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CASE REPORT

Simultaneous cryptococcal and tuberculous meningitis in a patient with systemic lupus erythematosus

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Simultaneous central nervous system (CNS) infection with *Cryptococcus* and tuberculosis (TB) is very rare. Despite improved therapeutic options, treatment of CNS cryptococcosis is still difficult and needs invasive treatment modalities, such as intrathecal or intraventricular amphotericin B, in refractory cases. We describe a patient with systemic lupus erythematosus diagnosed with simultaneous cryptococcal and TB meningitis who had a poor response to intravenous liposomal amphotericin B and fluconazole, but was successfully treated with intraventricular amphotericin B, in addition to anti-TB therapy.

Introduction

The etiology of central nervous system (CNS) infections in immunosuppressed patients varies widely. Opportunistic infections due to *Listeria monocytogenes*, *Mycobacterium tuberculosis*, or fungi such as *Cryptococcus* spp. should be considered in the differential diagnosis of meningitis in patients with systemic lupus erythematosus (SLE) receiving immunosuppressive agents.[1] Simultaneous CNS cryptococcosis and tuberculosis (TB) is a rare condition in immunosuppressed patients and even more rare in immunocompetent individuals.

Treatment of cryptococcosis has improved with the advent of polyene antifungal drugs. However, treatment may be difficult and invasive modalities may be needed in refractory cases of CNS cryptococcosis.[2] Here we present a rare case of CNS cryptococcal and TB infection.

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Case report

A 45-year-old woman with SLE was admitted to our clinic with headache, fever, nausea, vomiting, incontinence, somnolence, and convulsions. She had been diagnosed with SLE 10 years before on presentation with a malar rash and polyarthritis. She had lupus involvement of the kidney, but no CNS involvement. She was taking steroids (10 years, approximately 16 mg methylprednisolone/day), hydroxychloroquine and methotrexate (for 1 year; stopped 1 year before admission), and non-steroidal anti-inflammatory drugs (as needed). She had been on methylprednisolone treatment (16 mg/day) for the last 2 years. Her SLE *disease activity index (*SLEDAI*)* score was 10 on admission. Headache, nausea, and vomiting were present for the previous 4 months. During the previous 2 months, fever, incontinence, somnolence, and convulsions were added to the clinical spectrum. The patient was conscious with limited cooperation; she had neck stiffness and dysarthric speech. The bilateral muscular strength of her lower extremities was 3/5 and her deep tendon reflexes were hypoactive. Cranial magnetic resonance imaging (MRI) demonstrated lesions in the basal ganglia and hydrocephalus. Laboratory results for whole blood were as follows: leukocytes, 6200 /mm^3; hemoglobin, 12 g/dL; platelets, 324,000 /mm^3; C-reactive protein (CRP), 170 mg/L (normal range 0—5); erythrocyte sedimentation rate, 100 mm/hour; and anti-HIV, negative. CSF results were as follows: leukocytes, 160 /mm^3 (80% lymphocytes); protein, 174 mg/L; and glucose, 20 mg/dL (simultaneous blood glucose, 144 mg/dL). Empirical anti-TB therapy (rifampin + isoniazid + pyrazinamide + ethambutol) was initiated for a probable diagnosis of TB meningitis. One week later, acid-fast bacilli were detected in a CSF sample inoculated into mycobacterium growth indicator and were identified as *M. tuberculosis* complex using polymerase chain reaction (PCR). The isolate was found to be sensitive to all of the major anti-TB drugs tested.

