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(CASE REPORT)

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Exceptional metastatic glioblastoma: A case report of multifocal spread

Zineb El Ayachi *, Wissal Hassani, Kaoutar Soussy, Fatima Zahra Farhane, Zenab Alami and Touria Bouhafa

Department of Radiation Therapy, Oncology Hospital, HASSAN II University Hospital, Faculty of Medicine and Pharmacy Fez, University Mohammed Ben Abdellah, Fès 30000, Morocco.

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Abstract

Glioblastomas are aggressive primary brain tumors known for their local invasiveness but rarely associated with systemic metastases. We present a rare case of a 36-year-old male initially diagnosed with a spinal pilocytic astrocytoma (WHO grade I) following a traumatic event in 2018. Despite incomplete surgical resection and refusal of adjuvant therapy, the disease remained stable under surveillance for several years. In 2023, the patient developed neurological deterioration, dyspnea, and bilateral pleural effusion. Biopsy revealed transformation into a high-grade, IDH-wildtype astrocytic tumor with extensive metastases to pleura, lymph nodes, and bones. Imaging confirmed recurrence at the spinal level with widespread extension to the thoracic wall, paravertebral muscles, and multiple skeletal sites. Multidisciplinary evaluation led to palliative treatment with temozolomide and decompressive radiotherapy. Although transient symptomatic relief was achieved, disease progression was rapid, and the patient succumbed within three months. This case illustrates the potential for malignant transformation of low-grade gliomas and the exceptional occurrence of extracranial metastases in glioblastoma. Factors such as surgical disruption of anatomical barriers and genetic alterations may contribute to metastatic spread. Early intervention and careful surveillance in patients with incompletely resected tumors are crucial. Histological confirmation remains essential for diagnosis, and treatment in metastatic settings is primarily palliative.

Keywords: Glioblastoma; Metastasis; Astrocytoma; Spine; Radiotherapy; Temozolomide

1. Introduction

Glioblastomas are highly aggressive brain tumors with significant local-regional spread. Metastatic dissemination, however, is exceptional with extracranial metastases documented in approximately 0.4% to 0.5% of all cases of glioblastomas (1,2). We report the case of a patient who underwent surgery for a high-grade glial tumor and subsequently developed pleural, lymph node, and bone metastases during follow-up.

2. Case report

The patient, a 36-year-old Moroccan young man with no significant medical history, was diagnosed with a pilocytic astrocytoma of the spinal cord in 2018, discovered on an MRI following a car accident with dorso-lumbar spinal trauma. Clinically, the patient presented with Grade III paraparesis in both lower limbs but no other neurological abnormalities. The patient's history revealed that he exhibited heaviness in both lower limbs for a few months prior to the trauma. The spinal MRI revealed an extensive intracanalicular tumor from T-10 to L2, causing lytic and compression fractures of the vertebral bodies at T-12 and L1, with extension to the right posterior thoracic wall and myelopathy extending to the level of T-2.

