

Multiple Cystic Brain Metastases from Lung Adenocarcinoma: A Case Report and Literature Review

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Abstract

Case Report

Introduction: Multiple cystic brain metastases are a rare form of tumor dissemination, typically occurring in lung adenocarcinomas. Their management is complex and non-standardized, with cyst drainage playing an essential role in reducing intracranial pressure and controlling neurological symptoms. **Case Report:** We report the case of a 64-year-old female patient with no known history of neoplasia, who presented with progressive neurological symptoms (headaches, dizziness, memory disturbances) associated with chronic dry cough. Brain imaging revealed multiple intraparenchymal cystic lesions, bilateral, supratentorial and infratentorial, with slight peripheral enhancement. Staging workup revealed a tumor in the left upper lobe, mediastinal lymphadenopathy, and a suspicious adrenal nodule. CT-guided lung biopsy confirmed a moderately differentiated adenocarcinoma. The patient underwent whole-brain radiotherapy and chemotherapy, in the absence of driver mutations. The clinical course was marked by progressive neurological deterioration, and the patient died 8 months after diagnosis. **Conclusion:** This case illustrates the severity of multiple cystic brain metastases, whose prognosis is more reserved than that of solid metastases. In the presence of neurological signs in a cancer patient, this diagnosis should be considered. Management relies on a multidisciplinary approach combining surgical drainage, radiotherapy, and targeted therapies when possible.

Keywords: Cystic brain metastases, lung adenocarcinoma, whole-brain radiotherapy, intracranial hypertension.

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1. INTRODUCTION

Brain metastases are considered the most common malignant brain tumors in adults; they represent an extremely prevalent complication of cancers. Lung and breast cancers are the primary causes [1]. While the typical MRI appearance is that of a solid, nodular lesion with contrast enhancement and perilesional vasogenic edema, presentation as purely cystic lesions is exceptional and may mimic other pathologies (abscess, benign cyst, hemangioblastoma, or neurocysticercosis) [2].

Cystic brain metastases are defined as lesions where the cystic component represents more than 50% of the total volume [3]. Their management remains difficult and non-standardized. A recent retrospective study showed that the prognosis of patients with cystic metastases is poorer than that of solid metastases, with a median survival of 14.6 months versus 23.1 months, particularly in patients with EGFR-mutated lung adenocarcinoma [3].

We report the case of a 64-year-old female patient with stage IV lung adenocarcinoma who developed multiple cystic brain metastases, and we discuss therapeutic strategies through a literature review.

2. CASE REPORT

2.1. Patient and Methods

A 64-year-old female patient, with a history of cholecystectomy in 2019, presented to the emergency department with headaches, dizziness, and memory disturbances (amnesia) that had been progressively developing over 1 month, associated with chronic dry cough. For these symptoms, the patient was evaluated with computed tomography (CT) followed by brain MRI.

2.2. Clinical Examination

The initial neurological examination revealed signs of intracranial hypertension (severe headaches, nausea). The patient also presented with progressive decline in general condition, without focal neurological deficit.

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2.3. Diagnostic Workup

MRI (figure 1 and 2) Imaging studies revealed multiple intraparenchymal cystic lesions, bilateral, of varying sizes, supratentorial and infratentorial, with slight peripheral enhancement after contrast injection.

Additional thoraco-abdomino-pelvic (TAP) CT imaging revealed:

- A primary tumor process in the left upper lobe, measuring $68 \times 65 \times 62$ mm;
- Mediastinal lymphadenopathy, the largest located in the aortopulmonary window measuring 2 cm in short-axis diameter;
- A suspicious left adrenal nodule.

CT-guided lung biopsy revealed a moderately differentiated adenocarcinoma.

2.4. Therapeutic Management

The patient underwent whole-brain radiotherapy due to the multiplicity of lesions and worsening neurological symptoms. Chemotherapy was initiated, as driver mutation testing returned negative.

2.5. Clinical Course

The clinical course was marked by worsening neurological symptoms. After 8 months of follow-up, the patient died from progressive disease.

