INTERNAL MEDICINE

□ CASE REPORT □

Surgical Resection during Chemotherapy of Pulmonary Cryptococcoma in a Patient with Cryptococcal Meningitis

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Abstract

We herein report the case of a 72-year-old-man with pulmonary cryptococcoma along with cryptococcal meningitis who underwent surgery for pulmonary lesions while receiving chemotherapy. We noted two major clinical issues. First, the presence of pulmonary cryptococcoma had a detrimental influence on the cryptococcal meningitis. Second, resolution of the pulmonary cryptococcoma through antifungal therapy had a beneficial influence on the recovery from cryptococcal meningitis. As observed in the current case with pulmonary and meningeal cryptococcosis, surgery for pulmonary cryptococcoma with continuous antifungal treatment should be considered for cases where the symptoms respond poorly to antifungal therapy and radiographic abnormalities persist.

Key words: cryptococcal meningitis, pulmonary cryptococcoma, surgical resection, symptom responding poorly to antifungal therapy, persistent radiographic abnormality

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Introduction

Cryptococcosis is a global invasive mycosis associated with significant morbidity and mortality (1). The 2010 Infectious Diseases Society of America guidelines described the protocol for the management of cryptococcosis (1). However, the management of pulmonary cryptococcosis in the presence of cryptococcal meningitis has not been described. Several reports published years ago described surgical resection of pulmonary cryptococcoma in the presence of cryptococcal meningitis (2, 3), but no recent case reports or large-scale studies have been published. We herein report a case of surgical resection and chemotherapy of pulmonary cryptococcoma in an elderly patient with cryptococcal meningitis.

Case Report

A 72-year-old man with an old infarction of the left caudate nucleus and putamen developed a slight fever. After 1 month, he experienced headaches; subsequently, his level of consciousness declined, and he was admitted to our hospital. He had no history of immunodeficiency diseases or diabetes mellitus, and he had never gone abroad. As he was engaged in a profession related to forestry, he often visited mountainous regions but did not breed any animals. A neurological examination indicated a reduced consciousness (Glasgow coma scale; E4 V4 M5), meningeal irritation, hyperreflexia of all four extremities, and a positive Babinski response. A blood examination revealed normal levels of tumor markers, negative results for human immunodeficiency virus (HIV) antibody testing, increased β-D glucan levels (54.5 pg/mL; reference range, <20.0 pg/mL), and positive results for cryptococcus antigen testing. A cerebrospinal fluid (CSF) examination indicated a cell count of 9/μL (all lymphocytes); furthermore, the CSF protein level was 535 mg/dL (reference range, 10-40 mg/dL), and the CSF glucose level was 4 mg/dL (reference range, 50-75 mg/dL). An India ink smear of the CSF yielded a positive result, and cryptococcus antigen (glucuronoxylomannan) was detected. A mycological culture of the CSF indicated the presence of *Cryptococcus neoformans*.

Brain magnetic resonance imaging (MRI) revealed an old infarction of the left caudate nucleus and putamen but no abnormal enhancement (Figure A). Chest radiography and

