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Early Pulmonary Metastasis After a Surgical Resection of Glioblastoma Multiforme. A Case Report

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Male, 66-year-old
Final Diagnosis: Glioblastoma multiforme • pulmonary metastases
Symptoms: Hemiplegia and aphasia • nausea • vomiting
Medication: —
Clinical Procedure: Bronchoscopy • craniotomy
Specialty: Critical Care Medicine • Pulmonology

Objective: Diagnostic/therapeutic accidents

Background: Glioblastoma multiforme is one of the most aggressive types of tumors that affect the central nervous system. It has an extremely high morbidity and mortality rate despite immediate treatment and advances in chemotherapy, radiotherapy, and surgery. In the natural history of the disease, extracranial metastases of glioblastoma multiforme are a rare complication that can be localized in the lungs, bone, liver, and lymph nodes.





Case Report: A 66-year-old male presented with pulmonary metastasis after the surgical resection of a primary glioblastoma multiforme tumor. Seventeen days after surgery while in the intensive care unit, the patient had leukocytosis with a predominance of neutrophils. An exploratory bronchoscopy evidenced a white lesion that prevented the visualization of the bronchus. Consequently, a sample was taken for pathological study that demonstrated pulmonary metastasis due to glioblastoma multiforme.

Conclusions: Surgical resection of the tumor can precipitate the appearance of extracranial metastases, especially pulmonary metastases.

MeSH Keywords: Brain Neoplasms • Glioma • Neoplasm Metastasis

Abbreviations: **GBM** – glioblastoma multiforme; **CNS** – central nervous system; **BP** – blood pressure; **HR** – heart rate; **RR** – respiratory rate; **Chest x-ray** – chest radiography; **CT** – computed tomography; **MRI** – magnetic resonance imaging; **GFAP** – glial fibrillary acidic protein

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/922976>

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Background

Pulmonary metastases are extracranial manifestations that infrequently occur as a consequence of a glioblastoma multiforme (GBM). There is usually no invasion of blood vessels and, in rare cases, it spreads outside the central nervous system (CNS) [1]. Epidemiologically, younger patients are more susceptible to developing extracranial metastases, occurring in approximately 0.2% to 1% of cases [2]. The most common site of extracranial metastasis of GBM is the lung, although it may also spread to the liver, bone, or lymph nodes [3].

GBM is the most common and aggressive primary neoplasm that occurs in the brain. Its prognosis as a malignant tumor is discouraging due to its high rate of recurrence despite surgical resection, chemotherapy, and radiation. It should be emphasized that GBM resection is not usually complete due to the behavior of the tumor, which has an infiltrative growth pattern [4].

The literature reports cases of precipitation of postoperative metastases in patients mainly with GBM, but these metastases have been reported 4 to 6 months after surgical resection and treatment with radiotherapy or chemotherapy [5].

We report the case of a 66-year-old male patient who, 17 days after the resection of a right parietal GBM, had histopathological-proven pulmonary nodules consistent with pulmonary metastases of GBM.

Case Report

Our patient was a 66-year-old male had a history of arterial hypertension, was as a chronic smoker and a regular caffeine user. The patient had a clinical presentation of blindness and headache of great intensity of occipital location, which was

intensified over time, accompanied by nausea and vomiting, left hemiplegia, and aphasia. His condition was also accompanied by alleged tonic-clonic seizures that required several emergency visits to the hospital.

Initial chest radiography (chest x-ray) was observed as normal (Figure 1A). The patient's vital signs were as follows: blood pressure (BP) of 130/76 mmHg; heart rate (HR) of 86 beats per minute; respiratory rate (RR) of 12 breaths per minute; temperature of 36.5°C with oxygen saturation of 98% by pulse oximetry. During subsequent evaluations, a progressive deterioration of his neurological state was evident.

The magnetic resonance imaging (MRI) in sequence T1 (Figure 2A) showed an occupation zone of hererogenic intensity, with halo hypointense, which was compressing adjacent areas.

