Table 1. Summary of patients with severe acute respiratory failure due to legionella pneumonia who were treated with ECMO.

<table>
<thead>
<tr>
<th>Diagnosis, patient no./sex/age (y)</th>
<th>Method of diagnosis</th>
<th>Pre-ECMO data</th>
<th>Duration of ECMO (h)</th>
<th>Affected organ/system</th>
<th>Antibiotic regimen</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Vent D</td>
<td>PaO\textsubscript{2}/FiO\textsubscript{2} (mm Hg)</td>
<td>PaCO\textsubscript{2} (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presumptive</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/M/53</td>
<td>SFAT</td>
<td>3</td>
<td>64.0</td>
<td>51.8</td>
<td>113</td>
<td>...</td>
</tr>
<tr>
<td>2/M/42</td>
<td>SFAT</td>
<td>1</td>
<td>68.3</td>
<td>63.8</td>
<td>363</td>
<td>L</td>
</tr>
<tr>
<td>3/M/35</td>
<td>SFAT</td>
<td>13</td>
<td>71.3</td>
<td>63.8</td>
<td>720</td>
<td>R</td>
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<tr>
<td>4/M/41</td>
<td>SFAT</td>
<td>2</td>
<td>64.5</td>
<td>51.0</td>
<td>93</td>
<td>...</td>
</tr>
<tr>
<td>5/M/58</td>
<td>SFAT</td>
<td>1</td>
<td>37.5</td>
<td>N/A</td>
<td>105</td>
<td>R</td>
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<td>Confirmed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6/F/33</td>
<td>Urine</td>
<td>2</td>
<td>37.4</td>
<td>44.6</td>
<td>121</td>
<td>R</td>
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<tr>
<td>7/M/30</td>
<td>Cult</td>
<td>1</td>
<td>136.1</td>
<td>35.9</td>
<td>70</td>
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<tr>
<td>8/M/40</td>
<td>Cult/SFAT</td>
<td>2</td>
<td>46.0</td>
<td>46.0</td>
<td>337</td>
<td>R</td>
</tr>
<tr>
<td>9/M/49</td>
<td>Cult/SFAT</td>
<td>1</td>
<td>62.3</td>
<td>117</td>
<td>644</td>
<td>CNS, NB, R</td>
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<td>10/M/47</td>
<td>Cult/SFAT</td>
<td>4</td>
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<td>58.3</td>
<td>337</td>
<td>CF, L, R</td>
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<td>11/M/28</td>
<td>Urine</td>
<td>2</td>
<td>40.2</td>
<td>44.7</td>
<td>1</td>
<td>CF, L, R</td>
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<tr>
<td>12/M/49</td>
<td>Cult/SFAT</td>
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<td>69.0</td>
<td>48.0</td>
<td>261</td>
<td>L, R</td>
</tr>
<tr>
<td>13/F/46</td>
<td>Cult/SFAT</td>
<td>1</td>
<td>68.5</td>
<td>58.5</td>
<td>166</td>
<td>BMS, L, R</td>
</tr>
</tbody>
</table>

NOTE. BMS = bone marrow suppression; CF = cardiac failure; Clm = clarithromycin; CNS = CNS damage; Cpfx = ciprofloxacin; Cult = Legionella pneumophila was cultured from pulmonary secretions; Em = erythromycin; ECMO = extracorporeal membrane oxygenation; L = liver failure; NB = nasal bleeding; R = renal failure; Rif = rifampin; SFAT = serum immunofluorescent antibody titer; Urine = urinary antigen assay; Vent D = ventilation days.

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References


Invasive Sinusitis and Cerebritis Due to Curvularia clavata in an Immunocompetent Adult

We describe an unusual case of invasive dematiaceous fungal sinusitis in an immunocompetent patient infected with Curvularia clavata. The patient had cribriform plate involvement with destruction of bone, probable infection of brain parenchyma, and dramatic bifrontal cerebritis, and responded to complete surgical removal of the infected sinus tissue and prolonged antifungal therapy with amphotericin B followed by itraconazole.

