Epidemiological Analysis of Cancer Patients Diagnosed with Cranial Metastasis at Initial Presentation

Ercan Kaya[1]

[1]Kartal Dr. Lutfi Kirdar Education and Research Hospital, Istanbul, Turkey

A B S T R A C T

Introduction: Metastatic lesions are the most common brain tumors, comprising 52% of all cases. Early diagnosis is crucial to improve patient outcomes, but many cases remain undiagnosed until advanced stages. This study aimed to investigate the characteristics of patients diagnosed with brain metastasis concurrently with their primary malignancy, examine prognostic factors, and compare these findings with brain metastases of known primary origins.

Method: A retrospective analysis was conducted on 184 patients between 18-80 years diagnosed with brain tumors between January 2018 and January 2019. Patient data were collected from clinical records, and statistical analyses were performed using SPSS 26.0.

Results: Out of the total patients, 43% were diagnosed brain metastases. Among these, 33% had no known primary malignancy at diagnosis. In this group, 92.3% were over 50 years old, and 77% were male. The most frequent primary cancer was lung cancer (81%). Males had an average time to metastasis diagnosis approximately twice as long as females. A higher incidence of metastasis correlated with a lower Karnofsky Performance Score, indicating reduced operability and quality of life.

Conclusion: Early diagnosis is critical to improving outcomes. Routine cranial imaging for patients over 50 may aid in early intervention.

Keywords: Brain Tumor, Unknown Primary Malignancy, Brain Metastasis

A R T I C L E   I N F O

INTRODUCTION

Metastatic lesions are the most common brain tumors, comprising 52% of all cases. Approximately one-third of systemic cancer patients develop brain metastases, often due to the improved survival rates from systemic therapies and the inability of certain chemotherapeutic agents to penetrate the blood-brain barrier.[1-3]

Brain metastases typically spread hematogenously from the primary tumor, often localizing in gray and white matter due to the obstruction of tumor emboli in the brain's vascular structures. Although well-circumscribed, they may exhibit microscopic infiltration into the surrounding parenchyma, contributing to postoperative recurrence. Common primary malignancies include lung, breast, skin, kidney, and colorectal cancers, with lung cancer being the leading cause, responsible for 44-50% of cases. [4–7]

Patients often present with symptoms such as headaches, vomiting, memory problems, seizures and neurological deficits.[7,8] Approximately 15% of these patients have no prior cancer diagnosis, and their diagnosis is first established through cranial metastasis.[9] Imaging techniques like MRI, CT, and PET scans are vital for diagnosis, while biopsy remains the gold standard.[10]

Treatment modalities include corticosteroids, surgical intervention, whole-brain radiotherapy (WBRT), stereotactic radiosurgery (SRS), systemic chemotherapy, biological agents, and hormonal therapies, often combined. However, prognosis is generally poor. Critical prognostic factors include a Karnofsky Performance Score (KPS) above 70, solitary brain metastasis, absence of extracranial metastases, controlled primary malignancy, age below 65, and preserved cognitive function.[11]

This study aims to analyze the characteristics of patients diagnosed with cranial metastasis as their initial cancer presentation. Often, asymptomatic malignancies remain undetected until they present with advanced stages, emphasizing the importance of early diagnosis and the need for research into, screening protocols.

METHODOLOGY

This study included 184 patients aged between 18 and 80 who presented to neurosurgery department between January 1, 2018, and January 1, 2019, and were diagnosed with brain tumors for the first time. All patients' examination and hospitalization records were retrospectively reviewed in detail. Among the patients who underwent surgery, the mass in the brain of the patients whose pathology reports showed metastasis, and among the patients who did not undergo surgery, the mass in the brain of the patients with known primary malignancy or whose additional examinations (abdominal and thorax CT, PET CT, bone scintigraphy) showed a primary focus were considered as metastasis.

Statistical analysis was performed using SPSS 26.0. Findings were expressed as frequencies and percentages. The normality of continuous variables was assessed using the Kolmogorov-Smirnov test. Categorical variables were compared using the Chi-square test, independent samples t-test, one-way ANOVA, and post-hoc tests, while the Spearman test was used to analyze correlations between continuous variables. A p-value of <0.05 was considered statistically significant.

