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# Controversy of Surgical Intervention for Brain Metastases: Series of 27 Patients

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## Abstract

*Background:* The prevalence of brain metastases (BM) surpasses that of other intracranial neoplasms in adults. Surgical intervention for the management of brain metastases has led to considerable controversy. Patients exhibiting specific clinical characteristics may potentially achieve extended survival rates when undergoing resection as opposed to radiation therapy. Therefore, in the context of well-controlled systemic cancer, surgical intervention is strongly recommended for patients who have a single metastatic lesion. The combination of positron emission tomography and computed tomography (PET/CT) is a frequently utilized imaging technique in the field of oncology. It offers a distinct blend of cross-sectional anatomical data from CT and metabolic information from PET scans.

*Aim of Study:* To determine the efficacy of surgical excision of a single metastatic lesion and the diagnostic performance of brain-included whole-body PET/CT in the identification and assessment of brain metastases, this retrospective study was conducted.

*Patients and Methods:* The study was conducted over a period of 24 months on 27 patients having extra-cranial malignancies with single brain metastases with preoperative brain-included whole-body PET/CT.

*Results:* Male were predominant (3:1), and bronchogenic carcinoma was the most frequently primary malignancy. Headache, fits, heaviness, and vomiting were the most obvious symptoms. Out of the total of 27 patients, 18 (67%) had brain metastases of unknown origin, whereas 9 (33%) had brain metastases from recognized source tumors. Following a comprehensive FDG-PET/CT scan that covered the brain, it was determined that 12 patients (44.4%) had bronchogenic carcinoma, 3 patients (11%) had renal cell carcinoma, and 3 patients (11%) had breast cancer.

*Conclusions:* Surgery is a highly successful option for managing tumors, especially in situations of single brain metastasis. It is a crucial component of the treatment plan for brain metastases. Whole-body FDG-PET/CT, including the brain, offers significant additional information for assessing patients who are suspected to have brain metastases (BM).

***Key Words:*** *Brain metastases – PET scan – Computed tomography.*

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## Introduction

**METASTATIC** brain cancer is a significant obstacle in the field of neurological treatment. Brain metastases will ultimately occur in around 10% to 30% of those with systemic cancer **[1-5].** As the technical and medicinal advancements improve the survival rates of various diseases, the occurrence of brain metastases is expected to rise. Historically, the existence of metastatic brain lesions has been seen as a highly unfavorable prognostic indicator for patients with systemic cancer, resulting in unaddressed neurological impairments and ultimately death **[6-10].** The present therapeutic approach for brain metastases relies significantly on an integrated approach of surgical intervention and radiation therapy, aiming to effectively manage the advancement of both localized and expansive metastatic condition. As surgical methods and imaging investigations continue to improve, surgery will become increasingly important in the treatment of metastatic brain tumors **[11-23].**

*Objective:*

This study was conducted to evaluate the efficacy of surgical removal of a single metastatic lesion and the diagnostic accuracy of whole-body PET/CT

***List of Abbreviations:***

PET : Positron emission tomography.
CT : Computerized tomography.
KPS : Karnofsky performance status scale.
BM : Brain metastasis.
MRI : Magnetic resonance imaging.
LMD : Leptomeningeal dissemination.
WBRT: Whole body radiotherapy.
FDG : Fluorodeoxyglucose.

scans that include the brain in detecting and assessing brain metastases.

## Patients and Methods

*Study design:* This retrospective study was carried out at Benha University Hospitals over a period of 24 months starting from April 2020 on 27 patients having extra-cranial malignancies with single brain metastases using PET/CT imaging which involves the brain and the entire body.

*Inclusion criteria:*

1- Patients with single brain metastasis.
2- Patients with brain-included whole-body PET/CT.
3- Patients with neurological symptoms.

*Exclusion criteria:*

1- Patients with multiple brain metastases.
2- Patients who are not fit for surgery.

*Patient population:* 27 patients with single brain metastasis were operated on for surgical excision. Clinical and radiographic features were reviewed to evaluate the preoperative fitness, surgical results and prognostic factors. Preoperative brain-included whole-body PET/CT was done to exclude other brain lesions and discover the primary pathology in undiagnosed cases.

