Surgical Management and Postoperative Outcome in patients with Brain Metastases: Our Surgical Experience

Beyin Metastazı Olan Hastalarda Cerrahi Tedavi ve Postoperatif Sonuç: Cerrahi Deneyimimiz

Adem Doğan¹, Mehmet Ozan Durmaz², İnan Gezgin³, Ali Kapan²

¹Republic of Turkey Ministry of Health, Şehitkamil State Hospital, Gaziantep, Turkey.
²University of Health Sciences, Gülhane Training and Research Hospital, Department of Neurosurgery, Ankara, Turkey.
³Republic of Turkey Ministry of Health, Dr. Ersin Arslan Training and Research Hospital, Clinic of Neurosurgery, Gaziantep, Turkey.


ABSTRACT

Aims: Metastatic brain tumors are the most commonly seen intracranial lesion in adults and an important cause of morbidity and mortality in patients with cancer. This study aimed to evaluate the postoperative mortality, morbidity, and survival rates of patients who underwent surgery in our clinic for metastatic brain tumors.

Method: Clinical data of 131 patients, including age, sex, symptoms, localization, primer site, surgical methods, resection, complications and recurrence were collected.

Results: Fifty patients (38.1%) were female, and 81 (61.8%) patients were male. The average age of the patients was 54.9. The most common reason for hospital admission was headache (68.7%). Lesions were detected in the cerebral hemisphere in 108 (82.4%) patients and the posterior fossa in 23 (17.5%) patients, and 16 (12.2%) patients had multiple lesions. All patients (n=131) underwent surgery with neuronavigation. Total resection was performed in 25 (19%) patients, gross total resection in 83 (63.3%), subtotal resection in 18 (13.7%), and biopsy in 5 (3.8%). The most commonly seen tumor originated from the lungs (n=63, 48%), according to the histopathological examination. The mean overall survival was 5.3 (range, 1–36) months during the follow-up period. Twelve (9.1%) patients had recurrence and underwent surgery again.

Conclusion: Multidisciplinary treatment methods are used in the treatment of metastatic brain tumors. Effective surgical intervention to eliminate peritumoral edema and increased intracranial pressure improves postoperative survival rates. In addition, post-surgical whole-brain radiotherapy reduces recurrence and improves survival.

Keywords: Brain, metastasis, surgery, prognosis
INTRODUCTION

Brain metastases are the most common intracranial tumors in adults (11,19,29). Brain metastasis is the most important cause of morbidity and mortality in patients with cancer (29).

The incidence of brain metastases ranges from 8.3 to 14.3 per 100,000 (29). These tumors are estimated to occur 10 times more frequently than primary malignant brain tumors (20,29). However, these incidence rates vary according to the primary tumor, tumor stage, and even the subtype of cancer, among other factors. The most commonly detected brain metastasis originates from the lung upon diagnosis (10). The incidence of brain metastasis is 15%–40% in adults and 6%–10% in children among all patients with cancer (4). Brain involvement is a poor prognostic criterion because of its late occurrence in the course of metastatic cancer (2). In recent years, the number of confirmed brain metastases has increased because of the increased survival of patients with cancer and the widespread use of imaging modalities (3,24). Brain metastases are mostly seen in the fifth and seventh decades of life and are more common in men (1).

The most common source of brain metastasis is the lung (40%–50%), followed by the breast (15%–25%), malignant melanoma (5%–20%), kidney (5%–10%), and colon (4%–6%) (11,14,20,28,29,34). Sarcomas metastasizing to the central nervous system are very rare (17). The primary cancer site could not be identified in 5%–10% of the patients with brain metastases (29,35).

Approximately 80% of the metastases occur in the cerebral hemisphere, with less involvement of the cerebellum and brainstem (10%–15% and 2%–3%, respectively) (30). Unlike the cerebrum, primary parenchymal metastases to the spinal cord are rare (30).

