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A Rare Case of Extracranial Metastatic Glioblastoma: Lung Infiltration as an Uncommon Presentation

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Abstract

Background: Glioblastoma is the most prevalent and aggressive primary malignant brain tumor, known for its rapid growth and local invasion. While it predominantly remains within the central nervous system, extracranial metastasis is extremely rare, involving the liver, lymph nodes, thorax, spleen, and bones. Thoracic involvement is often associated with the worst prognosis. **Aim:** This paper presents a unique case of lung metastasis from glioblastoma, highlighting the diagnostic challenges and clinical implications associated with this phenomenon. **Case Presentation:** A 54-year-old male presented with a 10-day history of worsening headaches, dizziness, confusion, memory loss, and behavioral changes. A brain CT scan revealed a cystic mass in the left frontal lobe, raising suspicion of malignancy. A chest CT scan showed an irregular cavitary mass in the right lung. Surgical resection of the brain mass confirmed glioblastoma. Transthoracic fine-needle aspiration biopsy of the lung mass revealed metastatic glioblastoma cells. Immunohistochemical analysis indicated high Ki-67 proliferation rates, confirming the aggressive nature of the tumor. Despite adjuvant chemotherapy and radiotherapy, the patient's condition deteriorated, and he succumbed to the disease nine months post-diagnosis. **Conclusion:** This case underscores the importance of thorough diagnostic evaluation in patients with brain masses to avoid misdiagnosis and inappropriate treatment. It highlights the potential for glioblastoma to metastasize beyond the central nervous system, facilitated by systemic circulation and lymphatic spread. Timely surgical intervention and comprehensive treatment strategies are crucial in managing glioblastoma and improving patient outcomes. Further research is needed to understand the mechanisms behind extracranial metastasis in glioblastoma.

Subject Areas

Neurology, Oncology, Surgery & Surgical Specialties

Keywords

Glioblastoma, Metastasis, Brain Neoplasms, Lung Neoplasms

1. Introduction

Glioblastoma (GBM) is the most prevalent and aggressive primary malignant tumor of the brain, characterized by rapid growth and a propensity for local invasion. While it predominantly spreads within the central nervous system, extracranial metastasis is exceptionally rare, occurring in only a small percentage of cases. The majority of documented extracranial metastases involve the liver, lymph nodes, thorax, spleen, and bones, with thoracic involvement often associated with the most dismal prognosis [1]-[3].

Due to the rarity of this condition, several knowledge gaps still exist in the literature, particularly concerning its rare metastasis patterns. There is limited understanding of the molecular and cellular mechanisms driving high rates of *in situ* recurrence and insufficient data on the pathways and factors that enable occasional extracranial metastasis. Additionally, there is a need for more detailed case studies and reports on extracranial metastasis to provide deeper insights into the condition's progression. Addressing these gaps could enhance the management and treatment of this condition, especially in its uncommon metastatic forms.

This paper presents a unique case of lung metastasis from glioblastoma, highlighting the diagnostic challenges and clinical implications associated with this phenomenon. With advancements in imaging and treatment modalities, there is potential for increased recognition of extracranial metastases, underscoring the need for vigilance in monitoring patients with GBM.

2. Case Presentation

A 54-year-old male patient presented to the emergency department with a 10-day history of progressively worsening headaches, dizziness, confusion, memory loss, and notable behavioral changes. His medical history was significant for a 30-year smoking habit but no prior diagnosis of neurological conditions.

Upon examination, neurological assessments revealed cognitive impairment and altered mental status. A computed tomography (CT) scan of the brain was performed, revealing a cystic mass approximately 3 cm in diameter in the left frontal lobe, accompanied by marked vasogenic edema and a solid component (**Figure 1**). These findings raised suspicion of a malignant process, and further imaging was warranted to assess for possible metastasis. A chest CT scan was conducted to evaluate any potential thoracic involvement, revealing an irregular cavitary mass measuring approximately 6 × 5 cm with a thickened wall located in the apical segment of the

right lung (Figure 1(E)). The imaging characteristics raised concerns about a possible metastatic lesion.

