Pseudomonas denitrificans Meningitis

ROBERT A. FISCHER,1 GARY V. DOERN,1,2* AND SARAH H. CHEESEMAN1

Division of Infectious Disease1 and Department of Laboratory Medicine,2 University of Massachusetts Medical Center, Worcester, Massachusetts 01605

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An elderly male patient with Pseudomonas denitrificans bacteremia and meningitis is described. The antimicrobial susceptibility and minimum criteria necessary for the identification of this unusual and rare human pathogen are discussed.

Pseudomonas denitrificans has not, to our knowledge, been identified as a human pathogen. We report herein a patient in whom this organism was the cause of fatal systemic disease. Biochemical characteristics and antimicrobial susceptibilities are elucidated.

Case report. The patient was a 54-kg, 60-year-old male admitted to the hospital after having been found, by his daughter, lying on the floor of his room, unresponsive and incontinent. His past medical history was notable for systemic lupus erythematosus, chronic leg ulcers, mitral insufficiency, seizure disorder, and mild dementia. Three weeks before admission, his dose of prednisone had been increased because of an exacerbation of his systemic lupus erythematosus. He was in his usual state of health 2 days before admission and had no recent history of travel or exposure to animals.

At admission, he was noted to have a temperature of 39.3°C, nuchal rigidity, and a small, chronic-appearing ulcer on the left ankle. Lumbar puncture yielded cerebro spinal fluid (CSF) with 19,650 erythrocytes per mm3, 6,930 leukocytes per mm3 (100% polymorphonuclear leukocytes), 398 mg of protein per deciliter, and 2 mg of glucose per deciliter (112 mg of blood glucose per deciliter). His leukocyte count was 19,600/mm3 (89% segmented and 4% band forms). Tests of hepatic function were normal. Creatinine was 1.3 mg/deciliter, and blood urea nitrogen was 41 ml/deciliter. Cultures of blood, CSF, and the left ankle ulcer were obtained. A gram smear of the CSF revealed rare pleomorphic, faintly staining, gram-negative bacilli and coccobacilli, and the patient was begun on 12 g ampicillin per day intravenously and 4 g of chloramphenicol per day intravenously. Counterimmunoelectrophoresis analysis of the CSF was negative for the following: Haemophilus influenzae type b; Neisseria meningitidis groups A through D, X through Z, and W135; Streptococcus pneumoniae; Listeria monocytogenes; and groups B and D Streptococcus. X-rays of the left ankle were negative for osteomyelitis.

On hospital day 2, the patient defervesced and was alert and responsive to questioning. On hospital day 3, Pseudomonas denitrificans was identified in pure culture, by the criteria described below, in three of three blood cultures, CSF, and the swab specimen of the left ankle ulcer obtained upon admission. Susceptibility tests revealed that the organism was resistant to ampicillin, possessed intermediate susceptibility to chloramphenicol, and was susceptible to ticarcillin (Table 1).

That same day the patient developed coma, fever to 39°C, and adult respiratory distress syndrome. Lumbar puncture yielded CSF with 80,000 erythrocytes per mm3, 2,000 leukocytes per mm3 (99% polymorphonuclear leukocytes), 435 mg of protein per deciliter, 9 mg of glucose per ml (128 mg of blood glucose per deciliter). Gram stain revealed abundant pleomorphic gram-negative bacilli. Ampicillin and chloramphenicol were discontinued, an Ommaya reservoir was placed, and intravenous (30 g/day) and intraventricular (50 mg every 12 h) ticarcillin administration was begun. P. denitrificans was again recovered from the CSF and from two of two blood cultures.

No clinical improvement was noted during the next 2 days. Multiple cultures of lumbar and ventricular CSF remained positive for P. denitrificans. CSF leukocyte counts rose as high as 208,000/mm3. Computerized axial tomography of the head demonstrated enlarged ventricles and an old right frontal infarct, but no suggestion of an abscess.

On hospital day 5, the isolates of P. denitrificans recovered from CSF and blood cultures obtained on day 3 were found to be resistant to ticarcillin (minimum inhibitory concentration,
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VOL. 251, pg 59. "Ampicillin Resist 8.0
Resistant ND)
Resistant ND
Resistant ND
Resistant Intermediate
Resistant ND
Sulfamethoxazole
Sensitive 0.2/4.0

Antibiotic Disk diffusion susceptibility correlate

Ampicillin Resistant 25.0
Carbenicillin Sensitive 32.0
Ticarcillin Sensitive 8.0
Cephalothin Resistant ND
Tetracycline Resistance 2.0
Piperacillin ND
Gentamicin Resistance 32.0
Tobramycin Resistance 2.0
Amikacin Resistance ND
Chloramphenicol Intermediate 12.5
Polymyxin B Sensitive ND
Trimethoprim-sulfamethoxazole Sensitive 0.2/4.0

*a Isolates obtained from the blood, CSF, and ankle ulcer on admission all possessed this susceptibility pattern. Subsequent isolates, obtained after hospital day 2, varied only with regard to carbenicillin and ticarcillin, to which they were resistant.

*b Disk diffusion susceptibility tests were performed with Mueller-Hinton agar by the method of Bauer, et al. (1). National Committee for Clinical Laboratory Standards-approved zone diameter interpretive standards were applied (5). Ticarcillin susceptibility was determined by using disks impregnated with 75 ug of ticarcillin and a susceptibility correlate of 15 mm (6).