A 46-year-old woman with a history of asthma, hay fever, and chronic sinusitis presented for evaluation of a severe frontal headache, somnolence, and radiographic evidence of bifrontal cerebritis. She had undergone six operations required to manage her chronic sinusitis before her 1996 hospital admission, including several polypectomies and at least two intranasal ethmoidectomy procedures. CT and MRI of the sinuses and brain revealed severe mucosal thickening involving maxillary, frontal, and left sphenoid sinuses as well as postsurgical changes of the medial aspects of both maxillary sinuses. Extensive soft-tissue opacity was noted within the ethmoid air cells, with evidence of bony erosion. In addition, there appeared to be bony erosion of the cribriform plate and the medial walls of both orbits. Contiguous with and extending from the cribriform plate, a diffuse irregular area of enhancement was present in both frontal lobes (figure 1). Magnetic resonance T2-weighted images revealed vasogenic edema around the periphery with mass effect on the frontal horns of the lateral ventricles.

The patient was treated with intravenous dexamethasone and ampicillin/sulbactam. Within 12 hours, she had complete resolu-
The case of sinusitis due to *C. clavata* we described is unusual in at least three respects. Not only was sinus tissue invaded, but the cribiform plate was eroded, and marked bifrontal cerebritis was present in a host with no known systemic immunodeficiency. The patient, however, had significant local disease resulting from a prolonged history of hay fever, recurrent bacterial sinusitis, and multiple surgeries, which probably contributed to susceptibility for invasion by this organism. We suspect the organism at least partially invaded the base of the brain through the cribiform plate and caused an accompanying extensive inflammatory response in both frontal lobes. In addition, although several reports have emphasized the importance of prolonged follow-up because of possible persistent disease [5–7], to date (24 month follow-up) our patient has improved markedly with surgery limited to the sinuses, along with antifungal therapy. No drainage or excision of brain tissue has been required to achieve the dramatic, albeit slow, resolution of bifrontal cerebritis. In the only published report of frontal cerebritis we could find (case 4, [5]), *Exserohilum rostratum* invaded sinus tissue and tubinates, and the infection extended from the ethmoid sinus superiorly into the floor of the frontal sinus, with lateral erosion of the lamina papyracea. As in our patient, sinus but not brain surgery, accompanied by prolonged antifungal therapy, totaling 7 months of amphotericin B and 1 month of ketoconazole, was required to control the infection with nearly complete resolution of the frontal lobe lesions. Third, we have found only one report of *C. clavata* causing human disease. The single case was that of a 20-year-old woman with a recurring, but apparently superficial, skin infection [8].

Prior to the case we described, all isolates of *Curvularia* species associated with sinus disease were either not identified to the species level or determined to be *Curvularia lunata*, or, in one instance, *Curvularia senegalensis* [9]. Invasive dematiaceous fungal sinusitis in immunocompetent patients is unusual, especially when intracranial extension occurs. Clearly, more experience is needed in managing this difficult disease.

**Figure 1.** T1-weighted enhanced coronal MRI demonstrating opacification of ethmoid air cells and bilateral frontal lobe enhancement extending from the cribiform plate in a 46-year-old woman with invasive sinusitis and cerebritis due to *Curvularia clavata*.

**References**


Successful Treatment of Persistent Vancomycin-Resistant Enterococcus faecium Bacteremia with Linezolid and Gentamicin

Vancomycin-resistant enterococci (VRE) have emerged as an important nosocomial pathogens in medical centers throughout the United States. Recently, Enterococcus faecium isolates that are resistant to all currently available antimicrobial agents have been reported [1]. Therefore, therapy for patients infected with these multidrug-resistant organisms is particularly difficult, as many of the infections are virtually untreatable. In addition, serious enterococcal infections, such as persistent bacteraemia and endocarditis, may be associated with a high mortality [2, 3].

Linezolid (PNU-100766) is a member of a new class of antibacterial agents called oxazolidinones, which are chemically unrelated to currently available agents. This agent selectively binds to the 50S ribosomal subunit, thereby inhibiting protein synthesis. It is highly active against gram-positive organisms and is difficult to select for resistance in vitro [4]. To our knowledge, we report the first case of a neutropenic patient with persistent VRE bacteremia who responded clinically and microbiologically to therapy with linezolid and gentamicin.