The MRI using Gradient Sequence Echo showed an occupation mass with apparent vascularization that compresses callous rodent and displaces adjacent structures and hyperintense image (Figure 2B). The MRI using Flair (fluid attenuation inversion recovery) sequence, showed an occupational lesion that was having a mass effect, compressing adjacent areas, which was surrounded by a hyperintense halo that reached to the cerebral cortex (Figure 2C). The MRI using Diffusion image restriction of water diffusion was observed generating a central heterogeneous zone surrounded by a hyperintense halo (Figure 2D).

The patient became sleepy and non-collaborative, responding only to painful stimuli (Glasgow score of 10 out of 15). As such, a family member consented to our recommendation for surgical intervention and 3 days after he had the operation: a 6 by 6 craniotomy was performed by 7 trephines in the right parietal region plus excision of the tumor. A diffuse lesion was observed with necrosis of dark content and samples were taken for biopsy.

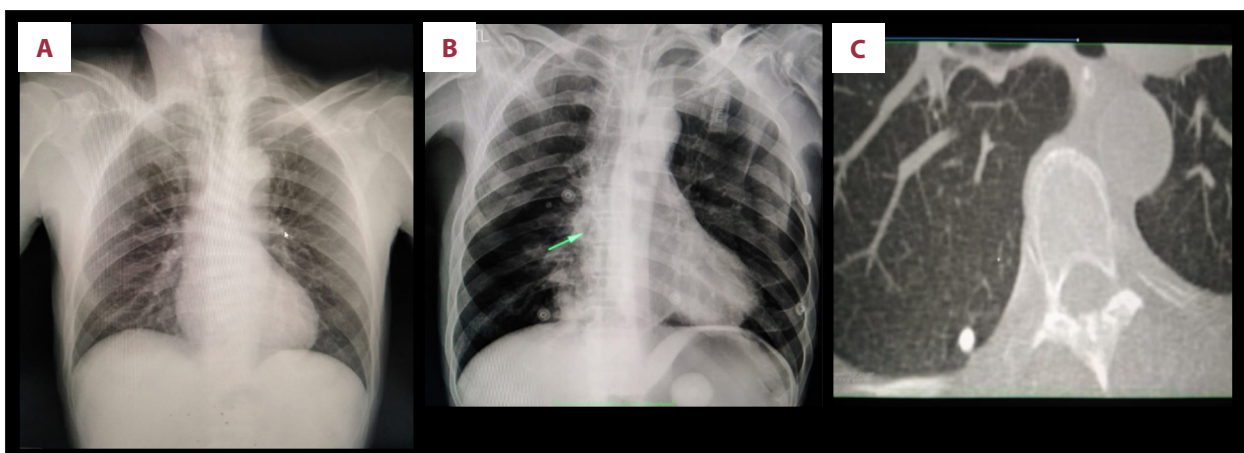


Figure 1. (A) Initial chest x-ray normal. (B) Chest x-ray and (C) computed tomography scan at 19 days later in which a unique nodular image is observed.