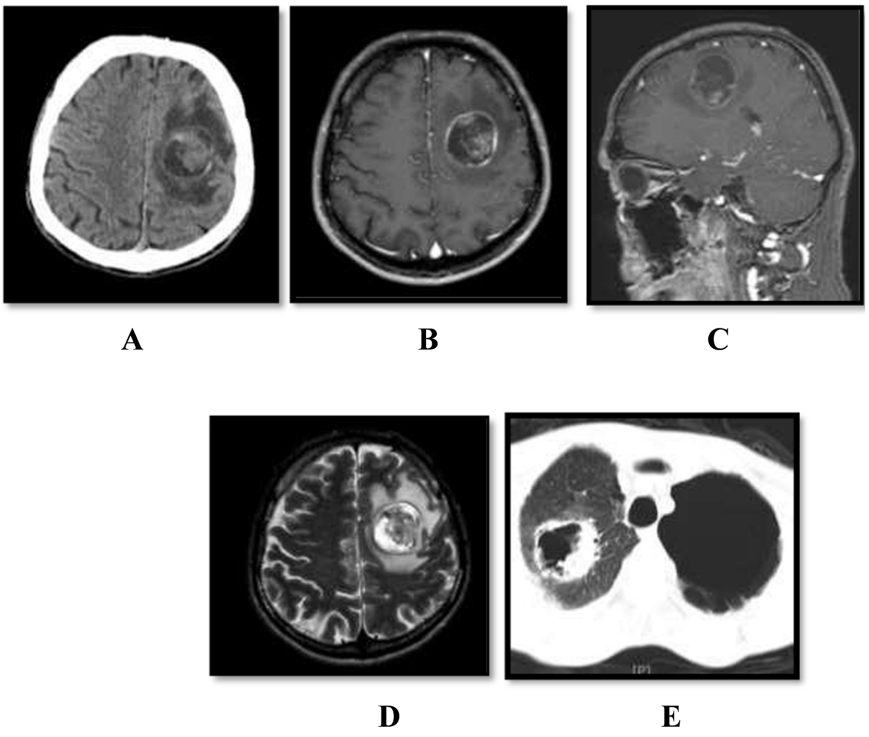

Figure 1. A 54-year-old male patient with a significant smoking history presented to the emergency department with progressive headaches, dizziness, memory loss, and behavioral changes. Brain imaging revealed a mass, and simultaneous examination detected a mass in the lung. Initially, it was suspected that the lung cancer had metastasized to the brain. (A) Brain CT scan; (B) MRI of the brain, T1 axial sequence; (C) MRI of the brain, T1 sagittal sequence; (D) MRI of the brain, T2 axial sequence; (E) CT scan of the thorax.

To establish a definitive diagnosis, the patient underwent surgical resection of the left frontal mass. Histopathological analysis of the excised tissue confirmed the diagnosis of glioblastoma. Subsequent tissue sampling from the right lung apex was performed via transthoracic fine-needle aspiration biopsy. Cytological evaluation of the samples revealed clusters of hyperchromatic neoplastic cells with small nucleoli and elongated oval nuclei set against a necrotic background.

Immunohistochemical analysis indicated that the tumor cells were negative for glial fibrillary acidic protein (GFAP) and oligodendrocyte transcription factor 2 (OLIG-2), with high Ki-67 proliferation rates suggesting aggressive tumor behavior. Additionally, the tumor cells were negative for cytokeratin and thyroid transcription factor-1 (TTF-1), ruling out the possibility of a lung tumor. When these findings were correlated with the patient's clinical history and imaging results, the diagnosis of lung metastasis originating from the glioblastoma was confirmed (Figure 2).

An inverted U-shaped incision was made, passing through the skin and subcutaneous tissue. The scalp was retracted. A 45 cm craniotomy was performed 1 cm

medial to the midline and 1 cm anterior to the coronal suture. Subsequently, the dura was opened and laid over the midline. The tumor, which was a gray-colored cystic structure, was totally excised. After the total excision of the tumor, hemostasis was achieved. The dura was repaired using galeal tissue to create a watertight duraplasty. The bone was secured back in place. After ensuring hemostasis, the layers were closed appropriately with a subcutaneous drain.

