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Case report

Cerebral mucormycosis masquerading as brain metastasis from lung cancer: A case report

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ABSTRACT

We report a rare case of concurrent pulmonary and cerebral mucormycosis initially misdiagnosed as a metastatic tumor. A 66-year-old man with a complaint of progressive right-sided limb weakness for 3 days. Head MRI showed a left parietal occupying lesion with severe edema, and a chest CT scan showed a parenchymal mass with speculation and pleural invasion in his left lung. The patient was initially diagnosed with brain metastases from lung cancer and underwent a craniotomy. Many fungal hyphae were found in the left parietal lesion, and the final pathological diagnosis of intracranial mucormycosis. After craniotomy and an entire course of treatment with liposomal amphotericin B, the patient was completely cured of both intracranial and pulmonary occupying lesions. We hope that this case experience will help expand neurosurgeons' differential diagnosis and treatment of such diseases.

1. Introduction

Mucormycosis is a very aggressive and rare fungal disease, with a case of lung cancer first reported by Arnold Paltauf in 1885 [1]. Hematological malignancies, uncontrolled diabetes mellitus, penetrating brain trauma, and prolonged ICU residence are the most common causative factors. The mortality rate of patients with mucormycosis remains high, ranging from 24% to 49% [2]. There are no standardized tests to detect mucorales-specific antigens, so it is likely to be under-detection by staff and consequently delayed treatment [3]. Moreover, some mucormycosis infections can mimic tumor-like lesions, leading to clinical misdiagnosis [4]. For instance, in the central nervous system, they may masquerade as skull base tumors by invading the skull base through the spinal cavity [5,6]. However, it is rare to have both pulmonary and cerebral mucormycosis infections [7], especially in patients without obvious immunocompromised etiologies.

We found a rare clinical case of a patient with both pulmonary and cerebral mucormycosis. He was misdiagnosed with brain metastases from lung cancer due to his imaging features and a series of negative laboratory tests. After adequate treatment, the patient was cured, and we hope that the patient here will cause clinical neurosurgeons to maintain a high level of attention to intracranial mucormycosis.

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2. Case report

A 66-year-old man with a past medical history of excessive smoking and thyroid nodules presented progressive right-sided weakness starting 3 days prior to the visit, with no headache, vomiting, unconsciousness or other symptoms such as seizures. He had no medical history of special conditions such as hypertension, diabetes, heart disease or organ transplants, and no intravenous drug use and steroid administration. On admission, physical examination demonstrated right hemiplegia (MRC 0/5) and cortical motor aphasia. Laboratory tests showed an increase in WBCs ($14.53*10^9$/L, the normal range is $3.5–9.5*10^9$/L), an increase in the ratio of neutrophils (79%, normal range is 40–75%), and average blood glucose (5.82mmol/L, normal range is 3.9–6.1mmol/L) and other indicators. The head MRI showed a left parietal occupying lesion that presented long T1 and T2 signals with severe edema (Fig. 1. A). Contrast-enhanced MRI T1 sequence showed circular enhancement considering tumors or abscesses (Fig. 1. B). A chest CT scan revealed a substantial mass in his left lung with pleural invasion (Fig. 1. CD).

Since the patient has a long-term smoking history, the possibility of brain metastasis from lung cancer should be considered. However, most serum tumor markers were regular. Computed tomography-guided needle biopsy of the lung revealed only inflammatory cell infiltrates and fibrin-like exudates, and no cancer cells were found (Fig. 1. E). An intracranial lesion was localized in the left parietal lobe and neurological deficits were evident. The patients signed a written consent and accepted craniotomy for occupying lesion resection. During the operation, the lesion was a jelly-like substance (Fig. 1. F). Many fungal hyphae were found and removed from the left parietal lesion, and pathological examination confirmed intracranial mucormycosis (Fig. 1.GH).

The acute management of intracranial mucormycosis involves surgical debridement and controlling elevated intracranial pressure. According to the guidelines, liposomal amphotercin B is recommended as the first-line antifungal treatment of mucormycosis in adult patients [2]. Analysis of cerebrospinal fluid from a lumbar puncture before antifungal treatment showed cell count of cerebrospinal fluid was 322*106/L (normal range: 0–10*106/L) which predominated by lymphocyte (64%), the total protein was 950 mg/L (normal range: 150–450 mg/L) and chloride was 109mmol/L (normal range: 110–120 g/L). Then, he was given 5 mg/kg liposomal amphotercin B intravenously for 6 weeks until CSF pleocytosis resolution (9 cells/mm^3). A review of the head MRI three weeks postoperatively showed that the lesion was replaced by cerebrospinal fluid and that the peripheral edema was reduced (Fig. 1. IJ).

