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Fatal Infection Caused by a Multiply Resistant Type 3 Pneumococcus

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The most virulent pneumococcal serotype (type 3) has not to date been associated with multiple antimicrobial resistance. We report an unusual gastrointestinal presentation of fatal septicemia caused by a multiply resistant type 3 pneumococcus in a setting of increasing prevalence of multiple resistance, including resistance to erythromycin, clindamycin, and tetracycline.

Pneumococcus type 3 is considered to be the most virulent pneumococcal serotype and is commonly responsible for human disease (7, 15, 16, 18, 20). Bacteremia caused by this organism is considered to have a 50% mortality rate, versus the 23 to 45% mortality rates for all serotypes combined (1, 16, 20).

Antibiotic resistance in pneumococci is well described (4, 8, 10), with a recent focus on organisms demonstrating high-level resistance to penicillin and to multiple antibiotics (4, 18). Multiply resistant but penicillin-susceptible organisms of serotypes 6B, 14, and 19F have also been documented (13, 14).

To date, multiple antimicrobial resistance of any type has not been described in type 3 pneumococcal infection. Here, we document a fatal bacteremia as a result of infection with a multiply resistant, penicillin-susceptible type 3 pneumococcus.

A 17-year-old schoolboy returned to Johannesburg, South Africa, after spending 2 weeks in a rural area. Three days later he complained of a sore throat, and subsequently he vomited repeatedly and consulted a family practitioner. Gastroenteritis was diagnosed and despite medication, the vomiting continued. Overnight he lost consciousness, and he was brought to the hospital where he suffered a cardiorespiratory arrest.

The patient was intubated, sinus rhythm was reestablished, and he was transferred to the intensive care unit. His blood pressure was 60/30 mm Hg, and his pulse was 114/min. His rectal temperature was 32.1°C. No skin rash or petechiae were detected. The patient's pupils were fixed and dilated with absent doll's eye movements. He had no reflex jerks and did not respond to painful stimuli.

A chest X ray revealed no abnormality. The patient's hemoglobin concentration was 13 g/dl, and his leukocyte count was 2.5×10^9/liter. The differential count revealed a left shift. The platelet count was 298×10^9/liter. Cerebrospinal fluid examination revealed four erythrocytes per ml and a protein concentration of 0.32 g/liter. Arterial blood gas on 100% oxygen showed a pH of 7.09, partial O_2 pressure of 84.4 mm Hg (1 mm Hg = 133.3 Pa) (normal on air is 75 mm Hg in Johannesburg [11]), and partial CO_2 pressure of 39.6 mm Hg. Inotropic support was initiated. Since the pulmonary capillary wedge pressure was 2 mm Hg, intravenous colloids were administered.

The patient was considered to have overwhelming bacterial infection and was given 2 g of ceftazidime, 500 mg of amikacin, and 500 mg of vancomycin intravenously. Despite prolonged resuscitation, the young man died 15 h later. Permission for postmortem examination was refused.

Blood cultures taken on admission revealed *Streptococcus pneumoniae*, identified by Gram stain and the colonial appearance on subculture overnight at 37°C in 5% CO_2 and confirmed by ethylhydrocupreine sensitivity and capsular typing with antipneumococcal serum as a type 3 strain (Quellung reaction; Statens Seruminstitut, Copenhagen, Denmark) (3). The strain was susceptible to penicillin but resistant to erythromycin, clindamycin, and tetracycline by the Kirby-Bauer disk diffusion method using a multidisk ring including oxacillin as the reference for penicillin susceptibility. MICs were >64 μg/ml for erythromycin and clindamycin, 16 μg/ml for tetracycline, and 0.03 μg/ml for penicillin, as determined by plate microdilution performed by established techniques (17).

The organism was not detected in the patient's cerebrospinal fluid or urine, and nasopharyngeal swabs from contacts did not reveal carriage of this strain.

Respiratory symptomatology was not prominent in the patient's history, and the primary focus of his symptomatology was gastrointestinal. A gastrointestinal presentation of pneumococcal bacteremia without an obvious source has recently been emphasized (2). The patient was not known to have any condition associated with an increased susceptibility to pneumococcal infection (2, 20), although a poor outcome could be predicted (18). Furthermore, Hook and co-workers (9) showed that patients admitted with pneumococcal bacteremia to an intensive care unit did not benefit from admission.

Type 3 pneumococci were isolated from 5.3% of 5,327 cerebrospinal fluid and blood culture isolates serotyped by our institute from 1979 to 1986. Type 3 ranks sixth in frequency of pneumococcal serotypes isolated from cerebrospinal fluid and blood in South Africa and fifth worldwide (19); yet despite the description of pneumococcal resistance to erythromycin in 1964 (5), to our knowledge erythromycin resistance has not been described in type 3 pneumococci. Tetracycline resistance has been described in many pneu-

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mococcal serotypes, including type 3 (6). The development of antibiotic resistance is believed to relate to prior exposure of patients or organisms to the antibiotic. Prior antibiotic exposure is associated with resistance to penicillin and with multiple resistance (10, 18). Erythromycin is a suggested alternative in penicillin-allergic individuals (18, 20) and in infections caused by penicillin-resistant strains (18), although in light of increasing erythromycin resistance in South Africa, we have recently cautioned against its use for penicillin-resistant strains (12). In a series of pneumonias treated by general practitioners in Norwich, England, erythromycin was prescribed in 20% of cases (21). Although no figures are available in Johannesburg, both drugs are used in this city and their widespread use may have resulted in the development of resistance in community-acquired organisms (13).

The development of a multiple pattern of antibiotic resistance in a type 3 pneumococcus (already a formidable organism) should be noted with concern.

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