BRIEF REPORTS

Infective Endocarditis Caused by *Streptococcus pneumoniae* with High-Level Resistance to Penicillin and Cephalosporin

Drug-resistant strains of *Streptococcus pneumoniae* are being increasingly reported as the causative agents of a variety of serious infections [1–3]. The pneumococcus causes a diversity of infections including endocarditis, and with its growing prevalence, one would anticipate that drug-resistant strains of *S. pneumoniae* would be isolated. Infective endocarditis due to drug-resistant strains of *S. pneumoniae* has been reported in a 2-year-old child from Japan [4]. We report a case of infective endocarditis in an adult that was caused by a strain of *S. pneumoniae* that was highly resistant to penicillin and cephalosporin (MIC of both, >2.0 µg/mL) and that was subsequently cured with vancomycin and rifampin therapy.

A 63-year-old female presented to the hospital with a 2-week history of tinnitus and otalgia that was associated with nausea and vomiting for the 2 days before admission. She also complained of a nonproductive cough and mild arthralgias. She denied headache, sore throat, chest pain, shortness of breath, abdominal pain, or urinary complaints. Of note, she reported that she had had a dental extraction ~ 1 month earlier.

When the symptoms began, the patient’s condition was diagnosed as otitis media, and an oral antibiotic was prescribed; she discontinued this medication after 2 days because of gastrointestinal intolerance. She denied the use of alcohol, intravenous drugs, or prescription medicines for chronic conditions.

Physical examination revealed that the patient was febrile (temperature of 103.7°F) and tachycardic. The right tympanic membrane was bulging and red with a diffuse light reflex. The pinna was nontender, as was the mastoid. Examination of the oropharynx did not reveal any abnormalities. The heart and lung examinations were unremarkable, and no murmur was heard on presentation. The remainder of the physical examination revealed no abnormalities.

The patient was admitted to the hospital with dehydration, otitis media, and possible sepsis, and she was treated with iv ceftriaxone. Although her symptoms decreased within 24 hours, her fever persisted. Reexamination on the second hospital day revealed a diastolic murmur that was best heard in the left second intercostal space. Cultures of blood drawn at the time of admission yielded *S. pneumoniae*.

A transthoracic echocardiogram showed a large vegetation on the noncoronary cusp of the aortic valve that was associated with moderate aortic insufficiency. With use of the Etest, the MIC of both penicillin and ceftiraxone for the blood culture isolate was 6 µg/mL. The MIC of rifampin was 1 µg/mL, and the MIC of vancomycin was 0.75 µg/mL. Therapy with vancomycin and rifampin was initiated, and therapy with ceftiraxone was discontinued.

The patient’s hospital course was further complicated by an episode of amaurosis fugax, but a head CT scan and ophthalmologic evaluation did not reveal any abnormalities. A prolonged PR interval developed on the patient’s electrocardiogram, but a transesophageal echocardiogram failed to demonstrate a perivalvular abscess. The patient was discharged to her home on the 18th hospital day and was asked to complete a 6-week course of vancomycin and rifampin. Eight weeks after completing the course of antibiotic therapy, her condition remained stable and blood cultures were sterile.

*S. pneumoniae* with high-level penicillin resistance is being increasingly reported in the United States [5, 6]. In the Memphis area, resistant pneumococci have been frequently isolated in children [6, 7] and adults [2]. Cleveland et al. recently reported the incidence of drug-resistant strains of *S. pneumoniae* in 100 adult Memphians with invasive pneumococcal infection [8]. These investigators reported that 20% of the isolates were resistant to penicillin and 3% were resistant to multiple antibiotics. Thus, one would anticipate identifying adult patients with infective endocarditis due to drug-resistant strains of *S. pneumoniae*.

practicing physicians and public health officials are concerned about the best empirical and definitive therapy for patients with drug-resistant strains of *S. pneumoniae*. Unfortunately, clear-cut recommendations for the treatment of such infections are not available. Treatment failures with third-generation cephalosporins for meningitis due to drug-resistant strains of *S. pneumoniae* have been reported in children [7, 9].

There are no clinical data regarding the best treatment regimen for patients with endocarditis due to drug-resistant strains of *S. pneumoniae*; however, experimental endocarditis in rabbits caused by pneumococci with intermediate and high-level resistance to penicillin was consistently eliminated with teicoplanin, an antibiotic chemically similar to vancomycin, and with cefotaxime when the MIC of cefotaxime was ≤0.5 µg/mL [10]. Only 88% of the animals had sterile vegetations when the levels of penicillin in the serum were three to four times the MIC for the organism.