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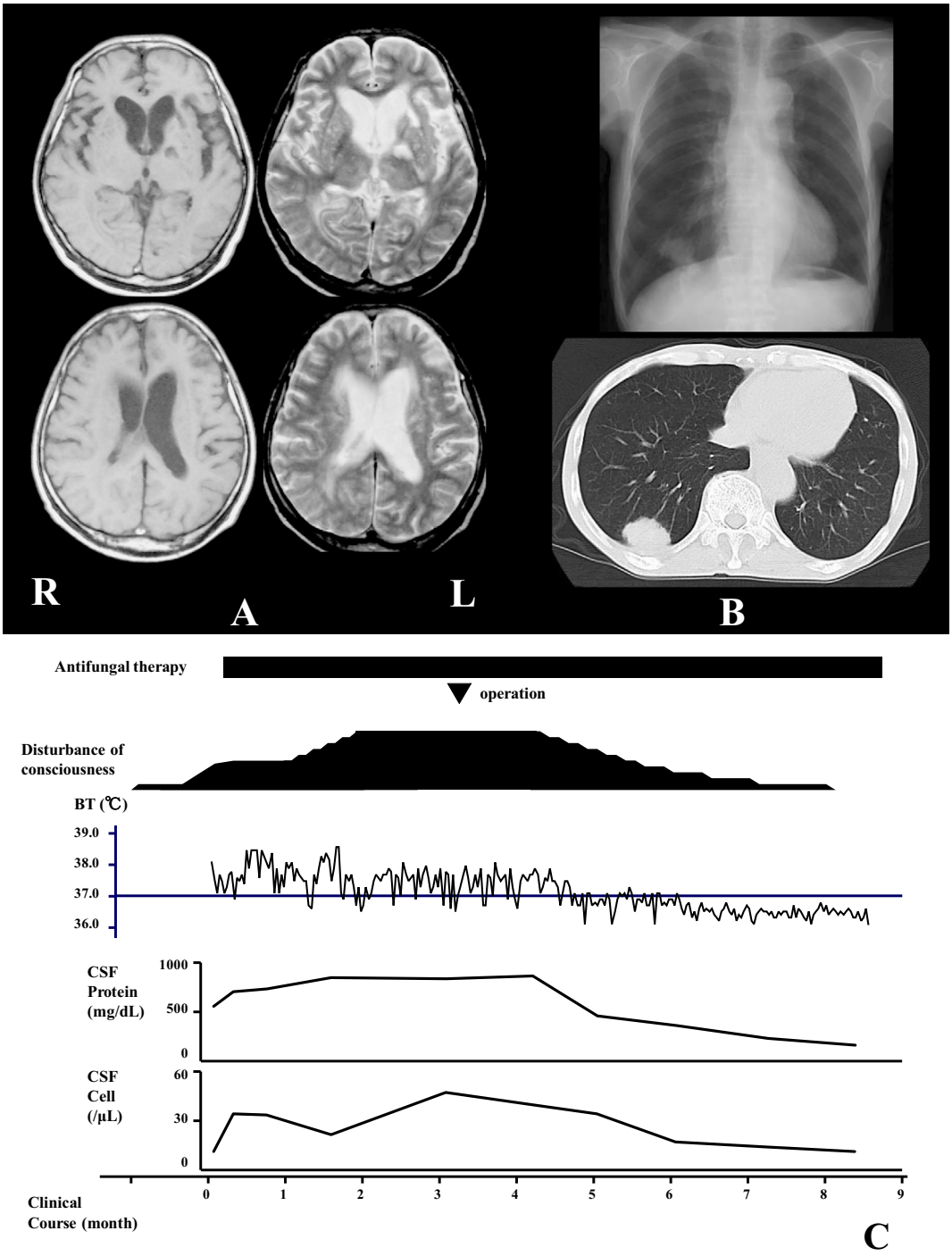

Figure. **The imaging findings for the present case. (A) Brain magnetic resonance imaging (T1-weighted image and T2-weighted image) showed an old infarction of the left caudate nucleus and left putamen but no abnormal enhancement. (B) Chest radiography and computed tomography revealed a solitary mass shadow in the right lower lung. (C) Clinical course. BT: body temperature, CSF: cerebrospinal fluid**

computed tomography (CT) revealed a solitary mass shadow in the right lower lung (Figure B). Bronchoscopy indicated pulmonary cryptococcoma. Based on these findings, the patient was diagnosed with cryptococcal meningitis along with pulmonary cryptococcoma.

As amphotericin B and flucytosine could not be administered due to their side effects, fluconazole (400 mg/day) was given instead. Despite the use of antifungal therapy for 3 months, the patient's symptoms persisisted, including his fever and disturbance of consciousness, and the CSF examination results worsened (Figure C). Because antifungal therapy for 3 months could not improve the radiographic abnormality of the pulmonary granuloma, the possibility that the pulmonary granuloma might be a malignant lesion remained. Therefore, surgery was considered and performed for the pulmonary granuloma. Histological and mycological exami-

nations revealed the presence of *C. neoformans* in specimens removed during surgery. Thereafter, antifungal therapy (fluconazole) for 6 months improved his symptoms and the CSF examination results. Brain MRI continued to show an old infarction, but no other abnormal findings were noted.