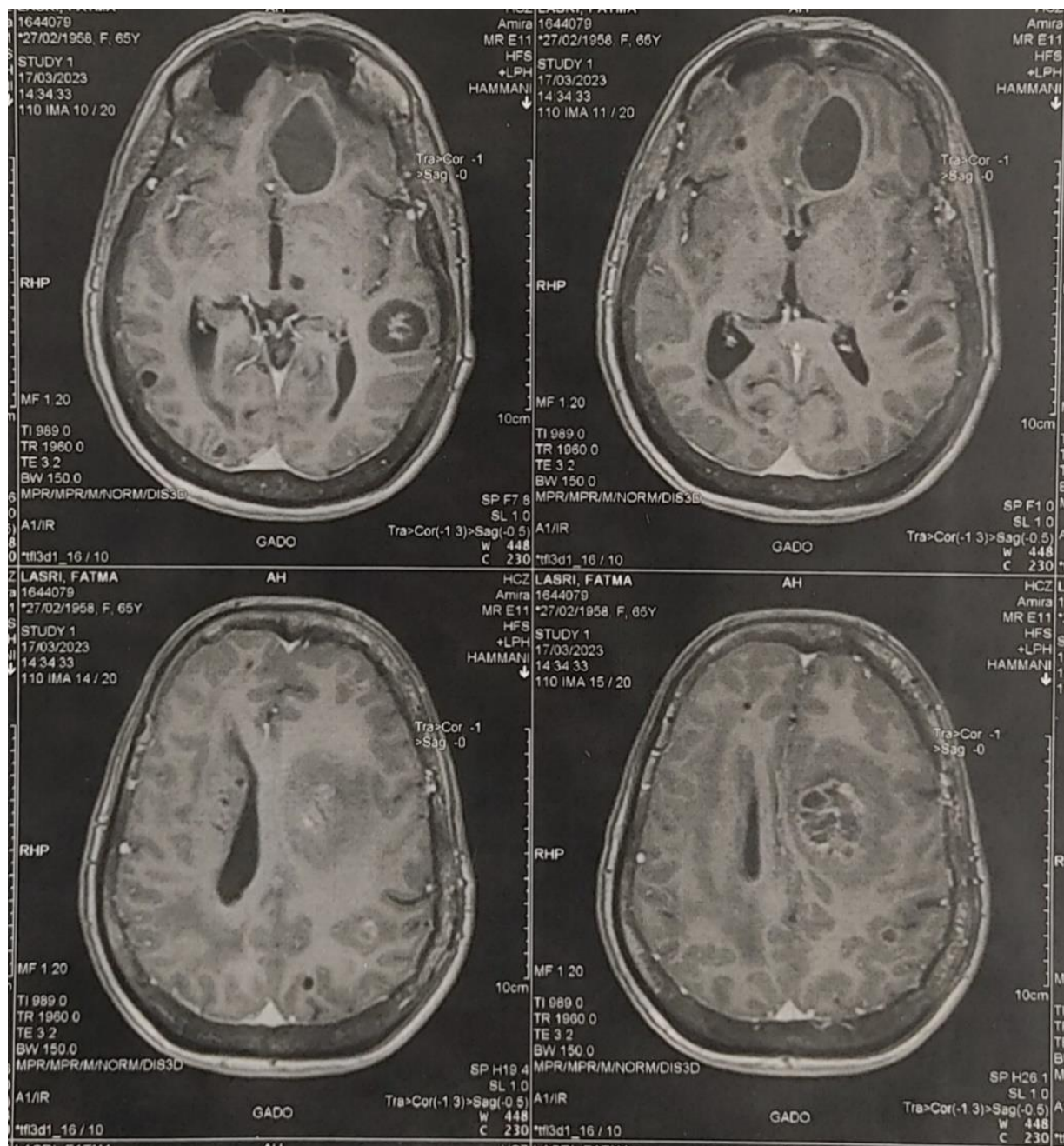


Figure 1: Brain MRI showing multiple cystic intraparenchymal metastases from lung adenocarcinoma