*Preoperative work-up:* Every patient got a standard physical examination, as well as a comprehensive neurological assessment. Furthermore, a comprehensive assessment of the patient's medical history was conducted, including an evaluation of their experience with headaches, feelings of heaviness, numbness, and instances of seizures. (Table 1 and Diagram 1).

We conducted preoperative imaging, which consisted of contrast-enhanced magnetic resonance imaging (MRI) (Fig. 2) and whole-body positron emission tomography/computed tomography (PET/CT) including the brain (Figs. 1,3). MRI is widely available and has great spatial resolution, making it the primary method for evaluating metastatic brain tumors. MRI enables the differentiation between bone marrow (BM) and possible imitators that likewise exhibit nodular or ring enhancement. A Positron Emission Tomography (PET) scan employs a range of radioactive tracers that specifically target diverse metabolic and molecular processes. PET imaging can offer valuable supplementary data that enhances disease evaluation, particularly in circumstances where clinical uncertainty exists, or to rule out other brain lesions and identify the underlying cause in patients with uncertain diagnosis.

*Location of the tumor:*

We found that the tumor's site was frontal in eight cases, parietal in five cases, temporal in five cases, and posterior fossa in nine cases.

Table (1): Clinical symptoms in 27 patients with single brain metastasis.

| Symptoms | No. of patient |
|---|---|
| Headache | 12 |
| Heaviness | 14 |
| Fits | 11 |
| Numbness | 9 |

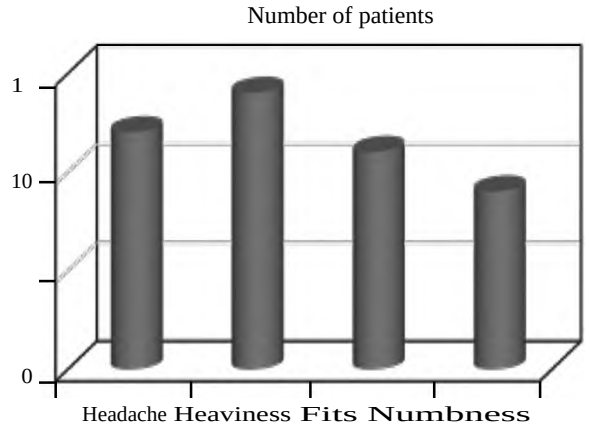


Diagram (1): Clinical symptoms in 27 patients with single brain metastasis.

*Operative note:* All studied cases underwent surgery under general anaesthesia, utilizing an operating microscope and microsurgical instruments. In our study, we operated on 12 patients in the supine position, 13 in the prone position, and 2 in the lateral position using a Mayfield pin fixation device.

*Surgical approach:*

We used various types of approaches, like the subfrontal approach in 3 cases, the bifrontal approach in 7 cases, the pterional approach in 8 cases, and the posterior fossa approach in 9 cases. In 10 cases, we used navigation to determine the location of deep-seated lesions.

The surgery's goal was to perform a complete microsurgical excision of a single brain lesion. We managed intraoperative complications such as brain oedema, bleeding, and brain herniation.

*Postoperative follow-up:*

We performed an early postoperative CT brain scan to show the excised tumor, brain edema, and early postoperative tumor bed hemorrhage (Fig. 4). We followed patients clinically first in our hospital, and then in an outpatient neurosurgery clinic. We collected and reviewed all intraoperative and postoperative findings, along with any new complaints.

Five cases had postoperative complications, including two cases of postoperative Hemorrhage, two cases of postoperatively worsening motor power, and one case of postoperative fits, all of which improved after six months with medical treatment and physiotherapy (Table 2).