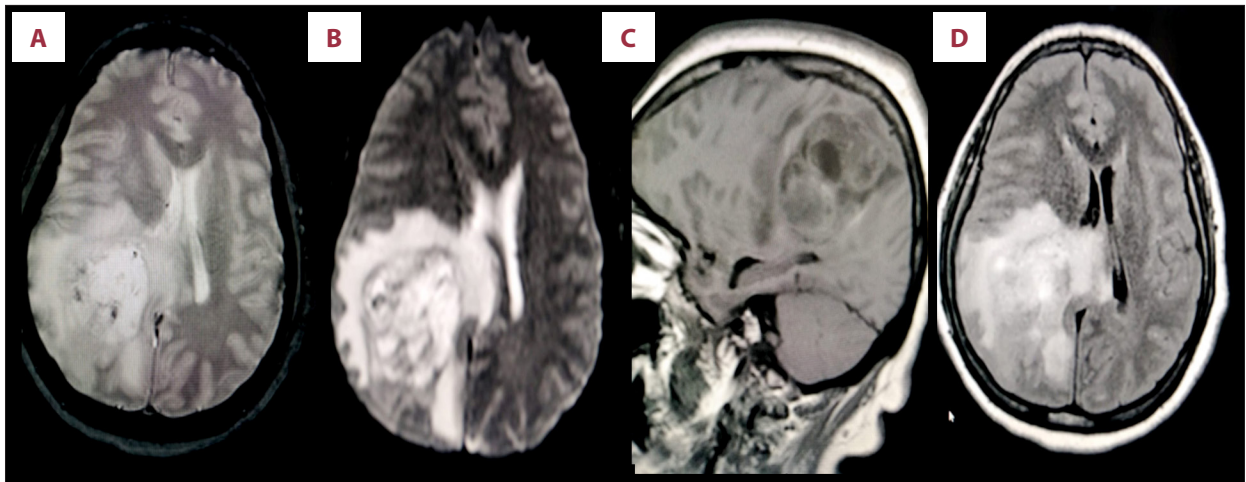


Figure 2. The magnetic resonance (MRI) in sequence T1. (A) Showed an occupation zone of hererogenic intensity, with halo hypointense, which is compressing adjacent areas. (B) MRI in Gradient Sequence Eco was observed an occupation mass with apparent vascularization that compresses callous rodent and displaces adjacent structures and hyperintense image. (C) MRI in Flair sequence, an occupational lesion was observed that is performing mass effect, compressing adjacent areas, which is surrounded by a hyperintense halo that reaches to the cerebral cortex. (D) MRI in Diffusion image restriction of water diffusion was observed, generating a central heterogeneous zone surrounded by a hyperintense halo.

Postoperative evaluation

Immediately after the procedure, the patient was transferred to the Intensive Care Unit (ICU) for monitoring. On the first post-operative day, the patient received invasive mechanical ventilation (IMV) in IPPV mode. Ampicillin+sulbactam antibiotic scheme was established at 3 g every 6 hours+dexamethasone 8 mg intravenous (IV) every 6 hours. Leukocytosis with a predominance of neutrophils was reported and blood, urine, and bronchial secretion samples were taken, evidencing no bacterial growth 48 to 72 hours later. The patient was extubated to 48 hours post-operative.

On the fifth postoperative day, a standard chest x-ray was performed, which reported findings within normal parameters. On the seventh day of hospitalization in the ICU, moderate hyponatremia was detected and was corrected with hypertonic saline. A brain computed tomography (CT) scan was obtained and revealed a hypodense image in the peripheral zone.

On the 15th day in the ICU, a chest x-ray revealed a diffuse alveolar infiltrate of left lung base without evidence of pleural effusion or masses. On the 17th day in the ICU, the patient presented new leukocytosis with predominantly neutrophils. Antibiotics were changed to IV cefepime 2 gr every 8 hours. An exploratory bronchoscopy revealed the presence of thickening of the mucosa and areas consistent with anthracosis protrusion area partially obstructing the bronchial lumen (Figure 3A).

A sample was taken for microbiological and pathological study. Images of chest-x ray and CT scan were evidenced 19 days later in which a unique nodular image is observed (Figure 1B, 1C).

The patient continued to deteriorate, sustained poor respiratory mechanics, and became hemodynamically unstable. The patient experienced cardiorespiratory arrest and after advanced cardiopulmonary resuscitation (CPR) was performed, he passed away.

Pathology of the brain lesion

A fragment of grayish brown tissue measuring 2.5×2.2 cm, friable, and with areas of hemorrhage was sent for biopsy. The histological sections revealed densely cellular neoplasia consisting of polygonal ovoid round cells and fusiform with signs of anaplasia evidenced by macronucleosis, hyperchromatism, pleomorphism, and intense mitotic activity (>25×10) with alteration of the polarity and the nucleus-cytoplasm relationship.

There were areas of necrosis surrounded by viable tumor cell palisades, as well as proliferation of glomeruloid vessels of swollen endothelium, typical of high-grade gliomas (Figure 4).

Biopsy of lung tissue

Minute fragments of tissue were observed consisting of a dense cellularity of round, ovoid and elongated elements, with signs of anaplasia evidenced by macronucleosis, nucleolar prominence, altered polarity and nucleo-cytoplasm relationship possibly corresponding to metastatic spread of brain neoplasia (Figure 3B).