Minimum inhibitory concentrations were determined by tube dilution by using Mueller-Hinton broth supplemented with calcium (50 mg/liter) and magnesium (25 mg/liter), and an inoculum of 10^4 to 10^6 colony-forming units per ml.

^ND, Not determined.

^Trimethoprim concentration, 0.2 ug/ml; sulfamethoxazole concentration, 4.0 ug/ml.

250 ug/ml) and carbenicillin. The remainder of the susceptibility profile was unchanged. Ticarcillin was discontinued, and intravenous administration of trimethoprim-sulfamethoxazole (960 and 4,800 mg, respectively, per day) was begun. CSF obtained on hospital day 11 remained positive for P. denitrificans. The patient remained comatose and expired on day 12 after admission.

At autopsy, abundant purulent exudate was observed covering both cerebral hemispheres, the base of the brain, and throughout the ventricular system. P. denitrificans was recovered from multiple postmortem central nervous system specimens. No other focus of infection was identified.

Discussion. P. denitrificans was identified by the criteria described by Weaver et al. (7). The organism, a gram-negative bacillus, grew well on MacConkey medium and was oxidase and catalase positive. Acid metabolic by-products were not detected when the organism was grown in Centers for Disease Control oxidative-fermentative basal medium, containing glucose, xylose, lactose, sucrose or maltose, either open or overlaid with sterile mineral oil. The organism failed to ferment the same sugars in purple broth. Growth was observed on salmonella-shigella agar (Scott Laboratories) and in 6.5% NaCl. The organism failed to hydrolyze esculin or to liquefy gelatin, did not grow on Simmons citrate agar, required 96 h to grow on cetrimide medium, and grew poorly at 42°C in tryptic soy broth (Scott). Indole, urease, and phenylalanine deaminase were not produced. Lysine decarboxylase, arginine dihydrolase, and ornithine decarboxylase were also not produced. The organism was nonhemolytic when grown on 5.0% sheep blood agar, forming small, grey, convex, glistening colonies of 1 to 2 mm in diameter when incubated at 35°C in 10% CO2 for 48 h. An alkaline slant with no reaction in the butt and no H2S production was observed when the organism was grown on a triple sugar iron agar (Scott) slant for 20 h at 35°C in air. Nitrates and nitrites were reduced with the production of copious amounts of gas. The ability to reduce nitrates with gas production was lost upon repeated subculture. The organism was motile and possessed 1 or 2 polar flagella.

Based on these observations, it is clear that this organism could easily be confused with Alcaligenes denitrificans (group V-C), an organism which is known to lose its ability to reduce nitrates with gas production upon repeated subculture (4). However, by the criterion of Weaver et al. (7), A. denitrificans usually grows on Simmons citrate agar with an alkaline reaction and possesses peritrichous flagella. Gilardi also states that A. denitrificans is characterized by peritrichous flagellation (3). Since the organism described in this report failed to grow on Simmons citrate agar and possessed 1 or 2 polar flagella, it was probably not A. denitrificans.

The precise taxonomic status of P. denitrificans awaits clarification. Based on DNA and RNA homology studies (2), it has been suggested that organisms previously designated as P. denitrificans might belong to other species and genera. It is not recognized in Bergey's Manual of Determinative Bacteriology (8th ed.), nor is it described in the Manual of Clinical Microbiology (3rd ed.). These considerations notwithstanding, the organism described in this report did meet the criterion for the identification of P. denitrificans as elucidated by Weaver et al. (7).

The initial isolate was resistant to all antibiotics tested except carbenicillin, ticarcillin, trimethoprim-sulfamethoxazole, piperacillin, and polymyxin B, to all of which it was susceptible,
and chloramphenicol, to which it exhibited intermediate susceptibility (Table 1). All isolates recovered after hospital day 3 of the patient yielded a similar susceptibility profile except that these isolates were resistant to carbenicillin and ticarcillin.

We believe this to be the first published report of systemic disease in humans caused by P. denitrificans. Although the pathogenesis of the meningitis described in this case is uncertain, an attractive hypothesis is that colonization of an old healing ulcer led to bacteremia with ultimate seeding of the leptomeninges. It is not surprising that, despite a transient clinical response, the condition of the patient worsened on combined ampicillin-chloramphenicol therapy, since the infecting agent was found to be resistant to ampicillin while possessing only intermediate susceptibility to chloramphenicol. It is also not surprising that the patient did poorly when treated with ticarcillin, despite the fact that the organism originally isolated from CSF was susceptible to this antibiotic. At the time the patient was begun on ticarcillin therapy, (hospital day 3), a second isolate of P. denitrificans recovered from CSF was found to be resistant to ticarcillin. The possibility exists that 3 days of ampicillin therapy selected for a population of organisms resistant to ticarcillin, another beta-lactam compound. That the patient continued to do poorly, despite being switched to trimethoprim-sulfamethoxazole on hospital day 5, probably reflects the general compromised status of the host as well as the extent of his disease. All isolates were found to be susceptible to trimethoprim-sulfamethoxazole. In addition, four determinations of the inhibitory titers of CSF (ventricular and lumbar) obtained during trimethoprim-sulfamethoxazole therapy indicated that sufficient CSF antibiotic levels had been achieved.

This report serves to illustrate that, in a given host, even the most uncommon organisms are capable of causing serious systemic disease. This report also emphasizes the need for clarification of the taxonomic status of P. denitrificans.

LITERATURE CITED