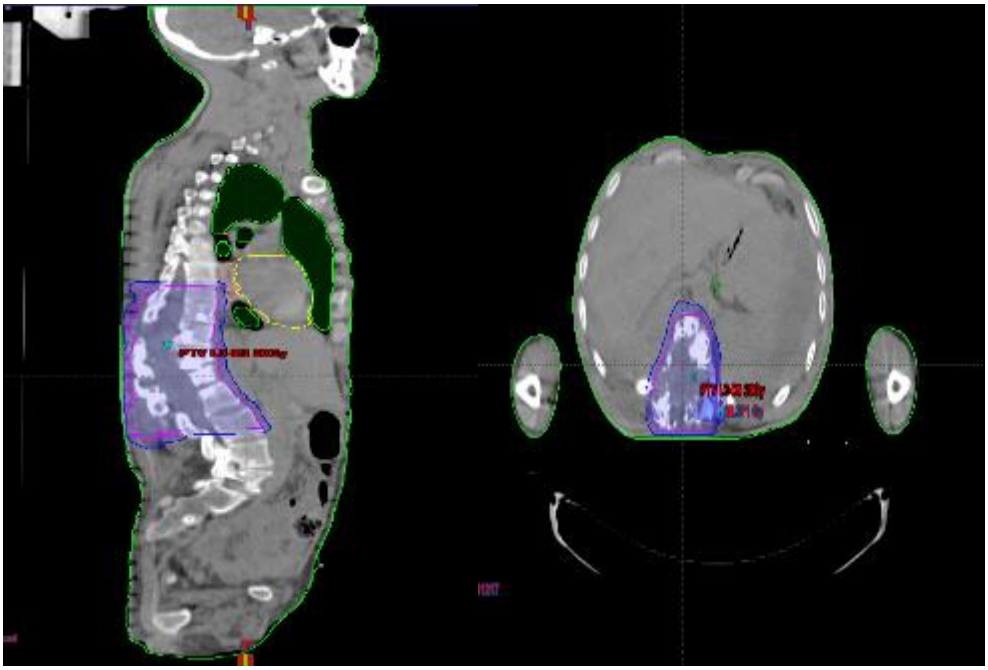
* Corresponding author: Zineb El Ayachi

Due to the tumor's extensive involvement and location, only a macroscopically incomplete resection was achieved. The decision for incomplete resection was due to the risk of causing significant neurological damage if a more aggressive resection was attempted.

The macroscopically incomplete resection of the mass confirmed the diagnosis of pilocytic astrocytoma. Because of the incomplete resection, adjuvant therapies were discussed with the patient who refused them. Close surveillance was initiated and MRI scans were conducted periodically between 2018 and February 2023 and showed stable disease for several years.

In February 2023, the patient developed gradually paraparesis and sphincter disturbances; then rapidly progressive dyspnea and pain due to bilateral pleural effusion, leading to hospitalization and a pleural biopsy that revealed pleural localization of a higher-grade (anaplasic) glial astrocytic medullary tumor IDH wildtype, non-1p/19q co-deleted. Cerebral and cervico-thoraco-abdominal CT scans, confirmed local recurrence from T10 to L2 with a large canalicular tumor measuring approximately 81 x 98 mm in axial diameter and extending over approximately 17 cm in height. The tumor invaded the pleura with the presence of tumor masses on both sides, and had focal contact with the abdominal aorta. Clinical evaluations did not show any signs of cardiac pathology that may have been impacted by the tumor's proximity to the abdominal aorta. The tumor also invaded the right paravertebral muscles and both diaphragmatic pillars.

The CT scan also revealed subphrenic and left internal mammary lymphadenopathies, as well as multiple secondary bone locations involving the axial and peripheral skeleton: The vertebral bodies, ribs, sacrum, and iliac bones. The case was discussed in a multidisciplinary team meeting. As surgical decompression was deemed not feasible, the decision was made to initiate chemotherapy with Temozolomide and provide decompressive radiotherapy. The patient underwent decompressive radiotherapy for his primary at a dose of 20 Gy in 05 fractions of 4 Gy **(Figures 1 & 2).**



Figures 1 and 2 Decompressive radiotherapy of the medullar glioblastoma

The patient experienced some initial benefits, mostly relief from severe pain and partially improved neurological symptoms, but the rapid disease progression led to a decline in quality of life. Unfortunately, the patient succumbed to the disease 3 months after the diagnosis of metastatic grade 4 Glioblastoma. The progression-free survival (PFS) period, was 2 months.

Our case highlights that grade I and II astrocytoma may evolve to a grade 4 Glioblastoma and rarely become metastatic **(Figure 3).**