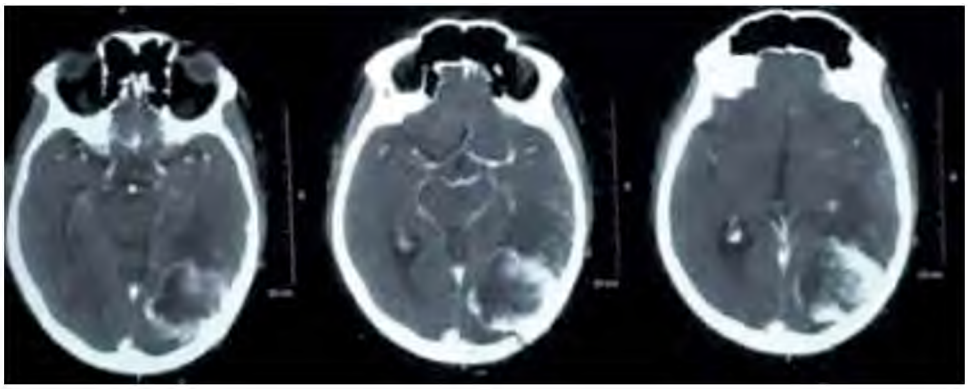

Fig (1): Case (1) Preoperative CT brain with contrast showing left occipital metastasis.

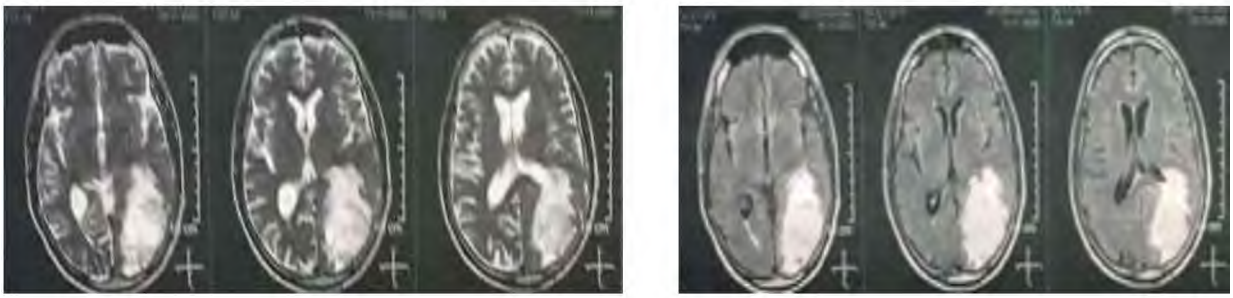

Fig (2): Case (1) Preoperative MRI brain showing left occipital metastasis.

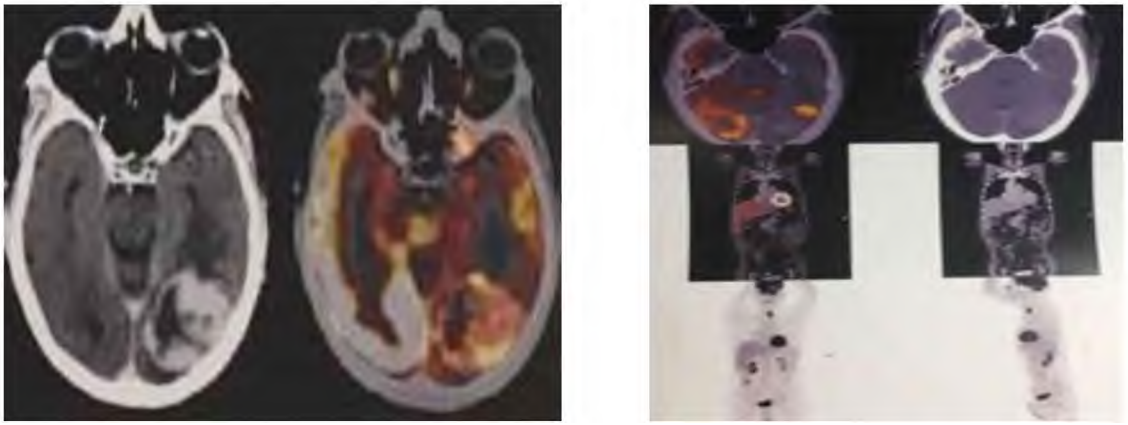

Fig (3): Case (1) Preoperative PET scan.