Symptoms caused by brain metastases may be the only sign of a certain cancer type such as lung cancer, breast cancer, or melanoma (8). Most brain metastases are diagnosed when they become symptomatic. Patients with brain metastases often present with neurological symptoms such as headache, cognitive impairment, seizure, and focal deficit, all of which accelerate the decline in the quality of life and survival (29). Brain metastasis usually presents with symptoms localized to that particular area of the brain (22,33). Seizures...
may be seen in 10%–20% of patients with brain metastasis (22). Seizures are more common in supratentorial and cortical lesions than in infratentorial masses (22).

Frequently used diagnostic tests aim to detect an underlying lesion. Computed tomography (CT) and magnetic resonance imaging (MRI) remain the most widely used imaging techniques. Positron emission tomography (PET) and single-photon emission computed tomography are used to evaluate the primary tumor site and to identify other possible metastases (1,25). Two MRI sequences, namely, diffusion-weighted MRI and diffusion-tensor imaging, can reveal the microstructure of the brain and its deterioration caused by tumor growth and edema (15). Histopathological examination is an important diagnostic tool that detects the morphology of metastatic malignancy and possible tumor origin (9).

Patients with brain metastases generally have a poor prognosis and survival of approximately 4 weeks without treatment (37). Depending on the primary tumor, the mean survival ranges from 2 to 27 months (37).

Radiation therapy, surgery, and chemotherapy are used in the treatment. Radiation therapy includes whole-brain radiotherapy (WBRT), stereotactic radiosurgery, or a combination of these modalities. WBRT has been accepted as the standard treatment of brain metastases (15).

This study aimed to retrospectively evaluate the clinicopathological features and postoperative survival rates of patients who underwent surgery for brain metastases in our clinic.

**MATERIALS and METHODS**

**Patient population**

This study was approved by the ethics committee (2020/304). In this study, we retrospectively analyzed 131 patients who were admitted with an intracranial mass and histopathologically confirmed metastasis between September 2016 and November 2020. Of these patients, 50 (38.1%) were female and 81 (61.8%) were male. The mean age was 54.9 (range, 2–82) years.

**Clinical and radiological evaluation**

The most common reason for admission was headache (68.7%, n=90). In addition, 30 (22.99%) patients were admitted with dizziness, 19 (14.5%) with seizures, and 3 (2.3%) with vision loss. CT and MRI were performed in all patients.

Radiological examination revealed that 108 (82.4%) patients had a supratentorial tumor, while 23 (17.5%) patients had a tumor at the posterior fossa. In addition, 16 (12.2%) patients had more than one lesion in the intracranial region. To reduce intracranial edema and high intracranial pressure caused by the lesion, dexamethasone (16 mg/day) was started in all patients preoperatively.

Tumor resection was classified as total, gross total, subtotal, and biopsy according to intraoperative surgical observation, and MRI was performed in the early postoperative period. Total resection included complete excision of the tumor and capsule, gross total resection meant excision of nearly all tumor tissues and capsule remnants are left, and subtotal resection was defined as cases where the tumor capsule and <10% of the tumor remained.
Surgical strategy
Neuronavigation (featured MRI) was used in all cases in addition to routine surgical preparations. After induction of anesthesia, the patient’s head was positioned in accordance with the localization of the lesion by wearing a head clamp.

After the neuronavigation installation, the skin and subcutaneous tissue were passed through an incision made in accordance with the lesion localization in all cases. Craniotomy and craniectomy were performed in cases with lesions located in the cerebral hemisphere and posterior fossa, respectively. Especially in cases with increased intracranial pressure and tight dura mater, mannitol (1 g/kg) was infused rapidly before dural opening (26). Tumor resection was performed by endoscopic methods (n=20, 15.2%) by placing a thoracoport in deeply located lesions. In other cases, tumor resection was performed by microscopic methods (n=111, 84.7%). After tumor resection, bleeding control was performed in all cases, and the dura was sutured. A bone flap was placed. The skin was properly closed.

