically significant (Chi-square test, *P*<.001). These findings suggest that the use of intraoperative technologies, particularly the combined use of neuronavigation and intraoperative ultrasound, may significantly reduce the need for reoperation by enabling more accurate and extensive tumor resection.

CONCLUSION

Brain metastases have become a significant cause of morbidity and mortality among cancer patients, and with advances in systemic treatment options, they now require more aggressive and multidisciplinary management. Surgical treatment plays a crucial role, particularly in providing rapid relief of mass effect and improvement of neurological symptoms.

In this study, the use of intraoperative technologies, including neuronavigation and intraoperative ultrasound, was associated with significantly lower reoperation rates compared to conventional surgery without additional tools (*P*<.001). These findings highlight the importance of intraoperative guidance in achieving maximal safe resection.

The presence of multiple brain metastases, extracranial metastases, comorbidities, and low Karnofsky Performance Status negatively affects prognosis and survival. Therefore, appropriate patient selection, meticulous preoperative planning, and the integration of advanced intraoperative imaging techniques are essential for optimizing surgical outcomes.

In conclusion, the combined use of modern surgical strategies and intraoperative technologies may improve clinical outcomes and contribute to better quality of life and prolonged survival in patients with brain metastases.

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