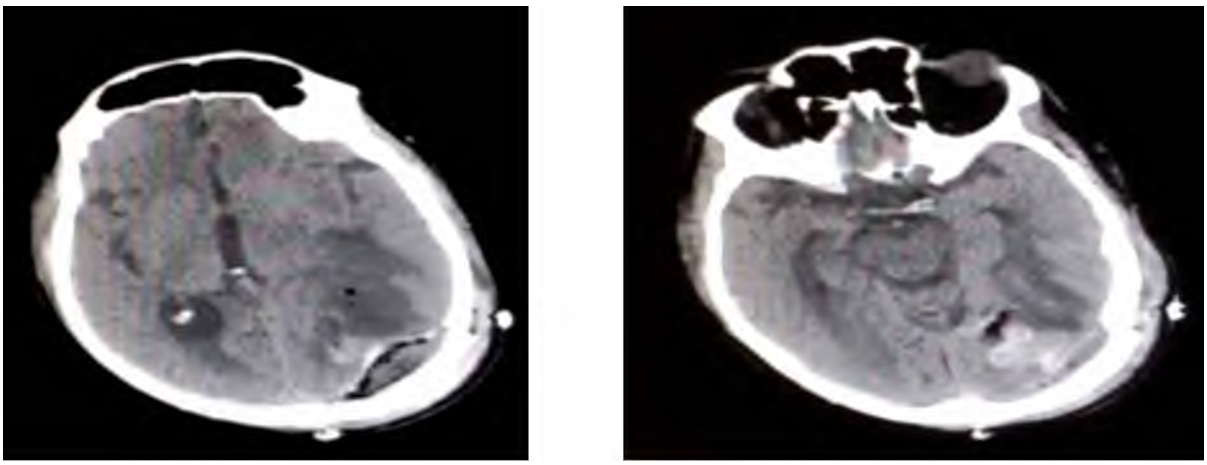

Fig (4): Case (1) Postoperative CT brain.

Table (2): Postoperative complications.

| Postoperative haemorrhage | Postoperative worsened motor power | Postoperative fits |
|---|---|---|
| 3 cases | 3 cases | 2 cases |

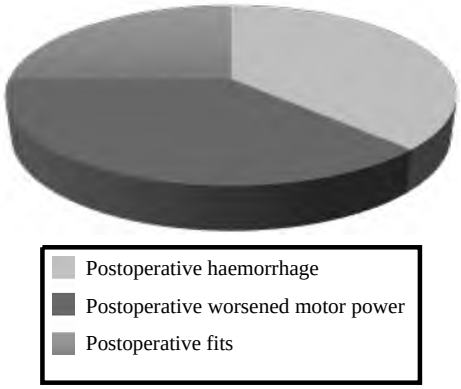


Diagram (2): Postoperative complications.

The Karnofsky performance status (KPS) is considered the primary prognostic factor influencing prognosis (Fig. 5). Studies have demonstrated that individuals who have a low-performance status at the time of diagnosis have a more unfavorable prognosis in comparison to those with a higher Karnofsky Performance Status (KPS). Another factor influencing the prognosis **[5].**

| | |
|---|---|
| - Able to carry on normal activity and to work; no special care needed. | 100 - Normal no complaints; no evidence of disease. |
| | 90 - Able to carry on normal activity; minor signs or symptoms of disease. |
| | 80 - Normal activity with effort; some signs or symptoms of disease. |
| - Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed. | 70 - Cares for self; unable to carry on normal activity or to do active work. |
| | 60 - Requires occasional assistance, but is able to care for most of his personal needs. |
| | 50 - Requires considerable assistance and frequent medical care. |
| - Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly. | 40 - Disable; requires special care and assistance. |
| | 30 - Severely disabled; hospital admission is indicated although death not imminent |
| | 20 - Very sick; hospital admission necessary; active supportive treatment necessary. |
| | 10 - Moribund; fatal processes progressing rapidly. |
| | 0 Dead. |

Fig. (5): Karnofsky performance status scale (Crooks, V, Waller S, et al. **[5]**.