Discussion

We noted two major clinical issues. First, the presence of pulmonary cryptococcoma had a detrimental influence on the cryptococcal meningitis. Second, the resolution of the pulmonary cryptococcoma through antifungal therapy had a beneficial influence on the recovery from cryptococcal meningitis.

The 2010 Infectious Diseases Society of America guidelines described the management protocol for cryptococcosis, with specific regimens recommended for three high-risk groups: HIV-infected individuals, organ transplant recipients, and non-HIV-infected and non-transplant individuals (1). In non-HIV-infected and non-transplant individuals, the treatment strategy for cryptococcal meningitis includes antifungal therapy, primarily with amphotericin B and flucytosine (1). Furthermore, among non-immunosuppressed patients with pulmonary and non-meningeal cryptococcosis, antifungal therapy should be initially administered, and surgery should be considered for cases with persistent radiographic abnormalities and symptoms that are unresponsive to antifungal therapy (1). For patients with isolated pulmonary cryptococcosis, surgery has two major roles (2-5). The first is to rule out malignancy by surgical excision of the pulmonary nodule (1). The second role concerns patients with persistent focal radiographic abnormalities despite conventional antifungal therapy; in this population with persistent symptoms or signs, some authorities have suggested surgical resection rather than continuing long-term antifungal therapy (1). However, the management of pulmonary cryptococcoma with cryptococcal meningitis has not yet been described.

Several reports published years ago described the surgical resection of pulmonary cryptococcoma in the presence of cryptococcal meningitis. One case report describes the successful treatment of two patients with co-existing pulmonary and meningeal cryptococcosis with pulmonary resection and chemotherapy (6). Another report describes a patient with combined pulmonary and neural cryptococcosis who was successfully managed with pulmonary resection and chemotherapy (7). Both cases have progressed favorably since the operation. Surgery for pulmonary granuloma may be effective as a radical cure for the pulmonary lesion as well as for preventing further dissemination to the brain. Although no similar cases have been reported recently, surgery for such cases may be a therapeutic option.

In the present case, the persistent radiographic abnormalities under chemotherapy suggested the possibility that the pulmonary granuloma might be a malignant lesion; therefore, surgery was performed. Although no clear standard has been established of surgical indications for pulmonary cryptococcoma in cases with cryptococcal meningitis, as in the present case, surgery for the pulmonary granuloma along with continuous antifungal treatment should be considered for patients with persistent radiographic abnormalities.

The authors state that they have no Conflict of Interest (COI).

References

1. Perfect JR, Dismukes WE, Dromer F, et al. Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the infectious diseases society of america. Clin Infect Dis **50**: 291-322, 2010.
2. Aberg JA, Mundy LM, Powderly WG. Pulmonary cryptococcosis in patients without HIV infection. Chest **115**: 734-740, 1999.
3. Pappas PG, Perfect JR, Cloud GA, et al. Cryptococcosis in human immunodeficiency virus-negative patients in the era of effective azole therapy. Clin Infect Dis **33**: 690-699, 2001.
4. Nadrous HF, Antonios VS, Terrell CL, et al. Pulmonary cryptococcosis in nonimmunocompromised patients. Chest **124**: 2143-2147, 2003.
5. Igai H, Gotoh M, Yokomise H. Computed tomography (CT) and positron emission tomography with [^{18}F] fluoro-2-deoxy-D-glucose (FDG-PET) images of pulmonary cryptococcosis mimicking lung cancer. Eur J Cardiothorac Surg **30**: 837-839, 2006.
6. Inoue N, Uozumi T, Yamamoto T, et al. Treatment of cryptococcal meningitis with pulmonary granuloma. J Neurol **231**: 109-111, 1984.
7. Sa'adah MA, Shakir RA, Jadaa SI, Bezjak V, Araj GF. Surgery in combined pulmonary and neural cryptococcosis. J Infect **15**: 263-268, 1987.