We describe an immunocompromised patient who developed a large frontal brain abscess caused by *Legionella micdadei*. This is, to our knowledge, a rare case of culture-proven *Legionella* central nervous system infection.
mented) agar. *L. micdadei* (>100 colonies) was isolated by culture after 72 h of incubation (O2, high humidity) from premortem abscess fluid and from brain abscess tissue, abscess fluid, and cerebrospinal fluid taken at the autopsy. The identification was confirmed by fatty acid analysis (MIDI) and 16S rRNA. Autopsy specimens from the lungs, heart valves, urine, and kidney were negative for *Legionella* by culture. Blood cultures were not available for subculture on BCYE. A single serologic test for *Legionella* (CDC in-house-derived protocol) was negative from serum taken the day following the craniotomy. Of note, *Mycobacterium avium* complex (MAC) was also isolated from postmortem lung tissue.

*Legionellaceae* species are fastidious, facultatively intracellular Gram-negative bacilli which fail to grow on the majority of standard media routinely used in clinical laboratories (1). Culture on specialized charcoal agar medium remains the gold standard for diagnosis of any form of *Legionella* infection. Clinical laboratories often rely on antigenuria, direct fluorescence antibody staining (DFA), serology, and molecular amplification to make the diagnosis. Except for the latter, these tests are somewhat more specific for *L. pneumophila* serotype 1 (2).

*Legionella* infections are generally associated with pneumonia or other respiratory tract infection. Extrapulmonary infections without lung involvement are rare (3). Systemic involvement, exhibited as renal impairment, cardiac manifestations, as well as gastrointestinal or neurological symptoms, can also occur (4). Early after the description of Legionnaires’ disease, several case reports, as reviewed by Johnson et al. (4), documented a greater-than-expected associated frequency of neurological signs and symptoms in an estimated 40 to 50% of patients. The described neurological disorders ranged from nonspecific alterations in the sensorium, including coma, to specific cerebellar dysfunction and an assortment of focal signs. However, an infective etiology for these associated neurologic conditions has evaded detection. In an autopsy-neuropathology study of 40 patients dying with *Legionella* pneumonia, 40% of whom had a neurologic disorder; Pendlebury et al. (5) were unable to attribute the cause to direct infection of the CNS. Therefore, it has been proposed that these neurological disturbances are due to either the effect of neurotoxins or immune-mediated mechanisms (5, 6). In regard to the latter mechanism, rare case reports of acute disseminated encephalomyelitis have been documented in the setting of Legionnaires’ disease (4, 7–9). Problematic in assessment are cases reported in the literature (4, 9–11), in which *Legionella* has been identified in CNS tissue or CSF by means other than culture (specific staining techniques, DFA, PCR) and for which there has been no clinical, radiological, or pathological correlation of infection. This difficulty in detection is likely a consequence of the subclinical nature of *Legionella* infections in the CNS.

![Figure 1](http://jcm.asm.org/)
may reflect the sensitivity of the diagnostic tools employed and the fastidious requirements of the organism for culture. Table 1 summarizes the reported cases of confirmed Legionella sp. central nervous system infection.

More than 90% of infectious Legionella isolates are L. pneumophila, while 60% of the remaining are attributed to L. micdadei and often affect immunocompromised patients (15). A PubMed search with the keywords “L. micdadei” and “brain abscess” produced only one case report. Fukuta el al. described a prosthetic valve endocarditis in a patient on immunosuppressive therapy for systemic lupus erythematosus complicated by L. micdadei brain abscess (14). As in our case, L. micdadei was detected with 16S rRNA PCR, and the organism was also visualized in the brain abscess exudate with a Warthin-Starry stain. Fukuta et al. however, did not isolate the organism by any culture method. Brain infection attributed to other Legionella species, specifically L. pneumophila and L. cincinnatiensis, have been reported, although again, the organism was never grown in culture (4, 10, 12, 13). L. micdadei has been identified in other infections, including prosthetic joint infections, lung abscesses, and necrotizing cellulitis (3), as well as in soft tissue abscesses, often in association with acquired or congenital immunosuppression (12, 16, 17).

The wide distribution of Legionella spp. in the environment complicates its identification as a pathogen, because the source and transmission route may be difficult to define. Our patient was immunocompromised and thus at risk for non-pneumophila legionellosis. It is possible that the patient’s initial respiratory symptoms may have been due to L. micdadei pneumonia (“Pittsburgh pneumonia”) or MAC infection, although the admission chest X-ray had no evidence of pneumonia. The low prevalence of legionellosis in Alberta, Canada; the ubiquitous nature of this organism; and the paucity of literature describing this agent as a cause of brain abscess led us to question the 16S rRNA results. Furthermore, recent reports have described Legionella spp. as possible contaminants of DNA extraction columns (18). The autopsy failed to identify any specific focus of infection aside from the brain. We were unable to identify, on history, the origin of the infection, as the patient’s family denied risk factors such as recent whirlpool use or travel.

Despite diagnostic and pharmacological advances, bacterial brain abscesses remain associated with a high morbidity and significant mortality (19-21). Detection and identification of causal agents is critical to direct therapy, although approximately two-thirds of brain abscesses have “negative” cultures. 16S rRNA gene sequencing may serve as an important identification tool when pathological findings and Gram stains suggest bacterial abscess, but attempts to isolate the organism by culture have failed (22, 23). As illustrated by this case, culture-negative brain abscess represents a clinical management challenge and, in such circumstances, 16S rRNA gene sequencing can be a useful adjunct test. It may also help identify agents not typically considered causes of brain abscess. Nonetheless, as with all new technologies, caution is required when interpreting the clinical significance of 16S rRNA results.

In summary, we describe the first case to our knowledge of an isolated brain abscess due to L. micdadei in an immunocompromised patient, diagnosed by culture and 16S rRNA sequencing of a direct specimen. This adds to the scant literature regarding this manifestation of Legionella infection and demonstrates how recent technologies can assist the clinician to better direct antimicrobial therapy.

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George Zahariadis is the senior author.

REFERENCES


TABLE 1 Summary of case reports of Legionella sp. confirmed central nervous system infection described in the literaturea

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age, sex</th>
<th>Underlying illness</th>
<th>CNS lesion</th>
<th>Detection method</th>
<th>Identification</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>5 mo, male</td>
<td>SCID, respiratory failure</td>
<td>Microabscess; midbrain</td>
<td>DFA, brain/liver; culture, lung</td>
<td>L. pneumophila</td>
</tr>
<tr>
<td>13</td>
<td>33 yrs, male</td>
<td>None</td>
<td>Temporoparietal abscess (CT)</td>
<td>Serology</td>
<td>L. jordanis</td>
</tr>
<tr>
<td>14</td>
<td>57 yrs, female</td>
<td>SLE</td>
<td>Frontal brain abscess (MRI)</td>
<td>16S rRNA, prosthetic valve</td>
<td>L. micdadei</td>
</tr>
</tbody>
</table>

*a SCID, severe combined immunodeficiency; DFA, direct fluorescent antibody; MRI, magnetic resonance image; CT, computed tomography; SLE, systemic lupus erythematosus.