The management of brain metastases is contingent upon many prognostic variables. Anticipated factors contributing to a more unfavorable disease prognosis include advanced age (over 65 years), poor functional level upon diagnosis [Karnofsky Performance Score (KPS) below 70], presence of many metastatic lesions, and untreated original malignancy, among other factors **[5].**

The Karnofsky Performance Scale Index allows for the categorization of patients according to their level of functional disability. This tool may be utilized to evaluate the efficacy of various treatments and determine the prognosis of specific patients. Survival rates for the most severe diseases are negatively correlated with lower Karnofsky scores.

The Karnofsky performance status scale establishes the parameters for rating (%).

## Results

We conducted surgical interventions on a total of 27 individuals who were diagnosed with brain metastases in our research. Our department accepted a total of 27 individuals, consisting of 20 males and 7 females, throughout the period from 2018 to 2020. In all instances, we conducted surgical excision en bloc. The mean age was 50 years with a range of 25 to 75 years.

There were six patients who had multiple lesions. We discarded patients who underwent Stereotactic Radiosurgery (SRS) or Whole Brain Radiation Therapy (WBRT) prior to surgery. Out of the total of 27 instances, a primary tumor diagnosis was established in 8 cases, however in the other 19 cases, the initial clinical presentation of cancer was in the form of brain metastases.

The histopathology of the lesions is presented in Table (3). The majority of brain metastases originated from the lung (15), with breast (6), kidney (4), and melanoma (2) being the subsequent sources.

Table (3): Histology and number of patients.

| Histology | Patients |
|---|---|
| Lung | 15 |
| Breast | 6 |
| kidney | 4 |
| Melanoma | 2 |

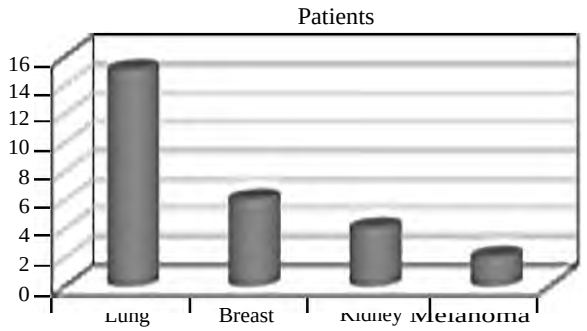


Diagram (3): Histology and number of patients.

Table (4) indicates that metastasis was detected in the posterior fossa (9 cases), frontal lobe (7 cases), parietal lobe (5 cases), occipital lobe (2 cases), and temporal lobe (2 cases).

Table (4): Localizations of lesions and number of cases.

| Localizations | Number of cases |
|---|---|
| Posterior fossa | 9 |
| Frontal | 7 |
| Parietal | 5 |
| Occipital | 4 |
| Temporal | 2 |

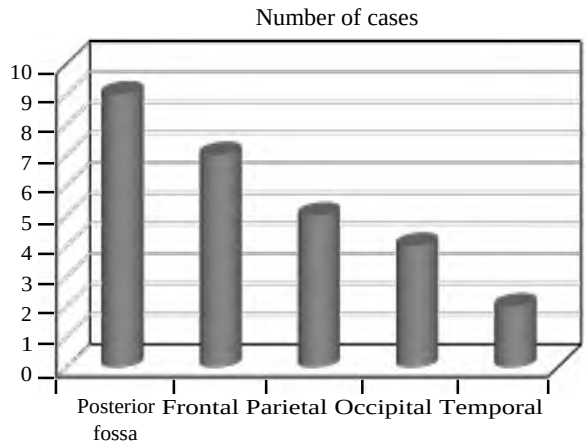


Diagram (4): Localizations of lesions and number of cases.

Upon admission, we conducted a calculation of the Karnofsky Performance Scale (KPS), yielding an average score of 78.5. The mortality rate during the perioperative period was less than 2.5%. After the surgical removal of tumors, oncologists chose patients for several supplementary medicinal interventions. More precisely, a total of 16 patients underwent both whole-brain radiation treatment (WBRT) and chemotherapy, whereas 5 patients exclusively received WBRT and 3 patients alone underwent chemotherapy. Three individuals were either untreated or provided with palliative care. We contemplated pursuing the follow-up until June 2020. The median survival period was 8 months.

