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Case Report

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A case of cystic brain metastasis from lung adenocarcinoma

Abstract

Background: Multiple cystic brain metastases are a rare form of cancer dissemination and usually originate from adenocarcinomas of the lung and breast. Managing these lesions is challenging, and cyst drainage plays an essential role in reducing intracranial pressure. This article presents a case of multiple cystic brain metastases from lung adenocarcinoma.

Case Presentation: A 40-year-old female with a two-year history of stage IV lung adenocarcinoma presented with debilitating progressive neurologic symptoms. Imaging studies showed multiple cystic lesions on brain MRI most consistent with brain metastases. She underwent a craniotomy to drain the biggest cysts, followed by whole-brain radiotherapy (WBRT). The patient experienced dramatic alleviation of symptoms. Following a year of follow-up, she had no neurological symptoms.

Conclusion: Despite the rarity of cystic brain metastases, these lesions should be ruled out in case of signs of increased intracranial pressure in a patient with a history of malignant disease.

Keywords: Adenocarcinoma, Brain metastasis, Cystic lesions, Lung cancer.

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Cystic brain lesions appear mostly as hypo-dense masses with ring enhancement in CT scans, and even with other imaging modalities, diagnosis remains challenging. Multiple cystic lesions in the brain can be classified as metastatic and rarely primary brain tumors, bacterial or fungal abscesses, parasitic lesions such as neurocysticercosis or toxoplasmosis, and hydatid cysts. Cystic brain metastasis is rare compared to solid ones and usually originates from breast or lung malignancies. Central necrosis, hemorrhage, or mucin secretion in a metastatic brain lesion can lead to cyst formation while preserving the ring enhancement, which is characteristic (1, 2).

Brain metastasis (BM) causes symptoms of headache, altered mental status, sensory and motor deficits, and seizures. Besides, cystic lesions may cause an accelerated decline in patients' condition due to rapid enlargement and consequent mass effect leading to increased intracranial pressure. Treatment is challenging because operating on patients with comorbidities and in unreachable areas is not feasible, and multiple masses are not great candidates for surgery. Radiotherapy modalities like radiosurgery or whole-brain radiotherapy (WBRT) can cause necrosis in cystic brain metastasis and deteriorate the situation. Drainage may be problematic if the fluid is viscous (2, 3). Therefore, encountering cystic brain metastasis is a dilemma. Brain metastasis imposes a poor prognosis on patients, and the lesion size is an important determinant (3). This article presents a case of multiple cystic brain metastasis from lung adenocarcinoma.

Case Presentation

A 40-year-old woman with a history of metastatic lung adenocarcinoma was admitted to the radiation oncology department. She was suffering from dyspnea, general bone pain, severe headache and true vertigo from couple of weeks earlier and wheelchair dependency from 5 days prior to admission.

She was conscious and well-oriented at neurological examination. Her T2N1M0 lung adenocarcinoma was diagnosed four years earlier. Following open lobectomy and dissection of inter- and intra-lobar lymph nodes (stations 10 to 14), she received four cycles of cisplatin/pemetrexed. After two years, she developed multiple symptomatic bone and liver metastases. Subsequently, molecular testing was requested and was reported negative for epidermal growth factor receptor (EGFR) mutation. Due to the appropriate time interval from the last platinum treatment and 24-month disease-free survival, cisplatin/pemetrexed rechallenge was considered, and four cycles of this regimen were prescribed every three weeks. Moreover, zoledronic acid was prescribed every four weeks.

The response to the palliative chemotherapy was significant, and the patient remained asymptomatic for the next two years. However, after 24 months, she was referred to the department of neurosurgery complaining of severe bifrontal headache, nausea, and vomiting while she was completely disabled with a score 4 Eastern Cooperative Oncology Group (ECOG) performance status. On magnetic resonance imaging (MRI), there were several well-defined increased signal intensity lesions on T2 and FLAIR with low signal intensity on T1 weighted images at both cerebral and cerebellar hemispheres, with no restrictions on DW1 (figure 1 A-D). The largest lesion measured 42*40 mm and was located at the left high frontal white matter. An intravenous contrast MRI and magnetic resonance spectroscopy (MRS) showed lesions with no surrounding edema but fine rim enhancement that was suggestive of metastatic nature (figure 2).