A 23-year-old woman, who was 18 weeks pregnant, was admitted to Northwestern Memorial Hospital (Chicago) and found to have a high-grade B-cell immunoblastic lymphoma with multiorgan involvement. Following the administration of chemotherapy, she had a spontaneous abortion and then developed acute renal failure resulting from tumor lysis syndrome. Prolonged neutropenia ensued complicated by fever. Initially, she received empiric therapy with ceftazidime and amikacin for 5 days; however, due to the persistence of fever, intravenous vancomycin was added. Two sets of cultures of blood obtained during a febrile episode revealed Candida krusei; therefore, amphotericin B cholesteryl sulfate complex was administered. She remained fungemic, despite removal of all central venous access devices. Ultimately, her fungemia cleared, then her neutropenia and acute renal failure resolved.

As the next part of her treatment regimen she received a second course of cytotoxic chemotherapy, which again resulted in prolonged neutropenia. It is noteworthy that before the initiation of chemotherapy, cultures of a rectal swab revealed vancomycin-resistant E. faecium. Twelve days after the initiation of this second course of chemotherapy, she developed a fever (temperature, to 38.9°C) and was started empirically on therapy with ceftazidime and amikacin. The following day, two sets of cultures of blood obtained from different sites (central venous catheter and peripheral) grew gram-positive cocci; consequently, vancomycin therapy was added. Both sets of cultures contained Staphylococcus aureus and vancomycin-resistant E. faecium. Due to her profound neutropenia (absolute neutrophil count, <100/µL), the patient was enrolled in a linezolid compassionate-use study.

Her antimicrobial regimen was changed to that with ceftazidime 2 g every 8 hours, linezolid 600 mg intravenously every 12 hours, plus gentamicin 1 mg/kg every 8 hours. Before the initiation of linezolid, blood cultures had yielded VRE for four consecutive days; however, no additional cultures yielded staphylococci. Due to this persistent bacteremia, all central venous catheters were removed and echocardiography was performed. No endovascular source of infection was identified. Therapy with linezolid and gentamicin was continued for 14 days, whereas the ceftazidime was discontinued following the resolution of her neutropenia on the ninth day of linezolid therapy. Blood cultures obtained after the first day of therapy with linezolid and gentamicin revealed VRE. All subsequent cultures of blood obtained while the patient was receiving antimicrobial therapy and at 14 and 30 days after completion of therapy were negative.

Antimicrobial susceptibility testing was performed according to National Committee for Clinical Laboratory Standards (NCCLS) guidelines [5]. Enterococcus faecalis ATCC 29212 was used as a control isolate and included each time a test run was performed. The antimicrobial agents were obtained from their manufacturers, and linezolid was generously provided by Pharmacia and Upjohn (Kalamazoo, MI). The provisional susceptibility breakpoints for linezolid are ≤8 µg/mL, susceptible; 16 µg/mL, intermediate; and ≥32 µg/mL, resistant. For each isolate tested, the inoculum was prepared from 18–24-hour-old colonies inoculated into 5 mL of trypticase soy broth. Just before testing, the broth was adjusted to a 0.5 McFarland turbidity standard to yield ~1 × 10^8 cfu/mL. Then 0.1 mL of the prepared inoculum was added to macrobroth dilution tubes.

A time-kill experiment was performed, according to methods previously described [6], to determine if the addition of gentamicin would provide in vitro synergy with linezolid. All testing was performed in duplicate.

The bacteremic isolates from this patient possessed high-level resistance to vancomycin (MIC, ≥256 µg/mL) and ampicillin (MIC, ≥128 µg/mL) and were resistant to all currently available antimicrobial agents except chloramphenicol (Table 1). The linezolid MIC was 2 µg/mL. Time-kill studies with the combination of linezolid and gentamicin failed to demonstrate any in vitro synergy.

Enterococci possess intrinsic resistance to many antimicrobial agents including the β-lactams and aminoglycosides. Therefore, for the treatment of serious enterococcal infections, a cell-wall active agent in combination with an aminoglycoside is required for synergistic, bactericidal activity [7]. However, for patients infected with VRE, treatment is problematic, especially for isolates that are also ampicillin resistant and/or highly aminoglycoside resistant. Although there have been no controlled clinical trials evaluating therapy for VRE, there are anecdotal reports of treatment using various different antimicrobial combinations [8, 9].

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