Although high doses of penicillin are adequate for pneumonia caused by strains that are highly resistant to penicillin, this does not seem to be true in cases of meningitis or endocarditis. Vancomycin has failed in cases of meningitis because of its variable CSF penetration. Intravenous vancomycin as a single agent may be used only if supplemented with intrathecal doses. Infections with strains for which the MIC of cefotaxime is ≥1 μg/mL may be treated with high doses of cefotaxime (300 mg/kg/d; maximum, 24 g) or with a combination of drugs such as cefotaxime and vancomycin, cefotaxime/ceftriaxone, and rifampin or vancomycin and rifampin.

Accordingly, in cases of endocarditis caused by S. pneumoniae with high-level resistance to penicillin, the possibility of meningitis should always be excluded before vancomycin is chosen as the single agent for therapy.

Fluconazole-Resistant Cryptococcus neoformans Isolated from an Immunocompetent Patient without Prior Exposure to Fluconazole

Fluconazole has been shown to be an effective alternative to amphotericin B in the treatment of cryptococcal meningitis [1–4] and is the most commonly used antifungal agent in maintenance therapy for this disease [5, 6]. A few cases of meningitis due to Cryptococcus neoformans resistant to fluconazole have been reported, all of which occurred in patients with AIDS who were previously treated with fluconazole [5–9]. Herein, we describe a case of meningitis due to fluconazole-resistant C. neoformans in an immunocompetent patient without prior exposure to fluconazole.

A previously healthy 32-year-old Philippine male employed as a nurse in Israel was admitted to the hospital with a 5-day history of headache, nausea, vomiting, and dizziness. Physical examination revealed only right-sided optic neuritis. Brain CT was unremarkable. During lumbar puncture, the opening pressure was 50 cm H₂O. Analysis of CSF revealed the following: fluconazole, <0.05 μg/mL; itraconazole, 0.38 μg/mL; ketoconazole, 0.32 μg/mL; and amphotericin B, 0.5 μg/mL. Resistance to fluconazole was also confirmed at the National Institute of Allergy and Infectious Diseases (Bethesda, MD). Although CSF remained sterile after the onset of treatment, clinical deterioration after the start of oral fluconazole therapy is highly suggestive of treatment failure and is in accord with the high MIC of fluconazole for the isolate.

All previously reported cases of meningitis due to C. neoformans resistant to fluconazole occurred in patients with AIDS who had been treated with fluconazole [5–9]. Petter et al. [9] showed heterogeneity in susceptibility when only 1% of cryptococci were resistant to fluconazole at the beginning of therapy, whereas 35% of isolates were resistant after the sixth episode of meningitis in the same patients.

To the best of our knowledge, this is the first reported case of meningitis due to fluconazole-resistant C. neoformans in an immunocompetent patient who had never been exposed to azoles. The increasingly wide use of azoles might cause an increase in resistance to these agents. Fluconazole susceptibility testing

References

should be performed whenever resistance is suspected clinically or epidemiologically.

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References


Brucella canis Endocarditis: Case Report

Brucella endocarditis, though uncommon, is found in almost 80% of fatal cases of systemic brucellosis at autopsy. We are unaware of any report in the English literature citing Brucella canis as a pathogen for this entity. A presumptive case of B. canis endocarditis, diagnosed by serology, is described.

A 49-year-old man was admitted to the hospital because of weight loss, heart murmur, and fever (temperature, 38°C), 3 months after returning from a trip to Kuwait. His history included Reiter’s syndrome, penicillin allergy, and no specific animal exposure. Echocardiography showed vegetations on the aortic valve and aortic insufficiency.

Two blood cultures were performed. Therapy with vancomycin and gentamicin was initiated. After heart failure occurred, transesophageal echocardiography showed a thickened aortic valve, vegetations, and severe aortic insufficiency. On day 10, he underwent aortic valve replacement.

Vancomycin and gentamicin were withdrawn when blood cultures were negative. The patient was discharged on hospital day 23, at which time he was being treated with oral ofloxacin (500 mg twice a day) and iv ceftriaxone (2 g every day). He had been afebrile since day 13.

The final pathology report showed fragments of aortic valve with bacterial endocarditis vegetations, in addition to the presence of microabscesses. The infectious agent was not identified. All 5 blood cultures were negative at 28 days.

The serology, performed at the Centers for Disease Control and Prevention (Atlanta), showed antibody to Brucella species (table 1), later identified as B. canis. The antibiotic therapy was changed to a regimen of oral ofloxacin (200 mg twice a day), rifampin (300 mg 3 times a day), and doxycycline (100 mg twice a day).

Brucellosis, though common worldwide, predominates in the Mediterranean and Middle East regions [1–3]. Brucella species frequently associated with human brucellosis are Brucella melitensis, Brucella abortus, and Brucella suis; B. canis is a rare cause [1–6]. Brucella endocarditis, despite its high mortality rate, has a low occurrence rate in cases of brucellosis (<2%) [1, 2]. Heart failure is the leading reason for death [1, 2]. The best outcome is associated with a combined medical and surgical approach [1, 2].

The clinical presentation, the operative findings of fibrinous vegetations within the mitral valve and subaortic septum, and the pathology report are all supportive data for the diagnosis of endocarditis. The serology showed B. canis as the probable etiologic agent in this case of endocarditis. Valvular immunofluorescent studies have been used diagnostically in cases of culture-negative endocarditis.

Table 1. Convalescent serological findings in a case of Brucella canis endocarditis.

<table>
<thead>
<tr>
<th>Date</th>
<th>B. canis antibody titer</th>
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<tr>
<td>January 1992</td>
<td>1: 2560</td>
</tr>
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<td>November 1994</td>
<td>1: 160</td>
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