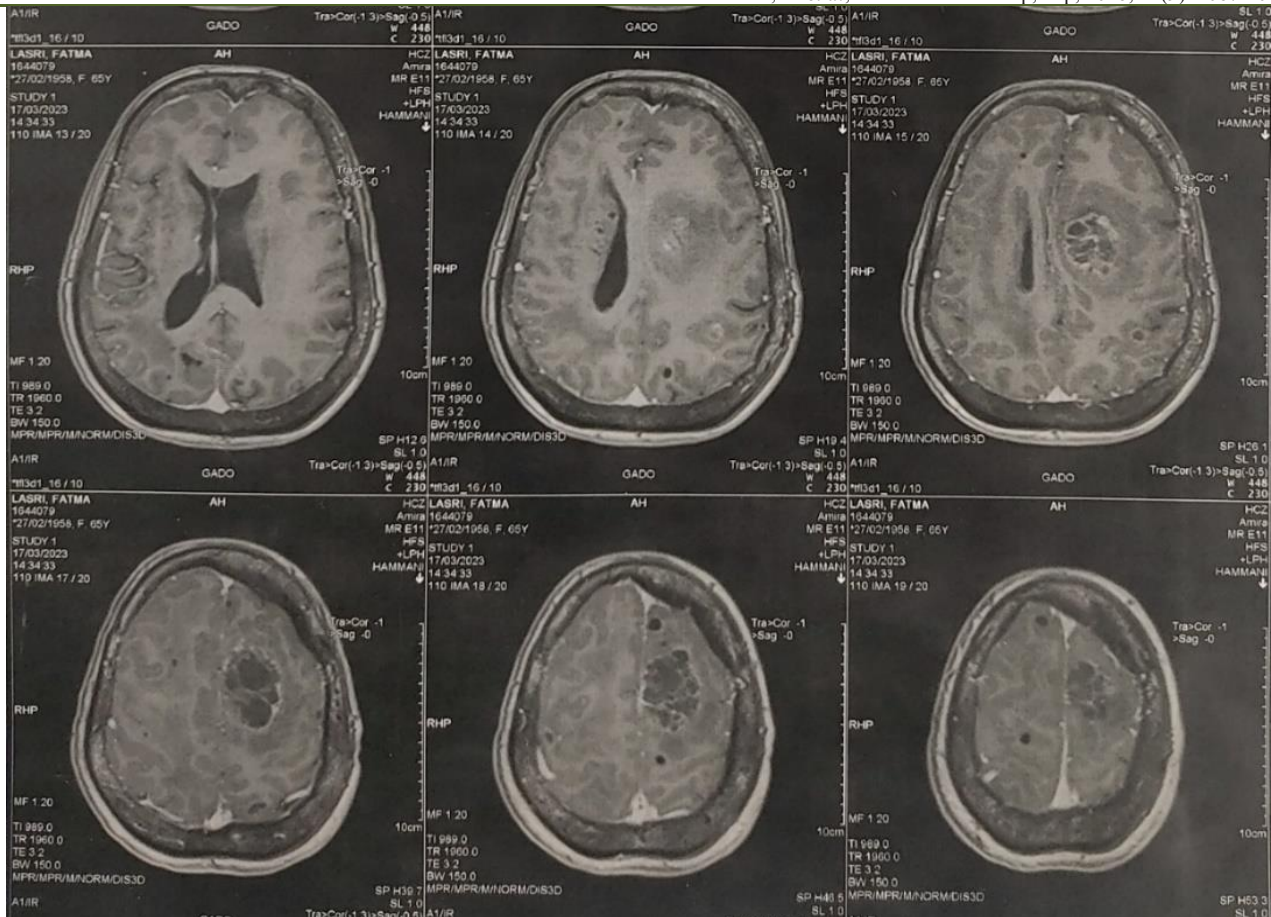


Figure 2: Brain MRI showing multiple cystic intraparenchymal metastases from lung adenocarcinoma

3. DISCUSSION

3.1. Epidemiological and Diagnostic Features

Cystic brain metastases from lung adenocarcinoma are rare, representing approximately 25% of brain metastases in series of patients who received radiotherapy [3]. Their presentation as multiple cystic lesions is even more exceptional. The age of onset in our case (64 years) aligns with reported series, ranging between 50 and 68 years [5].