RESULTS
Neuronavigation was used in all cases in addition to routine surgical preparations. Especially, in cases with increased intracranial pressure and tight dura mater, mannitol (1 g/kg) was rapidly infused before dural opening (26). Antiedema treatment (dexamethasone) was continued in all cases in the early postoperative period. In the postoperative period, pulmonary embolism developed in 2 (1.5%) patients, wound infection in 7 (5.3%), and cerebrospinal fluid fistula in 6 (4.5%). In the postoperative period, 3 (2.3%) patients were lost to follow-up because of various complications during the hospitalization period.

Total resection was performed in 25 (19%) patients, gross total resection in 83 (63.3%), subtotal resection in 18 (13.7%), and biopsy in 5 (3.8%) (Figs. 1–3). The patients were discharged after the improvement of the existing preoperative complaints and the wound had healed. The result of histopathological examination revealed that the most common tumor origin was the lung (n=63, 48%) (Table 1). PET was performed after histopathological diagnosis to detect other possible spread of the primary tumor. Subsequently, chemotherapy and radiotherapy treatments were planned.

<table>
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<tr>
<th>Characteristics</th>
<th>Number</th>
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<tr>
<td>Sex</td>
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<tr>
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Eight (6.1%) patients died within the first 3 months because of intracranial and primary tumor complications, and 25 (19%) patients were lost to follow-up. The mean overall survival was 5.3 (range, 1–36) months during the follow-up period, and 12 (9.1%) patients had a recurrence and undergo surgery again.

**REPRESENTATIVE CASES**

**Case #1:**
A 70-year-old male patient was admitted to our clinic with balance disorder. Neurological examination is normal. He has a history of surgery for gastric adenocarcinoma. On MRI, a 3.5x4 cm mass lesion was detected in the right cerebellar hemisphere. Gross total resection was obtained in the patient who was operated microscopically (Figure 1). Pathological examination was compatible with gastric adenocarcinoma. The patient was discharged on the 5th postoperative day and was referred to radiotherapy. The patient died in the 11th postoperative month due to complications arising from the gastrointestinal system.

**Case #2:**
A 69-year-old male patient applied to our clinic with complaints of headache and dizziness. In her neurological examination, her right upper and lower extremities were 2/5 paresis. He has a history of right nephrectomy for renal cell carcinoma. Cranial MRI revealed a 3x4 cm mass in the left parietal region. The patient was operated using endoscopic methods and thoracoport. The tumor was grossly excised (Figure 2). Pathological examination was consistent with renal cell carcinoma metastasis. The patient was discharged on the 5th postoperative day and received whole brain radiotherapy. He died at the postoperative 14th month due to non-intracranial complications.

**Case #3:**
A 61-year-old male patient applied to our clinic with the complaint of dizziness. In her neurological examination, tandem gate was unsuccessful, but other examination findings were normal. There was no significant pathology in his history. Cranial MRI revealed a 3x2.5 cm mass in the left cerebellar hemisphere. The patient was operated with microscopic methods. The tumor was grossly excised (Figure 3). Pathological examination was compatible with high-grade B-cell lymphoma. The patient was discharged on the 4th postoperative day and...
received whole brain radiotherapy. He died 6 months postoperatively due to complications related to multiple intracranial involvements.

DISCUSSION

Metastasis is the most common type of intracranial neoplasm (39). Its incidence is 10 times higher than that of primary brain tumors and occurs in approximately 25% of all patients with cancer (24). This number is expected to increase as more patients develop cancers, imaging technology becomes more common, and there was no progress in finding methods to prevent cancers from metastasizing to the brain (11).

Brain metastases are most commonly detected between ages 50 and 70 years (40). In this study, the mean patient age was 54.9 years.

The lung is the most common site of origin among all brain metastases. Generally, this is followed by the breast, gastrointestinal tract, lymphomas, renal tumors, and other tumors (5,31,35). Brain metastases are rare in sarcomas and are more common in undifferentiated sarcomas with previous metastases. The incidence of sarcoma metastasizing to the brain is <1% (14). In our study, metastases originating from lung cancer (n=63, 48%) were found most frequently.