We performed a preoperative PET scan in all cases to assess the presence of other brain lesions and other extracranial lesions, which can affect the prognosis of surgery.

Complete surgical removal of a single brain metastasis has a significant effect in enhancing the survival rate and reducing the likelihood of recurrence. Effective control of local recurrence is a crucial component of brain metastasis care. Out of the resected lesions, a significant 46% later had recurrence. In our investigation, we observed recurrence in 10 instances. The resection approach has a substantial influence on the rate of local recurrence. Researchers have discovered that tumors that are removed in separate pieces, without breaking the tumor capsule, have a recurrence rate that is twice as high compared to tumors that are removed as a whole (en bloc circumferential resection).

Postoperative follow-up showed complications in 8 cases in the form of deterioration of motor power in 3 cases, postoperative hematoma in 3 cases, and fits in 2 cases (Table 5).

Table (5): Postoperative complications.

| Postoperative complication | Number of cases |
|---|---|
| Deterioration of motor power | 3 |
| Hematoma | 3 |
| Fits | 2 |

## *Discussion*

Our study revealed a male predominance, with a male-to-female ratio of 20:7 and a mean age of 50 years, similar to the findings of Manuela Caroli and Andrea Di Cristofori in June 2011 *[11]*.

Grading systems, like the KPS, do not include patients' neurological problems *[5]*. For instance, the presence of substantial brain swelling leading to increased intracranial pressure causes a progressive rostrocaudal deterioration. This syndrome is associated with a decrease in KPS. Surgical debulking improves the Karnofsky Performance Status (KPS) by reducing pressure on important functional structures such the corticospinal tract, Broca's region, or Wernicke's area, leading to improvement in neurological condition. In addition, surgical decompression can effectively address issues related to the ascending reticular activating system, hence providing assistance to those experiencing confusion or comatose states, particularly those with a preexisting poor Karnofsky Performance Status (KPS) prior to the surgical intervention.

In our study, we calculated the preoperative KPS at admission; the average KPS was 78.5, a good indicator for the postoperative outcome, as reported in the June 2011 study by Manuela Caroli and Andrea Di Cristofori *[11]*.

Another issue lies in accurately identifying the location of metastatic lesions. Supratentorial lesions give rise to many clinical issues and cause several brain dysfunctions. Moreover, posterior fossa tumors present two significant challenges: They give rise to life-threatening diseases and are linked to a substantial risk of leptomeningeal dissemination (LMD). Our analysis identified nine instances of posterior fossa metastases, which emerged as the predominant site for brain metastases. However, according to a study conducted by Ostrom QT, Wright CH, and Barnholtz-Sloan JS *[23]*, supratentorial metastases were shown to be more prevalent.

Therefore, surgery is a successful approach that considers both prognostic markers and clinical state. In our view, KPS functions as a reliable measure of performance status. However, it has to be reassessed and adjusted to accommodate reversible neurological disorders. The preoperative Karnofsky Performance Scale (KPS) varies from the postoperative KPS in that the surgical procedure improves neurological impairments, edema, and seizures, resulting in a conclusive histology diagnosis. Oncological patients have the potential to develop a primary brain tumor or another kind of neoplasia. Patchell and colleagues have demonstrated that 11% of patients with brain metastases may exhibit nonmetastatic abnormalities, such as an abscess or a primary brain tumor.

The present study examined the efficacy of FDG-PET/CT as a diagnostic modality. The sensitivity and specificity of the test were reasonably good, with values of 78.1% and 92.6% respectively. There was no discernible variation in performance when compared to utilizing CECT alone. In accordance with our results, Hjorthaug et al. **[2]** conducted a study on lung cancer patients who were believed to have brain metastases (BM). They used FDG PET/CT as a method to prioritize individuals for further imaging. The study demonstrated that the PET/CT had a sensitivity of 72%, specificity of 100%, and a positive predictive value (PPV) of 97%.