Further investigations revealed multiple thoraco-abdominal lymphadenopathies with new metastatic pulmonary masses and pleural involvement. Open craniotomy was performed to alleviate the patient's symptoms, and all major cystic lesions were drained. On pathology, back-to-back mucinous glands with mildly atypical cells in mucin lakes were identified. Immunohistochemical study showed CK7 and TTF1 positive, CK20 and ER-negative cells with weakly positive CDx2 and CA-125 cells. These findings lead to the diagnosis of brain metastatic mucinous adenocarcinoma, most probably originating from the lungs. She was scheduled for whole-brain radiotherapy and received 10 fractions of 300 cGy for two weeks. Thereafter, maintenance chemotherapy using methotrexate was initiated. The ECOG performance score had improved significantly on the first- and sixth-month follow-ups, and there were no neurologic signs and symptoms. After a one-year follow-up, she had no neurological symptoms, and a brain MRI showed no active malignant lesions in the brain parenchyma (figure 1 F-I).

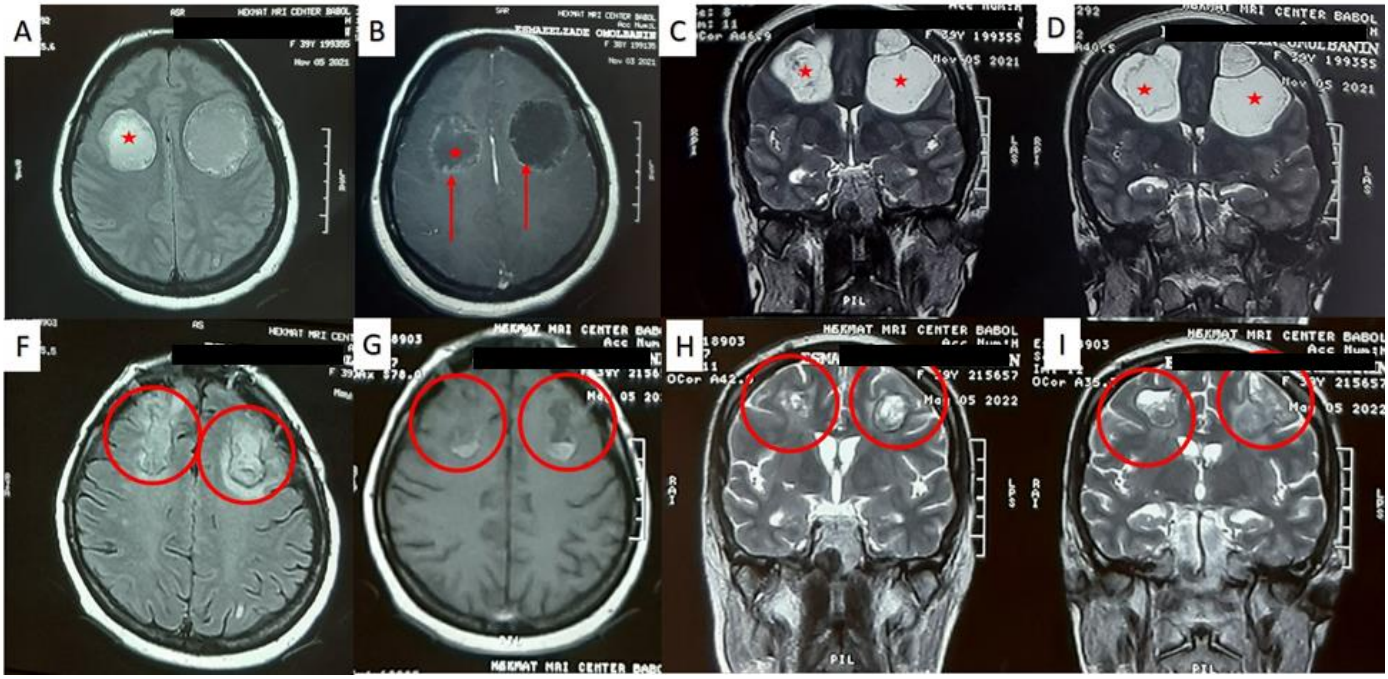

Figure 1. Magnetic resonance imaging of the patient. A-D) Pre-treatment brain MRI, A, and B show T2-weighted axial scan, T1-weighted with gadolinium (Gd) axial scan, respectively; C and D depict T2-weighted coronal scans. F-I) Post-treatment brain MRI (on one-year follow-up), F and G show T2-weighted axial scan, T1-weighted with Gd axial scan, C and D depict T2-weighted coronal scans, respectively; H and I represent T2-weighted coronal scans. Stars show the cystic lesions, arrows point to the rim enhancement area, and circles depict the post-treatment area of previous cystic lesions.