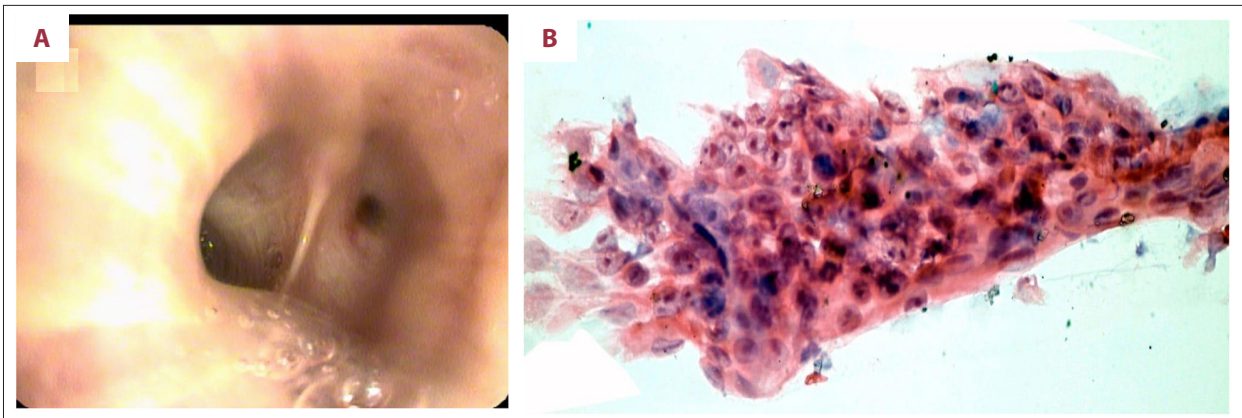


Figure 3. (A) Showed an exploratory bronchoscopy revealed the presence of thickening of the mucosa and areas consistent with anthracosis protrusion area partially obstructing the bronchial lumen and (B) dense cellularity of round, ovoid and elongated elements, with signs of anaplasia evidenced by macronucleosis, nucleolar prominence, altered polarity and nucleo-cytoplasm relationship possibly corresponding to metastatic spread of brain neoplasia.