*Conclusion:*

From our perspective, surgery remains the most efficient treatment choice for solitary brain metastasis. This is because it provides a conclusive histological diagnosis, alleviates epilepsy, and allows for rapid debulking of affected nervous structures. As a result, it improves the Karnofsky Performance Status (KPS) and enhances the overall prognosis.

Radiotherapy alone is not sufficient to improve these functions. However, it remains an effective treatment for lesions without a clear histological diagnosis, with minimal edema, under epilepsy medication, or with neurological abnormalities. Ultimately, we advocate for the development of more precise scoring grades, namely a grading system that considers these patients' reversible clinical situations.

The brain-included whole-body FDG-PET/CT is an important tool for assessing patients with suspected BM. It provides additional information that can help guide treatment decisions and serve as a preliminary diagnosis.

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# جدل التدخل الجراحى للأورام الثانوية فى الدماغ: سلسلة من ٢٧ مريضًا

**الخلفية:** انتشار الأورام الثانوية فى الدماغ يفوق تلك الأورام الأخرى فى الجمجمة عند البالغين. أدى التدخل الجراحى فى إدارة الأورام النخاعية فى الدماغ إلى جدل كبير. يمكن للمرضى الذين يظهرون خصائص سريرية محددة تحقيق معدلات حياة ممتدة بشكل محتمل عند إجراء الاستئصال بدلاً من العلاج الإشعاعى. لذلك، فى سياق سرطان النظامية المُضبَّطة بشكل جيد، يُوصى بشدة بالتدخل الجراحى للمرضى الذين يعانون من ورم ثانوى واحد.

**الهدف من الدراسة:** لتحديد فعالية استئصال الورم النخاعي الواحد وأداء التشخيص للفحوصات الطبية المشمولة بالدماغ بالكامل/التصوير بالتصوير المقطعى (PET/CT) فى تحديد وتقييم الأورام النخاعية فى الدماغ، تم إجراء هذه الدراسة الاسترجاعية.

**المرضى والطرق:** تمت الدراسة على مدار ٢٤ شهرًا على ٢٧ مريضًا يعانون من أورام خارج الجمجمة مع وجود ورم نخاعى واحد وخضعوا لفحص طبى مشمول بالدماغ بالكامل/التصوير بالتصوير المقطعى قبل الجراحة.

**النتائج:** كان الذكور هم الأكثر انتشارًا بنسبة (٣:١)، وسرطان الرئة كان الورم الخبيث الأساسى الأكثر شيوعًا. كانت الصداع والنوبات والثقل والقيء هى الأعراض الأكثر وضوحًا. من بين مجموع المرضى البالغ ٢٧ مريضًا، كانت لديهم أورام نخاعية فى الدماغ من مصدر غير معروف ١٨ مريضًا (٦٧٪)، فى حين أن ٩ مرضى (٣٣٪) كانت لديهم أورام نخاعية فى الدماغ من أورام معروفة. بعد إجراء فحص شامل بالطريقة الموجبة للإصدار الإيجابى/التصوير بالتصوير المقطعى (FDG–PET/CT) الذى شمل الدماغ، تبين أن ١٢ مريضًا (٤٤,٤٪) كانوا يعانون من سرطان الرئة، و٣ مرضى (١١٪) كانوا يعانون من سرطان الكلية، و٣ مرضى (١١٪) كانوا يعانون سرطان الثدى.

**الخلاصة:** الجراحة هي خيار ناجح للغاية لإدارة الأورام، خصوصا في حالات الورم الثانوى الواحد. إنها جزء أساسى من خطة العلاج للأورام النخاعية فى الدماغ. يقدم الفحص بالطريقة الموجبة للإصدار الإيجابى/التصوير بالتصوير المقطعى (FDG–PET/CT) للجسم بأكمله، بما فى ذلك الدماغ، معلومات إضافية هامة لتقييم المرضى الذين يشتبه فى إصابتهم بأورام ثانوية فى الدماغ.