Surgery, Whole Brain RT (WBRT), stereotactic radiosurgery, and chemotherapy are treatment options for brain metastasis (12,36). Many factors such as age, performance status, number of lesions, and treatment type affect the treatment modality. Aggressive treatment helps improve overall survival. Modi et al. reported that resection of metastatic lesions prolongs overall survival (27).

Surgery is an effective treatment modality in increasing survival. Surgical treatment is recommended, especially in brain metastases with large-scale, perilesional edema, neurologic deficits, and unknown histopathological diagnosis (28). Surgical treatment not only makes adjuvant therapy more effective but also provides benefits such as the alleviation of the mass effect, symptomatic improvement, and histopathological evaluation (21). However, it is more effective in single lesions (7). Solitary metastatic lesions have sharp margins and are amenable to surgical resection (23).
Surgery for deep-seated lesions is challenging and postoperative morbidity risk is higher. Such lesions are usually treated to provide palliation \(^{(11,21)}\). Minimally invasive approaches are used to reduce postoperative mortality and morbidity, especially in the surgical intervention of deeply located lesions, but studies on this subject are limited \(^{(13,23)}\). Hong et al. demonstrated the use of minimally invasive methods in 20 patients with deeply located metastatic lesions \(^{(23)}\). Many studies use tubular retractors for minimally invasive approach \(^{(6,21,23)}\). In this study, we also performed tumor resection with endoscopic methods by placing a thoracoport in 20 (15.2%) patients, especially in deeply located cases.

Bakhsheshian et al. reported gross total resection in 80% of 25 patients with deeply located metastatic brain tumors \(^{(6)}\). In the present study, total resection was performed in 25 cases (19%), gross total resection in 83 (63.3%) cases, subtotal resection in 18 (13.7%) cases, and biopsy in 5 (3.8%) cases.

WBRT is a frequently preferred treatment for brain metastases. The role of chemotherapy in the treatment of brain metastases is controversial because of the blood–brain barrier. Most authors argue that most chemotherapeutic drugs are unable to cross the blood–brain barrier; thus, the efficacy of chemotherapy in brain metastatic disease is low or nonexistent \(^{(18)}\). In cases with more than one metastasis, WBRT provided less recurrence in the postoperative period and longer survival than the group that did not receive radiotherapy \(^{(18)}\). In the present study, all \((n=98, 74.8\%)\) patients who were followed up in the postoperative period received WBRT.

Five (10%) new cases of neurologic deficits, one case of stroke (2%), and one case (2%) of exitus were reported after resection in a study that included deeply located metastatic brain tumors \(^{(21,23)}\). In another study, new-onset motor weakness and deep-vein thrombosis were reported in one (4%) patient \(^{(6)}\). In this study, pulmonary embolism occurred in 2 (1.5%) patients, wound infection in 7 (5.3%), CSF fistula in 6 (4.5%), and exitus in 3 (2.3%).

Patients with a single metastatic lesion had significantly higher survival rates than patients with multiple metastases \(^{(16)}\). In this study, multiple brain metastases were detected in the intracranial region in 16 (12.2%) patients, and 87.5% \((n=7)\) of the patients who died in the first 3 months after surgery were those with more than one metastasis.

Ekici et al. reported a mean survival of 6.7 months \(^{(16)}\). In the present study, the mean survival during the follow-up period was 5.3 months.

**CONCLUSION**

Brain metastases are an important cause of morbidity and mortality. The incidence, survival rates, and treatment modalities of brain metastases vary greatly according to the histopathological diagnosis of the primary tumor. Surgical intervention reduces intracranial pressure and eliminates tumor-related edema. Therefore, postoperative survival rates increase. In addition to surgical treatment, adjuvant WBRT reduces recurrence and increases survival in these cases. However, more clinical studies are needed to evaluate the efficacy of single or combined treatments in metastatic brain tumors.

**Ethical Approval:** This study was approved by the Scientific Research Ethics Committee of the Turkish Republic Health Sciences University (No: 2020-304 / 30.06.2020).

**Conflict of interest:** There is no conflict of interest in our study.
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