Title
Cryptococcus gattii Meningitis Complicated by Listeria monocytogenes Infection

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Among immunocompetent persons, 1% of individuals are susceptible to Cryptococcus gattii infection, commonly necessitating longer courses of treatment. We report a fatal case of C. gattii and Listeria monocytogenes co-infection in an immunocompetent woman with cryptococcomas.

The patient was a previously healthy 23-year-old Hispanic woman who was hospitalized in 2009 after weeks of headache and recent-onset diplopia. Lumbar puncture revealed elevated opening pressure of 52 cm H₂O; elevated leukocytes (1,030 cells/µL: 31% neutrophils, 55% lymphocytes, 14% monocytes); elevated protein concentration (117 g/L); and decreased glucose concentration (30 mg/dL). Cerebrospinal fluid (CSF) cryptococcal antigen (CrAg) titer was 1:64, and culture grew C. gattii. HIV antibody test result was negative. Magnetic resonance imaging of the brain demonstrated scattered enhancing round lesions within the cerebrum and cerebellum, consistent with cryptococcomas. The patient was prescribed intravenous amphotericin B (1 mg/kg/d) and intravenous fluconazole (2 g/6 h) (Table); after 5 days of therapy, culture of a repeat lumbar puncture sample was negative. The patient was then given intravenous liposomal amphotericin at 7 mg/kg, and after a 14-day induction period she was discharged with instructions to take fluconazole orally (400 mg 2×/d) and to continue amphotericin B infusions (3×/wk) (Table).
One week after hospital discharge, the patient experienced recurrent headache and low-grade fever and was readmitted. Repeat lumbar puncture indicated an opening pressure of 46 cm H₂O but improvement of all other clinical parameters (Table). CSF CrAg titer was 1:8 and culture result was negative (38). Corticosteroids are commonly used to treat immune reconstitution inflammatory syndrome. Although recently, they have been associated with adverse outcomes (7). As indicated by this case, corticosteroids remain a risk factor for secondary infection with several pathogens, including *Listeria*. No epidemiologic exposure to *Listeria* was identified for this patient.

*C. gattii* infection has been reported in 8 states, including California (3); we have found the pathogen in the soil south of Los Angeles, California, particularly in association with Canary Island pines and sweet gum trees (8). Some patients with *C. gattii* infection have autoantibodies to amphotericin B; *AMP*, ampicillin; *CrAg*, cryptococcal antigen; *CRO*, ceftiraxone; *DEX*, dexamethasone; *FLZ*, fluconazole; *L-AMB*, liposomal amphotericin; *M*, Monday; *NA*, not available; *q*, every; *TMP/SMX*, trimethoprim/sulfamethoxazole; *W*, Wednesday.

**Table.** Clinical events, management, and parameters for patient with *Cryptococcus gattii* meningitis complicated by *Listeria monocytogenes* infection