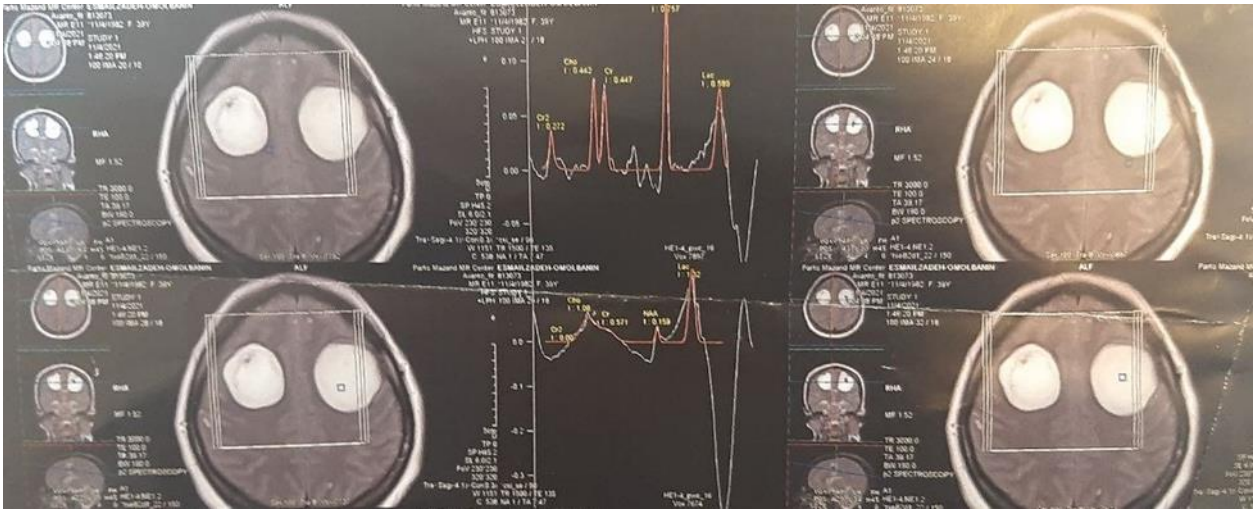

Figure 2. Magnetic resonance spectroscopy of the patient depicts lesions with no surrounding edema but fine rim enhancement at both cerebral hemispheres.

Discussion

Brain metastasis is ten times more prevalent than primary brain tumors. Estimations show that roughly 30% of patients with lung cancer will develop BM eventually, and the risk highly depends on the disease stage (4-6). Based on the type of the original malignancy, metastatic cyst formation rarely occurs, with a prevalence of up to 12% of all BMs in non-small-cell lung carcinoma and scarce case reports of cystic BM from small-cell lung carcinoma (7, 8). Our patient developed BMs two years after the initial diagnosis of her metastatic lung adenocarcinoma, a subtype of NSCLC; early workups showed no BMs. Following her acute symptoms investigations revealed multiple cystic BMs. Normally BMs present with focal signs and symptoms related to specific brain regions like motor or sensory disturbances. But generalized signs and symptoms like nausea, vomiting, headache, lethargy, cognitive impairment, and seizure also happen. The reason behind the later presentations is elevated intracranial pressure due to mass effect, blockade in the cerebrospinal fluid stream, or edema (6, 9). They are more seen in multiple BMs and cystic BMs because of their rapid growth (6, 7). Our patient with multiple cystic BMs experienced acute debilitating symptoms, and she rapidly reached ECOG performance status 4. All imply intracranial hypertension. Therefore, prompt treatment was demanded.