RESULTS

Out of the 184 patients included in the study, 105 (57.1%) were diagnosed with primary brain tumors, while 79 (42.9%) were diagnosed with brain metastases. Among the patients with metastases, 53 (67.1%) had a known primary malignancy before the diagnosis, whereas 26 (32.9%) received their initial diagnosis through brain metastasis.

The distribution of brain lesions according to gender was balanced for both primary brain tumors and metastases with known primary diagnoses, showing no significant difference. However, among patients with newly diagnosed metastases, 77% were male, and only 23% were female (p<0.05).

Similarly, when examining the time since primary diagnosis, females received their diagnoses significantly sooner than males. In patients with known primary malignancies, males were diagnosed with metastases on average at 25.4 months, while females were diagnosed at 12.5 months (p<0.05). (Table 1)

Table 1: Evaluation of the incidence of brain metastases according to the age parameter of 50 years and comparison with glial tumours

	Brain metastases (%)	Glial tumors (%)
5th decade and earlier	7 (9)	42 (40)
6th decade and later	72 (91)	63 (60)

Comparing patients above and below 50 years of age in terms of KPS, operability status, and presence of extracranial metastases revealed that patients over 50 were disadvantaged in all three aspects (p<0.05).

Among patients diagnosed with brain metastases, 45 (57%) had primary lung cancer. Among lung cancer types, adenocarcinoma was the most common at 44.4%. (Table 2)

Table 2: Location and frequency of primary malignancy in newly diagnosed patients

Location	Cases (%)
Lungs	21 (80.8)
Stomach	3 (11.5)
Colon	1 (3.8)
Ovaries	1 (3.8)

No significant relationship was found between the solitariness or multiplicity of metastases, localization, and the origin of the primary malignancy. Additionally, although there was no significant difference between the time of primary diagnosis and the number of extracranial metastases, an increase in metastasis numbers was correlated with the delay in diagnosis.

A negative correlation was observed between the number of brain metastases and KPS and between the number of extracranial metastases and KPS (p<0.05). The KPS tended to decrease as the number of brain or extracranial metastases increased.

KPS was considered among the indication criteria when making surgical decisions for patients with metastases. A KPS below 70 indicated that surgery should be avoided. In solitary metastases, 6.2% of patients had a KPS below 70; in multiple metastases, this rate was 22.6% (p<0.05).

DISCUSSION

This study aimed to investigate the characteristics of patients who received their primary cancer diagnosis concurrently with brain metastasis and to explore the differences and relationships between primary brain tumors and metastases with known primary origins.

Our findings indicate that the frequency of metastasis in patients diagnosed with brain tumors was 43%, which is lower than expected. This rate may be attributed to the exclusion of oncology clinics during sample selection, where a substantial number of brain metastasis diagnoses occur, and patients are treated with SRS or WBRT without surgical intervention. The higher frequency of unknown primary metastases, nearly double the rates reported in many studies, could be due to societal reluctance to seek medical attention, underestimation of symptoms, and consequently delayed diagnoses. Additionally, the high proportion may result from the predominance of asymptomatic, especially lung cancer-related malignancies.

The study highlights the significance of the 50-year age threshold, aligning with Barnholtz-Sloan et al.'s findings.[12] Metastasis frequency increases markedly in patients over 50 across almost all cancer types, except for a balanced distribution in breast cancer regions. Alongside the increased frequency, the rate of multi-organ metastases rises, complicating the control of the primary disease and maintaining a high KPS, thereby reducing expected survival and quality of life.

The higher proportion of known primary malignancies at the time of metastasis diagnosis in females compared to males is likely due to breast cancer. Breast cancer metastases are often detected through self-examination, supported by public awareness campaigns, leading to earlier diagnoses and longer intervals between primary and metastasis diagnoses. Conversely, other malignancies like lung cancer may remain asymptomatic until advanced stages, resulting in a higher incidence of concurrent primary and metastasis diagnoses.