<table>
<thead>
<tr>
<th>Clinical event (day)</th>
<th>Therapy (days)</th>
<th>Opening pressure, cm H₂O (day)</th>
<th>Leukocyte count, cells/μL (day)</th>
<th>Protein, g/L (day)</th>
<th>Glucose, g/L (day)</th>
<th>CrAg titer (day)</th>
<th>Culture result (day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1–15: induction therapy</td>
<td>AMB 1 mg/kg (1–4); 5FC 2 g q6h (1–14); L-AMB 7 mg/kg (5–14)</td>
<td>52 (1), 12 (12)</td>
<td>1,030 (1), 123 (12)</td>
<td>117 (1), 104 (12)</td>
<td>30 (1), 29 (12)</td>
<td>1:64 (1)</td>
<td><em>Cryptococcus gattii</em> (1), negative (12)</td>
</tr>
<tr>
<td>Days 16–30: discharge, outpatient infusion, readmission</td>
<td>L-AMB 7 mg/kg M, W, F (15–22); FLZ 400 mg q12h (15–22); L-AMB 5 mg/kg (23–30); FLZ 600 mg q12h (23–30); 5FC 3 g q6h (23–30)</td>
<td>46 (23)</td>
<td>111 (23)</td>
<td>81 (23)</td>
<td>64 (23)</td>
<td>NA</td>
<td>Negative (38)</td>
</tr>
<tr>
<td>Days 31–45: inpatient therapy</td>
<td>L-AMB 5 mg/kg (31–45); FLZ 600 mg q12h (31–45); 5FC 3 g q6h (31–45)</td>
<td>44 (38)</td>
<td>17 (38)</td>
<td>66 (38)</td>
<td>64 (38)</td>
<td>NA</td>
<td>Negative (38)</td>
</tr>
<tr>
<td>Days 46–60: inpatient therapy</td>
<td>L-AMB 5 mg/kg (46–60); FLZ 600 mg q12h (46–60); DEX 2 mg q6h (46–60)</td>
<td>35 (48)</td>
<td>18 (48)</td>
<td>25 (48)</td>
<td>85 (48)</td>
<td>NA</td>
<td>Negative (48)</td>
</tr>
<tr>
<td>Days 61–75: discharge and outpatient infusion</td>
<td>L-AMB 5 mg/kg (61–65); FLZ 600 mg q12h (61–75); DEX 2 mg q6h (61–75); L-AMB 7 mg/kg M, W, F (66–75)</td>
<td>13 (63)</td>
<td>8 (63)</td>
<td>28 (63)</td>
<td>91 (63)</td>
<td>1:4 (63)</td>
<td>Negative (63)</td>
</tr>
<tr>
<td>Days 76–83: readmission/coma (80); death (83)</td>
<td>L-AMB 7 mg/kg M, W, F (76–79); DEX 2 mg q12h (76–79); FLZ 600 mg q12h (76–83); CRO 2 gm q12h (80–83); AMP 2 gm q4h (80–83); TMP/SMX 320–1,600 mg (2 double-strength tablets) q6h (80–83)</td>
<td>&gt;55 (80)</td>
<td>1,010 (80)</td>
<td>258 (80)</td>
<td>17 (80)</td>
<td>1:4 (80)</td>
<td><em>Listeria monocytogenes</em> (80)</td>
</tr>
</tbody>
</table>

*5FC, fluconazole; AMB, amphotericin B; AMP, ampicillin; CrAg, cryptococcal antigen; CRO, ceftiraxone; DEX, dexamethasone; FLZ, fluconazole; L-AMB, liposomal amphotericin; M, Monday; NA, not available; q, every; TMP/SMX, trimethoprim/sulfamethoxazole; W, Wednesday.*
granulocyte–macrophage (GM) colony-stimulating factor (9). Although these autoantibodies have not been reported in patients with *Listeria* infections, susceptibility to infection caused by this bacterium is increased in GM–colony-stimulating factor −/− mice (10). Autoantibodies against GM–colony-stimulating factor or perhaps other cytokines might have impaired the patient’s host defense against these organisms; unfortunately, our report is limited by lack of serum for further testing.

This case demonstrates the difficulties of managing patients with *C. gattii* infection and an unusual co-infection with *L. monocytogenes*. Initiation of corticosteroids for the management of severe cryptococcal disease should be undertaken with caution. The differential diagnosis for worsening cryptococcal disease should include acute or subacute bacterial meningitis, particularly when the patient is receiving corticosteroids for the management of immune reconstitution inflammatory syndrome or associated complications.

Acknowledgments

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References


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**Melioidosis in Travelers Returning from Vietnam to France**

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To the Editor: Melioidosis, a potentially fatal infectious disease, occurs predominantly across much of Asia and in northern Australia because of the soil and water bacterium *Burkholderia pseudomallei* (1). We report 2 related cases of suppurative cervical lymphadenitis, an unusual adult presentation of melioidosis, in 2 men who returned to France from Vietnam on the same trip (2).

Patient 1, a 28-year-old previously healthy man, was admitted to our hospital in Lyon, France, in October 2013 for the evaluation of a palpable neck mass, which had been growing steadily for the previous 2 months. Examination of the head and neck revealed a fluctuant, tender mass located in the inferior angle of the right side of the mandible, mimicking lymph node tuberculosis. Ultrasonographic investigation confirmed a level II enlarged cervical lymph node

1These authors contributed equally to this article.

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