Although appropriate therapy was administered, the clinical state of the patient deteriorated. She lost consciousness during Week 2 of anti-TB therapy. Her Glasgow coma scale score was 10/15 and left hemiparesis developed. A repeat CSF examination on Day 15 of therapy revealed capsulated yeasts using Indian ink staining, and *Cryptococcus neoformans* was isolated. Although liposomal amphotericin B (5 mg/kg/day) was added to treat her cryptococcal meningitis, the patient became unresponsive to external stimuli by Week 3 of antifungal therapy. After progression of hydrocephalus was detected by cranial MRI, an external ventricular drain was applied to control CSF pressure and fluconazole was added to liposomal amphotericin B as flucytosine is not available in our country. Repeated CSF cultures became sterile on this combination therapy. The patient showed some improvement and recovered minimal consciousness after 1 month of combination antifungal therapy, and CSF cultures were negative; however, her fever persisted and MRI revealed ventriculitis (Fig. 1). Although it did not fulfill the definition of persistent infection, we decided to add intraventricular liposomal amphotericin B based on the insufficient clinical response to treatment. Following three doses of intraventricular liposomal amphotericin B (1 mg/day every 72 hours), her fever

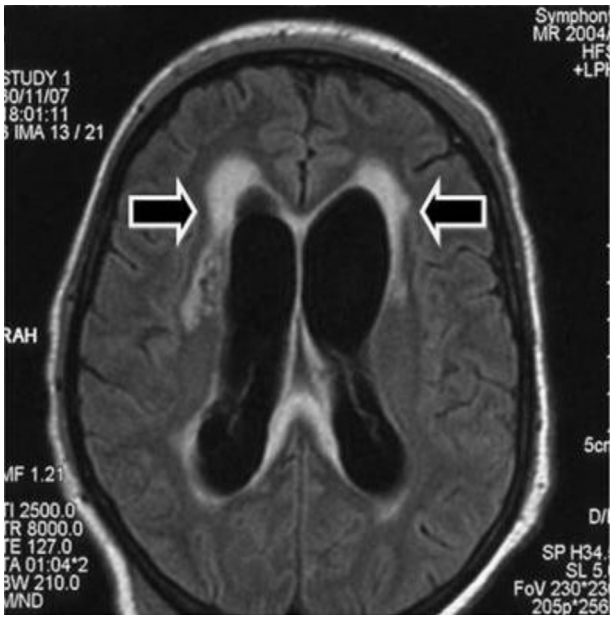

Figure 1. Magnetic resonance image demonstrating bilateral ventricular ependymal contrast enhancement indicative of ventriculitis (arrows).

subsided, CRP levels decreased, and radiological improvement (Fig. 2) was observed. Repeated HIV tests remained negative. Systemic liposomal amphotericin B was stopped in Week 14 and oral fluconazole was discontinued after 6 months of treatment. Anti-TB treatment was continued for 1 year. The patient was referred to a physical therapy unit for rehabilitation. Two years after completion of the therapy, she was mobile with support and had only residual speech impairment.

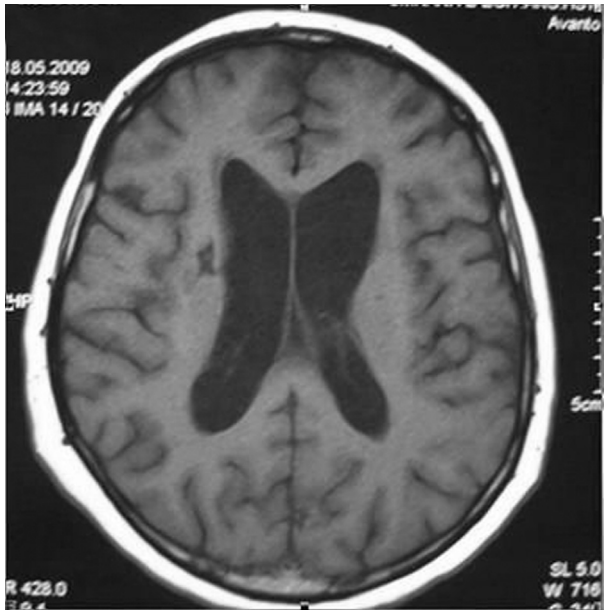

Figure 2. MRI demonstrating complete regression of ventriculitis after intraventricular amphotericin B.