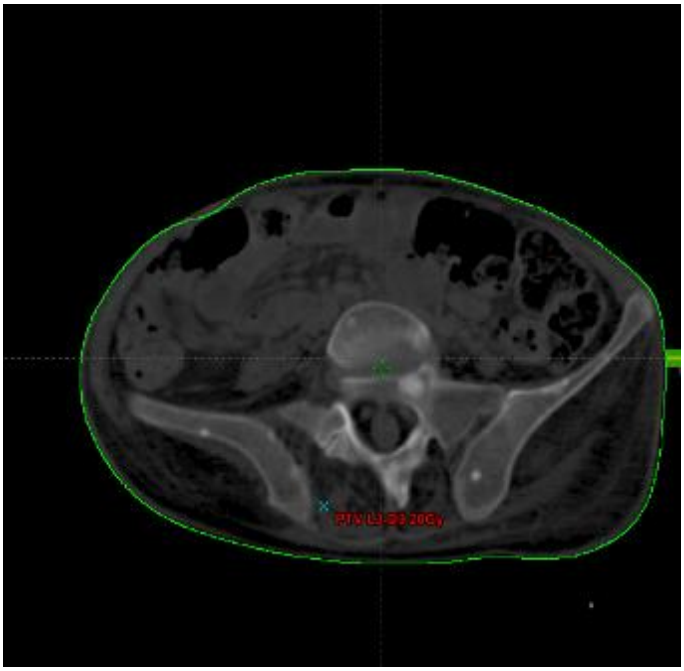


Figure 3 Multiple secondary bone locations of glioblastoma involving the axial skeleton

3. Discussion

The progression of a grade I glioma (pilocytic astrocytoma) to a grade 4 glioblastoma is a complex process involving multiple mechanisms: Genetic mutations; Specifically, the PI3K/Akt pathway, whose activity is normally suppressed by the tumor suppressor PTEN, can become overactive in the presence of PTEN mutations, driving tumor growth. Additionally, the MAPK pathway, involving RAS, RAF, and ERK proteins, can also contribute to tumor progression when altered, with BRAF mutations commonly implicated in pilocytic astrocytomas.

In cases of pilocytic astrocytoma, several studies have documented cases where residual tumor following subtotal resection led to local tumor recurrence. Gupta et al. reported that maximizing tumor resection is crucial for reducing recurrence and improving survival in Low Grade Glioma patients. After such surgeries, adjuvant therapies should be considered. Unfortunately, our patient's refusal of further treatment after surgery likely contributed to the recurrence of the tumor. This case also underscores the importance of early detection in patients with incompletely resected tumors. Close monitoring allows for early intervention in the event of recurrence. Glioblastomas, traditionally considered non-metastatic tumors confined to the central nervous system, have increasingly shown instances of metastasis in recent reports (3). The prevailing hypothesis for the rarity of such metastases revolves around the lack of lymphatic drainage from the CNS (4). However, despite being rare, the acceptance of metastatic potential is growing, with indications that the number of cases might be underestimated due to the unfavorable survival outcomes associated with these tumors; and depending on the localization of symptoms, investigations should be pushed to detect metastatic spread early.

Understanding the mechanisms underlying metastatic dissemination in glioblastomas remains an ongoing challenge. Surgical interventions have been implicated as potential contributors to the development of secondary metastases. The breach of anatomical barriers during surgery could facilitate the spread of tumor cells either through the lymphatic system, leading to lymph node metastases, or via hematogenous dissemination, resulting in visceral metastases (5). Notably, there have been reported cases of metastasis even in the absence of surgical interventions (2,6,7), suggesting that tumor cells may acquire genetic alterations that confer migratory capabilities (8). The overall incidence of such metastatic spread remains very low. But when they occur, metastatic glioblastomas tend to manifest in specific sites, with the pleuropulmonary region being the most common (59.7%), followed by lymph node involvement (51.4%), bone metastases (30.5%), and liver metastases (22%) (9).

The confirmation of metastatic lesions requires histological examination. Treatment approaches for metastatic glioblastomas remain primarily palliative, with chemotherapy playing a central role. Palliative radiotherapy can also be

considered as an option, aiming to alleviate symptoms and reduce tumor burden. In our patient's case, radiotherapy was employed with the intention of relieving compression (10).

4. Conclusion

This case demonstrates the rare occurrence of metastatic dissemination in glioblastoma, which led to rapid clinical decline and death. It contributes to better clinical awareness of glioblastoma's metastatic potential and emphasizes the need for vigilant follow-up and timely intervention in managing low-grade gliomas.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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