Other than supportive care with glucocorticosteroids to diminish edema and temporarily alleviate neurologic symptoms, available treatment modalities for BMs are: surgery, radiotherapy, chemotherapy, and targeted therapy (10). The benefits of surgical intervention followed by WBRT in solitary BMs are well documented. In a review article, Goldberg et al. stated that there is not enough evidence whether surgery in multiple BMs improves the outcome or not. However, they inferred that patients with limited brain metastases (fewer than 3) also benefit from surgical resection (5). Form results of a case series study, Weil et al. suggested that simultaneous surgical resection of multiple BMs is safe and may improve the overall survival and quality of life (4). However, they limited the number of lesions to three. In a retrospective study of BMs from NSCLC, patients had significantly longer survival in the brain surgery group compared with those without surgical intervention (40.3 months vs. 8.4 months). However, the former group had fewer metastatic lesions inside and outside the brain (11). Despite multiple lesions, our patient experienced dramatic alleviation in her neurologic symptoms, and her functions improved after the cyst drainage, with no postsurgical complications. She received WBRT as guidelines suggest. While evidence shows no improvement in survival after postsurgical WBRT but its efficacy in local disease control has been established (10). Our patient has been symptom-free since the surgery and subsequent WBRT.

Newer radiotherapeutic modalities like radiosurgery are now available. Radiosurgery is an option for patients who are not candidates for craniotomy, but large cystic BMs do not usually respond to it. Furthermore, intracranial hypertension is a well-known adverse effect of radiosurgery, and it can be life-threatening in patients with prior increased intracranial pressure (12, 13). Although radiosurgery preceded by stereotaxic aspiration or Ommaya reservoir placement are other available treatment options (2-4), as our patient suffered from multiple cystic BMs,

radiosurgery was not an option for her. In line with the recommendation Yen et al. made to consider brain surgery in NSCLC patients with BMs not suitable for radiosurgery (11). Besides, our patient was diagnosed with multiple large cystic BMs, which made Ommaya reservoir placement ineffective and impossible, let alone the mucinous nature of brain cysts may block the shunt and deactivate the catheter (14). Furthermore, obtaining specimens from BMs, in spite of known primary malignancy or other accessible secondary lesions, is recommended for molecular subtyping and planning treatment strategy (6). Despite the increased risk of leptomeningeal dissemination after surgery (15-17), our patient was considered to most benefit from craniotomy followed by WBRT.

In the literature, we found a few similar cases: A 66-year-old woman with a two-year history of stage IV lung adenocarcinoma and progressive neurologic symptoms for the last three months; was diagnosed with multiple cystic BMs after stereotaxic brain biopsy. Unlike our patient, she presented atypical imaging features like partial ring enhancement and no edema surrounding the lesions. No further information on treatment and outcomes was provided (18). Two other cases of multiple BMs from lung and prostate carcinomas with rapidly deteriorating neurologic symptoms have been reported. Both cases had confirmed diagnoses with brain biopsies and were deceased within months of WBRT (18, 19). A 68-year-old man with speech difficulties was diagnosed with stage IV lung adenocarcinoma in the initial investigations. Brain imaging showed multiple BMs with a large cyst, which was resistant to WBRT and enlarged continuously. An Ommaya reservoir was inserted into the largest cyst and alleviated the patient's symptoms. He was still well-performed a year after the procedure (20). Despite the rarity of cystic brain metastases, these lesions should be ruled out in case of increased intracranial pressure in a patient with a history of malignancy. Although surgery has a limited role in managing multiple BMs, metastatic cysts should be adequately drained before WBRT to reduce the intracranial pressure.

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Conflicts of interest: The authors have no conflicts of interest to declare.

Data availability statement: All data generated and analyzed during this study can be accessed through direct communication with the corresponding author and the agreement of all research team members. Further enquiries can be directed to the corresponding author.

Authors' contribution: D.F, H.F and M.F contributed to the study design. S.K contributed to perform femoral fixation surgery. H.Y contributed to perform chest tube insertion. D.F and M.F contributed to perform radiation treatment. B.P and S.R contributed to perform chemotherapy. A.A contributed to neurologic medical treatment. H.H contributed to perform biopsy from brain. N.A and A.E contributed to translate the manuscript. S.J contributed to drafting the manuscript. D.F, A.S and H.F contributed to manuscript revision. All authors have read the manuscript and approved its final version.

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