The cystic appearance of brain metastases can pose a diagnostic challenge, particularly with neurocysticercosis, as reported in the literature [2]. In some cases, the appearance may be that of "true" cysts, without contrast enhancement or peripheral edema, making brain biopsy necessary to confirm the diagnosis [4].

3.2. Pathophysiological Mechanisms

Several hypotheses explain the formation of these cystic lesions. Some authors suggest that treatment with tyrosine kinase inhibitors (such as erlotinib) could induce lysis of metastatic deposits, leading to cystic transformation [4]. Other cases report cysts without prior treatment, suggesting a process related to tumor biology itself, such as mucin production by adenocarcinoma cells [6].

3.3. Prognosis: Cystic vs. Solid Metastases

A recent study of 168 patients showed that patients with solid metastases had a significantly longer median overall survival than those with cystic metastases (23.1 months vs. 14.6 months, $p=0.04$). This difference was particularly marked in patients with EGFR-mutated lung adenocarcinoma (23.1 months vs. 6.43 months, $p=0.01$) [3]. Metastasis volume and biologically effective dose (BED) emerged as significant prognostic factors for cystic metastases [3].

3.4. Therapeutic Options

Management of cystic brain metastases is particularly challenging because they are generally resistant to radiotherapy [5]. Several approaches have been described in the literature:

- **Simple surgical drainage:** Craniotomy with drainage can be effective in reducing mass effect and rapidly improving neurological status. This option was not pursued in our patient due to the multiplicity of lesions [7].
- **Ommaya reservoir placement:** This technique is particularly useful for large cysts, especially in patients with poor general condition. Toyokawa et al. reported the case of a 68-year-old patient in whom Ommaya reservoir placement reduced a large

cystic lesion from 4.7 to 2.9 cm, with improvement in neurological symptoms and performance status [5]. Yatsushiro *et al.*, also reported a case where the combination of Ommaya reservoir and radiosurgery (Gamma Knife) led to a dramatic improvement in consciousness, with the patient subsequently benefiting from pembrolizumab immunotherapy [7]. Lv *et al.*, emphasized the importance of the Ommaya reservoir in preventing fluid reaccumulation and avoiding a second surgical intervention [8]. Takeda *et al.*, reported a similar case where the Ommaya reservoir enabled prolonged control of a radiotherapy-resistant cystic metastasis [6].

- **Stereotactic radiosurgery:** Often used in combination with drainage, it can be effective after cystic volume reduction. An Ommaya reservoir allows for cyst size reduction before radiosurgery, thereby improving treatment efficacy and reducing the risk of radionecrosis [8].
- **Whole-brain radiotherapy:** Our patient received whole-brain radiotherapy without surgical drainage due to the multiplicity of lesions. However, its efficacy on purely cystic lesions is debated [3].
- **Targeted therapies:** When mutations are identified, tyrosine kinase inhibitors can be effective. A case of a patient with an EGFR mutation responding to gefitinib after five months of treatment has been reported [4]. In our patient, driver mutation testing was negative, so this option was not available.

3.5. Limitations of the Case Report

Our case has certain limitations: it is a single observation, and the precise MRI characteristics (exact lesion size, exact number, exact location) are not detailed. Nevertheless, this case illustrates the importance of considering this diagnosis when neurological signs present in a cancer patient, and highlights the severity of the prognosis of multiple cystic brain metastases [3].

4. CONCLUSION

Multiple cystic brain metastases from lung adenocarcinoma are rare but potentially severe, with a less favorable prognosis than solid metastases. In the presence of neurological warning signs in a patient with a history of cancer, this diagnosis should be

systematically considered. Management generally combines surgical drainage and radiotherapy, with satisfactory results. Less invasive techniques such as Ommaya reservoir placement appear promising, particularly in patients with poor general condition, enabling rapid improvement in performance status and providing a therapeutic window for systemic treatments. Molecular mutation testing (EGFR, ALK, ROS1, PD-L1) is essential to propose effective targeted therapy and improve the prognosis of these patients.

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