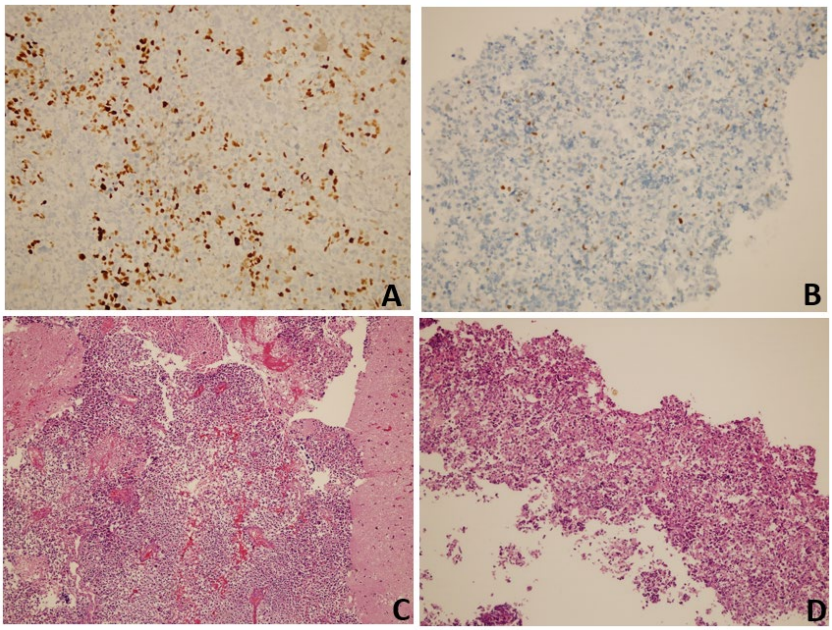

Figure 2. Cell block sections from the transthoracic needle aspiration (TTNA) biopsy of the right lung apex exhibit the same immunohistochemical characteristics as the brain tumor, including oligodendrocyte transcription factor 2 (OLIG-2) positivity. (A) Brain; (B) Lung; (C) Brain, high-grade glial tumor, H&E ×100; (D) Lung, cell block—malignant cytology, consistent with metastasis, H&E ×100.

Following surgical intervention, the patient was initiated on adjuvant chemotherapy and radiotherapy as part of a multidisciplinary treatment approach. Unfortunately, despite these interventions, the patient's condition deteriorated, and he succumbed to the disease 9 months post-diagnosis.

3. Discussion

This case presents a rare instance of simultaneous intracranial and pulmonary involvement in a patient with glioblastoma. Initially misdiagnosed as a thoracic malignancy, further investigation revealed that the brain glioblastoma had metastasized to the lung, highlighting the necessity of thorough pathological evaluation in similar cases.

In the literature, the mean age of glioblastoma diagnosis is typically around 62 years, with an average survival prognosis of approximately 11.6 months [4]. While glioblastoma is known for its rapid proliferation and local spread within the central nervous system, instances of extracranial metastasis remain exceptionally rare

[5]. Recent advances in treatment, particularly in chemotherapy and radiotherapy, have led to an increase in documented cases of extracranial spread, including metastases to the liver, lymph nodes, thorax, spleen, and bones [6]. Our findings are consistent with previous studies that have reported thoracic involvement in glioblastoma, which may manifest as nodular lesions within lung parenchyma or as pleural effusions [7] [8].

Table 1. Review the literature on extracranial metastases of extracranial metastatic glioblastomas.