Among lung cancer types, adenocarcinoma was the most frequent source of metastases (44%), contrary to some studies that report small cell carcinoma as the predominant source. However, studies like that of Ziyal et al. have also identified adenocarcinoma as a more common metastatic source.[13]

In patients with multiple metastases, surgical removal of all metastases showed no survival benefit compared to solitary metastasis resections. Therefore, when multiple metastases are present, surgery should be considered only if all metastases are resectable, except in severe neurological symptoms or life-threatening masses. In our center, surgeries for patients with multiple metastases and low KPS are primarily performed for acute symptom relief and palliation, explaining the low surgery rates in these groups, consistent with the literature.

The negative correlation between the number of brain metastases and KPS suggests that multiple metastases impact motor and cognitive functions, reducing KPS as metastasis numbers increase. Delayed diagnosis leads to increased metastasis numbers and a subsequent decline in KPS.

As discussed, both the delay in primary diagnosis and metastasis diagnosis in older patients complicate disease control, shortening expected survival and diminishing quality of life. Prospective studies with larger samples are necessary to confirm these findings.

Considering that some cancers are asymptomatic and the frequency of unknown primary malignancies increases at metastasis diagnosis, the 50-year age threshold identified in our study is significant. Similar to routine screening recommendations for colonoscopy in individuals over 50 or ultrasound and mammography for breast cancer, routine cranial imaging may be beneficial for early detection of brain metastases.

CONCLUSION

This study provides valuable data on the diagnostic processes of cranial metastases and the prognostic factors utilized in these patients. Our findings are broadly consistent with existing literature, reaffirming the importance of early diagnosis and appropriate treatment methods. Therefore, more extensive and prospective studies are essential for a deeper examination of these findings and their effective integration into clinical practice.

REFERENCES

1. Gaspar L, Scott C, Rotman M, et al. Recursive partitioning analysis (RPA) of prognostic factors in three Radiation Therapy Oncology Group (RTOG) brain metastases trials. Int J Radiat Oncol Biol Phys. 1997;37(4):745–51.

2. Lang FF, Wildrick DM, Sawaya R. Management of cerebral metastases: the role of surgery. J Moffitt Cancer Cent. 1998 Mar; 5(2):124–9.

3. Youmans JR, Winn HR. Youmans neurological surgery. Vol. 2. Philadelphia: Elsevier/Saunders; 2011. p. 3342–61.

4. Lippitz B, Lindquist C, Paddick I, et al. Stereotactic radiosurgery in the treatment of brain metastases: the current evidence. Cancer Treat Rev. 2014;40(1):48–59.

5. Matsuo T, Shibata S, Yasunaga A, et al. Dose optimization and indication of linac radiosurgery for brain metastases. Int J Radiat Oncol Biol Phys. 1999;44(5):1069–73.

6. Wowra B, Muacevic A, Tonn JC. Quality of radiosurgery for single brain metastases with respect to treatment technology: a matched-pair analysis. J Neurooncol. 2009;94(1):69–77.

7. Wang ZZ, Yuan ZY, Zhang WC, et al. Brain metastasis treated with Cyberknife. Chin Med J (Engl). 2009 Aug 20;122(16):1847-50.

8. Murai T, Ogino H, Manabe Y, et al. Fractionated stereotactic radiotherapy using CyberKnife for the treatment of large brain metastases: a dose escalation study. Clin Oncol (R Coll Radiol). 2014;26(3):151–8.

9. Brem S, Panattil JG. An era of rapid advancement: diagnosis and treatment of metastatic brain cancer. Neurosurgery. 2005;57(5 Suppl)–S10.

10. Young RJ, Sills AK, Brem S, et al. Neuroimaging of metastatic brain disease. Neurosurgery. 2005;57(5 Suppl)–S16.

11. Lagerwaard FJ, Levendag PC, Nowak PJ, et al. Identification of prognostic factors in patients with brain metastases: a review of 1292 patients. Int J Radiat Oncol Biol Phys. 1999;43(4):795–803.

12. Barnholtz-Sloan JS, Sloan AE, Davis FG, et al. Incidence proportions of brain metastases in patients in the Metropolitan Detroit Cancer Surveillance System. J Clin Oncol. 2004; 22(14): 2865–72.

13. Ziyal İM, Müslüman M, Türkmen CS, et al. The metastatic brain tumors. Med Bull Sisli Etfal Hosp. 1997;31(3):43–8.