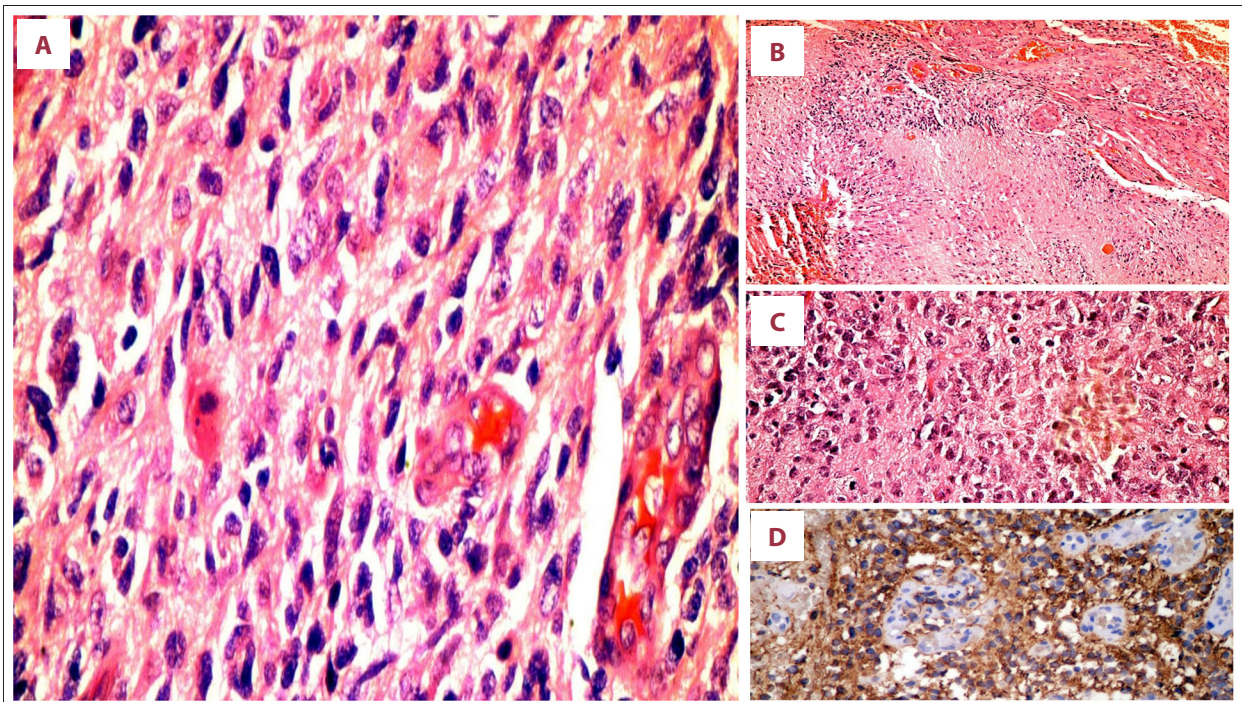


Figure 4. (A) Showed histological sections reveal densely cellular neoplasia consisting of polygonal ovoid round cells and fusiform with signs of anaplasia evidenced by macronucleosis, hyperchromatism, pleomorphism, and intense mitotic activity ($>25\times 10$) with alteration of the polarity and the nucleus-cytoplasm relationship. (B, C) Showed areas of necrosis surrounded by viable tumor cell palisades, as well as proliferation of glomeruloid vessels of swollen endothelium, typical of high-grade gliomas. (D) Showed immuno-staining for glial fibrillary acidic protein (GFAP) is intensely positive in tumor cells and verifies their glial lineage.

Discussion

Extracranial metastases of GBM are rare, with a reported incidence of less than 2% [6]. In most documented cases, these patients have undergone a resection by means of open craniotomy, which suggests the hypothesis of iatrogenic exposure

of tumor cells through blood vessels. Due to the rarity of this condition, it is not clear if overall survival in GBM is diminished in the context of extracranial GBM metastasis [1].

The preoperative assessment of the extent of the lesion, as well as certain preoperative inflammatory markers, have recently

been highlighted for their important value in the prognosis and survival of patients.

Our patient underwent a GBM resection and developed pulmonary nodules identified as extracranial GBM metastasis in the lung. The mechanism of dissemination is not clear, however, as mentioned in the literature, post-surgical iatrogenic sowing is suggested [6].

Extracranial metastases are usually rare due mainly to 1) the absence of lymphatic vessels in the CNS, 2) the absence of communication between the peri-vascular and extracranial spaces, 3) the fact that intracranial veins are thin-walled, and 4) the fact that meningeal tumors grow in the dura mater and remain only on the surface. The dural veins are protected by a dense connective tissue. Therefore, for the tumor to metastasize, it must follow different routes. These routes are mainly hematogenous, either by invasion of the primary or lymphatic tumor after the infiltration of the skull or to the extracranial soft tissue, which can be precipitated by the surgical intervention [7].

Craniotomy alters the mechanism of innate defense of the CNS and facilitates tumor cells entering the blood vessels hematogenously, which is the main route for the metastasis of other solid organs (lung, bone, and spleen) [8]. The lungs are the first filter for the tumor cells. Tumor cells that are mechanically trapped in the lung, might result in lung metastasis [9].

Among the limitations found for the diagnosis and correct evaluation of this patient, some histochemical characteristics of the tumor were not analyzed. Furthermore, some studies have

linked subclones [10] that are genetically altered in the primary tumor to the presence of extracranial metastases. However, advanced age and postoperative infections have been related to survival [11].

The preoperative assessment of the extent of the lesion, as well as certain preoperative inflammatory markers, have recently been highlighted for their important value in the prognosis and survival of patients [12].

Conclusions

In this clinical case study, the rapid presentation of pulmonary metastasis was the main clinical presentation that was related to surgical resection. Although pulmonary metastases are rare events and the mechanisms through which they develop are not fully defined, clinicians must take this clinical possibility into account post-brain-tumor resection to achieve adequate and effective diagnostic management and thus improve the quality of life of our patients.

Department and Institution where work was done

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Conflict of interest

None.

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