It is difficult to determine with certainty whether the brief use of ceftiraxone therapy had a beneficial effect on our patient’s outcome. Data are insufficient to assess the role of drug-resistant strains of *S. pneumoniae* on the lethality of infective endocarditis, and the results of additional clinical studies are needed. Since our patient’s endocarditis was successfully cured with vancomycin therapy, we believe that this treatment should be considered for patients with serious infections due to strains of *S. pneumoniae* that are highly resistant to penicillin and cephalosporin.

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References

patients. Two of these four patients died soon after enrollment, before enrollment in this study.

Association of Plasma Levels of Tumor Necrosis Factor α with Severity of Disease and Mortality Among Patients with Leptospirosis

Circulating TNF-α has been detected in patients with leptospirosis [1] and associated with the Jarisch-Herxheimer reaction [2]. However, an association between the levels of TNF-α and the severity of disease has not been clearly demonstrated. The aim of this study was to investigate the presence of circulating TNF-α in patients with leptospirosis to determine if there was an association between the levels of TNF-α and disease severity and outcome.

Eighteen patients with a diagnosis of leptospirosis who were treated consecutively at Hospital São Paulo and Casa de Saúde Santa Marcelina, both tertiary care hospitals located in São Paulo, Brazil, were enrolled between November 1993 and March 1994 and evaluated daily until discharge from the hospital or death. Diagnoses were made on epidemiological and clinical grounds as well as on the results of microagglutination tests.

Serological tests of the first blood sample were negative for four patients. Two of these four patients died soon after enrollment, and the diagnosis of leptospirosis was made on clinical grounds (previously healthy young men with myalgia, severe jaundice, renal failure, and hemorrhage), epidemiological grounds (they were caught in a flood in an area infested by rats), and laboratory abnormalities (e.g., thrombocytopenia and a markedly elevated level of creatine phosphokinase). Involvement of the liver or kidney was considered for patients whose serum levels of transaminases, bilirubin, or creatinine were above the normal range. Involvement of the lungs was assessed by the presence of dyspnea or tachypnea as well as by changes on chest roentgenograms or hypoxemia or hypercapnia.

The mean age of the patients enrolled in our study was 34.8 years. Eighteen healthy adults were used as controls. For measurement of TNF-α levels, three blood samples were collected from each patient in the first 24 hours after admission and three were collected on the second hospital day. Only three samples were collected from three patients who died in the first 24 hours. One blood sample was obtained from each control. Levels of TNF-α were determined with use of a commercially available ELISA kit (Genzyme Corporation, Cambridge, MA). Differences between subgroups of patients and between patients and controls were analyzed with use of Fisher’s exact test.

The clinical signs and symptoms of leptospirosis observed in this series were myalgia (94% of patients), jaundice (83%), fever (78%), headache (61%), and dyspnea (56%). In all cases the liver was involved, in six cases the liver and kidney were involved, and in nine cases the liver, kidney, and lungs were involved (hemorrhaging occurred in six of these nine cases). The mortality among the 18 patients with leptospirosis was 22% (4/18).

TNF-α was detected in four patients, but it was not detected in any of the controls (P = .10). In one patient’s case, TNF-α was detected in only one sample (141.3 pg/mL); in two patients’ cases, it was detected in two of three samples (patient 1, 185 pg/mL and 190 pg/mL; patient 2, 159.8 pg/mL and 67.4 pg/mL); and in one patient’s case, it was detected in all three samples (14.3 pg/mL, 10.5 pg/mL, and 16.8 pg/mL).

Detection of circulating TNF-α was associated with kidney, liver, and lung involvement as well as bleeding in four of six patients, whereas none of 12 patients for whom TNF-α was not detected had such dysfunction (P = .005). Detection of circulating TNF-α was also associated with higher mortality among the 18 patients with leptospirosis (TNF-α was detected in 1 of 14 patients who survived vs. in 3 of 4 patients who died; P = .02).

The role of TNF-α in the inflammatory response that occurs during endotoxia and sepsis has been extensively investigated [3, 4]. In this study we found an association between the presence of TNF-α and the severity of disease and mortality among patients with leptospirosis, a finding that suggests that TNF-α may also be involved in the inflammatory response observed in this disease and that detection of circulating TNF-α may be indicative of a poor prognosis. However, TNF-α plays a dual role in the host response to infections. Although there is strong evidence of its deleterious role in patients with sepsis, there is also an increasing body of evidence that it plays a pivotal role in host defense in...