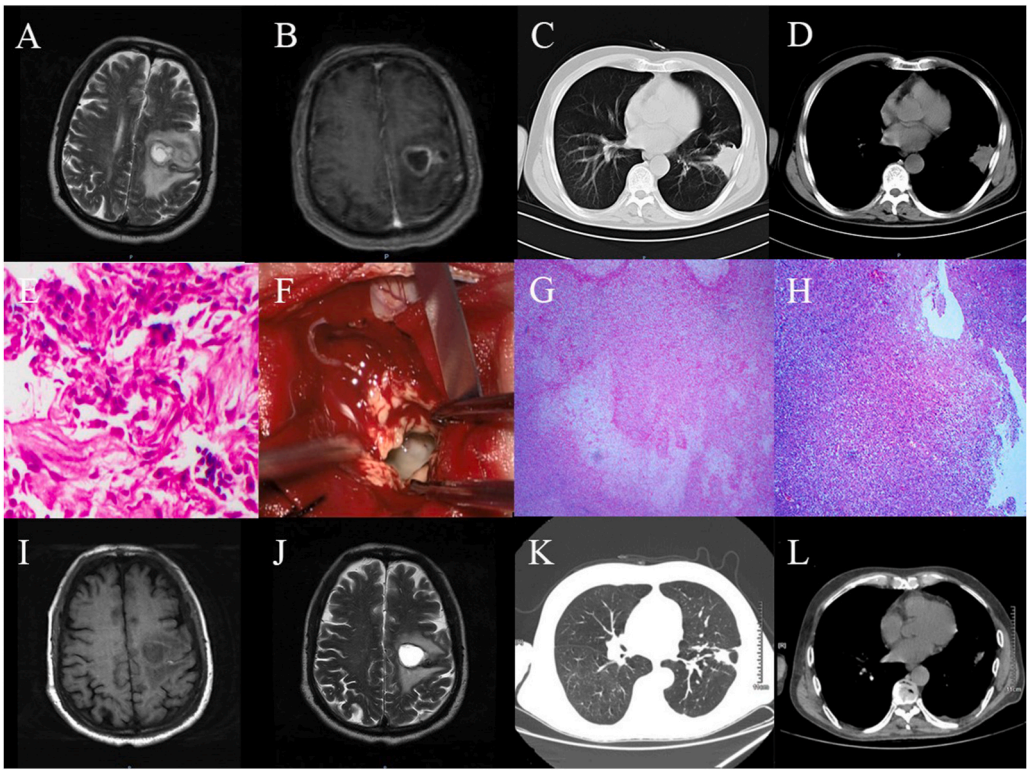

Fig. 1. Head MRI, chest CT scan, histopathology of lung mass and naked-eye sight of intracranial lesions.
(AB) The left parietal occupying lesion presented long T2 and high Flair signals with surrounding severe edema. Contrast-enhanced MRI T1 sequence showed circular enhancement. (CD) Chest CT scan showed an irregular mass with lobulation, spiculation, pleural invasion located in the left lower lung. (E) Lung biopsy revealed only inflammatory cell infiltrates and fibrin-like exudates, and no cancer cells were found. (F) Jelly-like substance was observed during the left parietal occupying lesion resection (black arrow). (GH) Histopathology of the cerebral mucormycosis showed massive fungal mycelium. (IJ) postoperatively head MRI showed that the lesion was replaced by cerebrospinal fluid and that the peripheral edema was reduced. (KL) Follow-up chest CT in the 6th week after discharge showed that the lung mass was eventually absorbed, leaving some fibrous strips present.

Although a chest CT review after 6 weeks showed a shrinking of the lung lesion, the lesion had not disappeared. The patients were discharged after partial recovery of hemiparesis (MRC 4/5) and speech (improved fluency) and were started on oral posaconazole 2 days before discharge until 6 weeks after discharge. Follow-up chest CT in the 6th week after discharge showed that the lung mass was eventually absorbed, leaving some fibrous strips present (Fig. 1. KL).

3. Discussion

The patients/participants provided their written informed consent to participate in this study. For solitary intracranial MRI ring-enhancing lesions, we should consider the following differential diagnosis based on the clinical symptoms: Glioblastoma, multiple sclerosis (MS), brain abscess, brain metastatic tumors, intracranial tuberculoma, toxoplasmosis and so on. Our patient presented with both left lung and intracranial occupying masses without fever, so we first considered the diagnosis of brain metastasis from lung cancer. However, the diagnosis of cerebral mucormycosis was confirmed in the final histopathological examination.

Mucormycosis is a highly invasive opportunistic fungal infection that occurs almost exclusively in immunocompromised hosts [1]. Intracranial mucormycosis is usually associated with intracranial spread of fungal sinusitis [8]. Invasive central nervous system mucormycosis were characterized by prominent infarcts (94%), angioinvasion (100%) and prominent perineural invasion (90%) in biopsies [3]. If intracranial mucinosis is considered as a suspicious diagnosis, histopathological examination is urgently needed. Liposomal amphotericin B efficacy is dose-dependent which could reach higher lung concentrations, better fungal tissue clearance and more effective in reducing brain fungal burden than amphotericin B lipid complex [2]. Posaconazole was used as remedial treatment to Mucor at a high dose of 200 mg four times a day. In our study, although the patient's lung biopsy didn't confirm the diagnosis of mucormycosis, the patient was sensitive to liposomal amphotericin B and the lung lesions disappeared at follow-up after posaconazole treatment, which should be considered also as a mucormycosis according to the monism of the disease.

Besides patients with the typical risk factors described above, mucormycosis has also been reported to occur in seemingly healthy populations, especially in the elderly. But we don't know if these patients are really "healthy". In our study, the patient was negative for rheumatologic, anti-HIV and onconeuronal antibodies. Hormone concentrations, glycosylated hemoglobin, randm blood glucose were almost normal. He had no medical history of diabetes, organ transplants, intravenous drug use or steroid administration. Therefore, we speculate whether there are other causes of mucormycosis that we did not find in this patient. Interestingly, his lymphocyte flow cytometry results showed normal B-cell and T-cell counts but extremely low proportion and absolute count of $CD16^{+}CD56+$ NK cells, respectively were 3.3% (normal range:7.92–33.99%) and 44/μL (normal range:210–1514/μL). NK cells participate in innate immunity which plays a major role in the fight against cancer cells, aging cells, microbial infection [9]. This result indicates that the patient may have an inherent immunodeficiency. However, we do not know if this was the cause of both pulmonary and cerebral mucormycosis in this patient.

4. Conclusion

Although mucinosis usually occurs in immunocompromised patients, its highly invasive nature makes it important to remain highly alert to seemingly normal patients, especially in the elderly. We hope that this patient will provide some inspiration and guidance to physicians managing intracranial mucormycosis.

Declarations

Author contribution statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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