No	Age/Sex	Primary Location	Metastatic Location	Diagnosis	Interval	Survival	Adjuvant Therapy
Index Case	54/M	L Frontal Lobe	Lung	GBM	0	9	Adjuvant chemotherapy and radiotherapy
1	65/M	R occipital lobe	Bones (femur, ilium, sacrum)	GBM	13	11	Concurrent radiochemotherapy
2	20/W	L temporal lobe	Lung, lymph gland	GBM	NS	NS	Chemotherapy (temozolomide)
3	48/W	L temporal lobe	Bone, lung, pleura, liver, mesentery	GBM	13	11	Concurrent radiochemotherapy
4	43/W	L frontal lobe	Lung, pleura	GBM	38	2	Concurrent radiochemotherapy
5	49/M	R temporal lobe	Lung, cerebrospinal fluid	GBM	12	10	Concurrent radiochemotherapy
6	56/W	R temporal lobe	Parotid, lymph node, lung	GBM	14.5	11	Concurrent radiochemotherapy
7	32/M	L basal ganglia region	Lymph nodes, bones (ribs, scapula, spine)	GBM	22	3	Concurrent radiochemotherapy
8	41/W	R temporal lobe	Lymphatic, spinal column	GBM	10	1	Concurrent radiochemotherapy
9	43/M	R temporal lobe	Multiple bone metastases	GBM	3	2	Radiotherapy
10	38/W	R temporal lobe	Lymph gland, bones	GBM	10	6	Concurrent radiochemotherapy
11	47/M	R temporal lobe	Scalp, lymph gland ribs, spine, liver, lungs	GBM	13	6	Concurrent radiochemotherapy
13	20/W	L temporal lobe	Lumbar vertebrae, appendages, and bilateral ilium, sternum	GBM	35	4	Concurrent radiochemotherapy
14	23/W	R parietal lobe	Thigh		10	16	Concurrent radiochemotherapy

Interval: Time from diagnosis of primary to diagnosis of metastasis in months; Survival: Survival after diagnosis of metastasis in months. R: Right; L: Left; M: Male; F: Female; NS: Not stated or not known; GBM: Glioblastoma.

The occurrence of extracranial metastasis in glioblastoma could be attributed to several factors, including the patient's advanced age and the aggressive nature of the tumor. The barriers typically hindering metastatic spread from the central nervous system—such as the lack of a lymphatic system in the brain, dense dura mater around intracranial vessels, and minimal stroma—may help explain the low

incidence of these metastases [7]. However, the simultaneous presentation of intracranial and thoracic lesions in our case suggests that the glioblastoma could infiltrate beyond its typical confines, possibly facilitated by systemic circulation and lymphatic spread during the advanced stage of the disease [9]. The stage of glioblastoma is a significant factor, with extracranial metastases typically emerging in the advanced stages of the disease [10].

According to the literature, nearly all cases of metastatic glioblastoma are linked to prior surgical interventions on the primary tumor [8] [9] (**Table 1**). The timing and manner of metastasis can often be traced to surgical seeding and/or meningeal spread [7]. However, in our presented case, both the brain mass and thoracic involvement were detected simultaneously, indicating that the spread was not attributable to surgical seeding, which emphasizes the importance of this case.

The strength of this case lies in its contribution to the understanding of glioblastoma's metastatic potential, particularly to the lung, and emphasizes the importance of biopsy for accurate diagnosis and appropriate treatment planning. However, the limitations include the single-case nature of the report, which may not be generalizable to the broader population of glioblastoma patients.

4. Conclusion

This case underscores the critical need for accurate diagnosis in patients presenting with brain masses, as misdiagnosis can lead to inappropriate treatment strategies that may diminish the patient's prognosis. Our findings indicate that when glioblastoma is identified, timely surgical intervention is essential, as it significantly influences survival outcomes. The dual presentation of the primary brain tumor and lung metastasis in our patient emphasizes the need for heightened awareness and further research into the mechanisms behind extracranial metastasis in glioblastoma.

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Data Availability Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval Statement

This study was conducted in Kartal Dr. Lutfi Kırdar Training and Research Hospital and the ethical approval was waived for case reports by the polices of the hospital.

Informed Consent

Informed consent was obtained from the participants to participate in the current study.

Conflicts of Interest

The authors declare no conflicts of interest.

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