Enclosed and silent growth of chronic cryptococcal meningitis

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Description

A man in his 70s with a history of stable, idiopathic pulmonary fibrosis and without HIV infection visited our hospital for transient paraesthesia in the left extremities. Results of the neurological examination were normal, except for finger escape and Babinski sign on the left. Sensory disturbance and meningism were negligible. He had a history of breeding zebra finch for 3 years before the onset. Findings on chest CT were unremarkable. Brain MRI revealed abnormal signals on the right fronto-parietal meninges (figure 1A). Although the physician recommended further examinations, the patient refused because the paraesthesia occurred rarely and disappeared abruptly.

He revisited our department 6 months later, as he occasionally exhibited transient paraesthesia every month. Neurological findings did not deteriorate. However, the brain MRI region gradually enlarged during the follow-up period (figure 1B). The work-up for malignancy and autoimmune diseases had unremarkable findings. His cerebrospinal fluid (CSF) cytology was negative, and a lip biopsy revealed negative findings. His cerebrospinal fluid (CSF) cytology was negative, and a lip biopsy revealed negative findings for IgG4-related disease. Although mild CSF pleocytosis (10 cells/µL) was visible, Gram and acid-fast staining and India ink preparation were negative. No growths were detected on repeat CSF cultures for bacterial, acid-fast bacilli and fungi. Repeat cryptococcal antigen tests of serum and CSF samples were negative. Thus, a right frontal meningeal and brain biopsy was performed (figure 2). We made a diagnosis of cryptococcal meningitis. Intravenous administration of antifungal drugs (amphotericin B and 5-fluorocytosine) ameliorated the transient paraesthesia in the left extremities, and the abnormal signals on the brain MRI region gradually ceased. Cryptococcal antigen tests were still negative following treatment.

The cryptococcal antigen test is usually highly reliable, as serum cryptococcal antigen has sensitivities of 99.7% and 98.8% and CSF cryptococcal antigen has specificities of 94.1% and 99.3%. Additionally, concordance between CSF cryptococcal antigen test and CSF culture is excellent. However, antigen tests occasionally show false-negative results, particularly in immunocompromised cases, for example, a case with a postzone phenomenon (a false-negative test caused by excessive antigen), with cryptococcal antigenemia and symptomatic meningitis but without microbiological evidence of CSF infection, or with Cryptococcus gattii meningoencephalitis. However, our patient does not have HIV infection and the postzone phenomenon was negligible because cryptococcal antigen tests were still negative following the initial treatment. A histopathological meningeal biopsy revealed cryptococcosis; the fungal bodies that were trapped by a necrotising granuloma were visible (figure 2A). Thus, a necrotising granuloma trapped the fungal bodies in the Th1 cell immune response background, resulting in mild chronic meningitis with false-negative laboratory results. We considered that Cryptococcus entered via the airway without causing an infected lung region and reached the intracranial area in our case. Thus, the cryptococcal antigen test may give false-negative results in non-HIV cases. Although not within the scope of this study, capsule-deficient C. neoformans (the susceptibility of the capsule-deficient form to phagocytosis) could also give false-negative results in cryptococcal antigen tests in a non-HIV case.

Figure 1 Brain MRI fluid attenuated inversion recovery (FLAIR) image (A) at first visit and (B) 6 months later.

Figure 2 (A) H&E stain showing a necrotising granuloma in the subarachnoid space that entraps the fungal bodies (black arrows). (B) Positive for Alcian blue staining and periodic acid-Schiff staining.
Images in...

Patient’s perspective

Following the initiation of antifungal therapy, my symptoms improved.

Learning points

► Cryptococcal antigen test may give false-negative results in non-HIV cases.
► Necrotic tissue enclosing fungal bodies may result in false-negative laboratory results.

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Contributors

RK and MN treated the patient, analysed the data and drafted the manuscript. SN designed and conceptualised the study, analysed the data and drafted the manuscript, including intellectual content. HM interpreted the data and revised the manuscript for intellectual content.

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