Standard antifungal therapy for pulmonary cryptococcosis to improve prognosis

Masaya Taniwaki and colleagues[1] report an interesting case of pulmonary cryptococcosis mimicking lung cancer. The patient was confirmed to have pulmonary cryptococcosis through both bronchoscopic examination and CT-guided biopsy. After antifungal treatment for several days, the mass in the lungs had not decreased in size and the patient refused to continue therapy, continuing only with observation. After a discussion about the antifungal therapy given and a review of the literature, we concluded that the effect of therapy might have been more obvious if standard treatment had been given.

The clinical practice guidelines for cryptococcal disease, updated in 2010 by the Infectious Diseases Society of America,[2] are the most authoritative source on crypotoccal disease. According to the guidelines, once a diagnosis of cryptococcal disease has been confirmed, the clinician should establish whether or not the patient is in a state of immunosuppression, which is not mentioned in the Clinical Picture. If the patient is not immunosuppressed, they should receive oral fluconazole therapy (400 mg per day) for 6–12 months, whereas if the patient is immunosuppressed, a more complex therapy should be given. However, in this case, the patient received oral fluconazole 200 mg daily for 9 days, which is a lower dose and shorter course than recommended. If the patient had received a more standard therapy of fluconazole initially, in terms of dose and course, the effect might have been more obvious and he might have decided to continue treatment.

It is difficult to observe remission of pulmonary cryptococcosis on imaging in only a few weeks. We suggest that the authors contact the patient to persuade him to continue antifungal treatment for at least 6 months, until the mass shadow improves, instead of observation only, to guarantee the treatment effect.

We declare no competing interests.

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1 Taniwaki M, Yamasaki M, Ishikawa N, Kawamoto K, Hattori N. Pulmonary cryptococcosis mimicking lung cancer. *Lancet Infect Dis* 2019; **19:** 1033.
2 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* 2010; **50:** 291–322.

Authors' reply

We thank Boyou Zhang and colleagues for their interest in and comments on our Clinical Picture.[1] To the best of our knowledge, our patient was not immunosuppressed because none of the following causes of immunosuppression were present: HIV infection, human T-cell leukaemia virus type 1 infection, immunosuppressive drugs, malignant diseases, diabetes, splenectomy, renal disease, or liver disease.

We treated the patient for cryptococcosis according to the Japanese national guidelines.[2] We first administered oral fluconazole 200 mg daily for 9 days, but this did not lead to improvement on chest radiography. Because we considered his infection to be severe, we then administered oral voriconazole 600 mg daily for 1 day, and then 400 mg daily for 3 days.

It has been reported that cryptococcal infection can lead to granuloma formation.[3] It has also been reported that cryptococcosis can cause organising pneumonia.[4] In the present case, granuloma formation and organising pneumonia might have been present when mass enlargement was observed on CT scan. In cryptococcal disease, fluconazole resistance has been reported.[5] The patient might have had fluconazole-resistant cryptococcal infection. Cryptococcosis with granuloma and organising pneumonia might gradually improve only after treatment with several antifungal agents.

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VIVIANE study of HPV vaccination

Since the 2018 Cochrane meta-analysis on human papillomavirus (HPV) vaccination[1] quotes the VIVIANE publication,[2] we found it interesting to analyse some results of this study on the most relevant clinical endpoints—namely, cervical intraepithelial neoplasia grade 2 or