Among immunocompetent persons, the emergence of the mcr-1 gene is unknown, indicating a need to conduct accurate surveillance of the gene’s prevalence in humans. Additional mechanisms unique to the mcr-1 gene may contribute to colistin resistance, suggested by the wide variation in colistin MICs among mcr-1–carrying Enterobacteriaceae.

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References

Cryptococcus gattii Meningitis Complicated by Listeria monocytogenes Infection

Robert G. Deiss, Michael Bolaris, Angel Wang, Scott G. Filler

Author affiliations: Uniformed Services University of the Health Sciences, Bethesda, Maryland, USA (R.G. Deiss); Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda (R.G. Deiss); Naval Medical Center of San Diego, San Diego, California, USA (R.G. Deiss); Harbor-UCLA Medical Center, Los Angeles, California, USA (M. Bolaris, A. Wang, S.G. Filler); David Geffen School of Medicine at UCLA, Los Angeles (S.G. Filler)

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To the Editor: Among immunocompetent persons with cryptococcal disease, infection with a second organism is rare; all reported cases have involved concomitant mycobacterial infections (1). Immunosuppression is not a necessary precondition for infection with Cryptococcus gattii (2), and among immunocompetent persons, C. gattii infection confers high mortality rates: up to 24% according to a large case series (3). In addition, cryptococcomas are frequently observed in patients with C. gattii, as opposed to C. neoformans, 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 flucytosine (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. Repeat brain magnetic resonance images revealed no hydrocephalus, minimal edema, and decreased size and number of cryptococcomas. She was again given amphotericin B (5 mg/kg/d) and intravenous flucytosine (3 g/6 h) and fluconazole (600 mg q6h). Placement of a ventricular-peritoneal shunt was deferred, and the patient required frequent lumbar punctures to relieve elevated intracranial pressure. After 3 weeks of therapy, she began taking oral dexamethasone (2 mg 4×/d) to reduce intracranial pressure and control symptoms consistent with immune reconstitution inflammatory syndrome. After 30 days of antifungal therapy, she experienced head‐ache over 3 months and symptom relapse during 10 weeks of antircryptococcal therapy. As was done in this case, practice guidelines recommend a longer duration of polyene antifungal induction for patients with cryptococcomas than for those without (4), and longer courses of therapy are commonly described for infections caused by C. gattii than for those caused by C. neoformans (5). Corticosteroids are commonly used to treat immune reconstitution inflammatory syndrome associated with cryptococcal meningitis (6), 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 C. gattii in serum and CSF (9), and titers are used to monitor treatment success (10). In this patient, cryptococcal meningitis complicated by Listeria monocytogenes 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

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**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)</td>
<td>1,030 (1)</td>
<td>117 (1)</td>
<td>30 (1)</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>1:8 (23)</td>
<td>Negative (23)</td>
<td></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, flucytosine; AMB, amphotericin B; AMP, ampicillin; CrAg, cryptococcal antigen; CRO, ceftriaxone; DEX, dexamethasone; F, Friday; 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.

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References

Address for correspondence: Robert G. Deiss, Division of Infectious Diseases, Naval Medical Center of San Diego, 34800 Bob Wilson Dr, San Diego, CA 92134, USA; email: robert.g.deiss.ctr@mail.mil