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Associated Mortality and Clinical Characteristics of Nosocomial *Pseudomonas maltophilia* in a University Hospital

ALLAN J. MORRISON, JR.,†‡* KAREN K. HOFFMANN, AND RICHARD P. WENZEL

Department of Internal Medicine, University of Virginia Hospital, Charlottesville, Virginia 22908

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We studied the spectrum of clinical disease in 99 patients with nosocomial *Pseudomonas maltophilia* isolates at the University of Virginia Hospital from 1981 through 1984. The annual rate of isolation increased from 7.1 to 14.1 per 10,000 patient discharges. A crude mortality rate of 43% was documented in all patients from whom the organism was cultured, and the data include 12 patients with nosocomial bacteremia (four deaths). Risk factors associated with death for patients having a *P. maltophilia* isolate included the following: requirement for care in any intensive care unit during hospitalization ($P = 0.0001$), patient age over 40 years ($P = 0.002$), and a pulmonary source for the *P. maltophilia* isolate ($P = 0.003$). All *P. maltophilia* isolates were susceptible to trimethoprim-sulfamethoxazole, 60% of the isolates were resistant to all aminoglycosides (amikacin, tobramycin, and gentamicin), and more than 75% of the isolates were resistant to all β-lactam antibiotics. The antibiotic susceptibility pattern allows for a niche exploitable in the hospital microbial environment by an organism with a marked associated mortality.

The appellation *Pseudomonas maltophilia* was first proposed by Hugh and Ryschenkow in 1961 (20), and taxonomic status was verified in 1981 (18). Recently, Swings et al. (35) proposed that this bacterium be transferred to the genus *Xanthomonas* as *Xanthomonas maltophilia*. The organism is an aerobic, gram-negative, motile bacillus possessing polar multitrichous flagella. It should not be misidentified as other *Pseudomonas* species, because it possesses distinct biochemical characteristics, including a positive reaction for lysine decarboxylase and DNase and often has a negative reaction for indophenol oxidase (19, 26). Early isolates were recovered from various locations, including well and river water, raw milk, frozen fish, raw sewage, rabbit and human feces, contaminated tissue culture, and various human body fluids (20). More recently, the organism has been identified as a cause of bloodstream infections (11, 24, 33, 41), endocarditis (5, 9, 40), infections of traumatic and postoperative wounds (6, 13, 14, 28), urinary tract infections (13, 14), pneumonia (7, 12, 31), meningitis (4, 27), epididymitis (34), eye infections (2, 4, 34), and mastoiditis (16). This report describes the spectrum of clinical disease in 99 patients from whom nosocomial *P. maltophilia* was isolated between 1981 and 1984 at the University of Virginia Hospital. Furthermore, risk factors associated with fatal outcome after *P. maltophilia* acquisition are delineated.

MATERIALS AND METHODS

Patient source and period of study. The University of Virginia Hospital is a 700-bed teaching hospital serving the city of Charlottesville, Va. (population, 40,000), and the western half of the state of Virginia. Approximately 22,500 patients are admitted annually for a mean hospitalization time of 9 days. Six intensive care areas account for 8% of hospital beds. The study period extended from 1 January 1981 through 31 December 1984.

Case definition. Computerized microbiologic data were reviewed for all specimens submitted to the clinical laboratory during the study period. *P. maltophilia* isolates were considered to be nosocomially acquired under any of the following circumstances. (i) The body site from which the isolate was obtained had been culture negative on prior determination or culture positive for other microbiologic floras ($n = 62$). (ii) The isolate was obtained at or near the time of hospital admission when a prior hospital discharge had occurred within the previous 7 days ($n = 10$). (iii) The isolate was obtained from a body site which on previous diagnostic testing had been documented to be normal by the admitting physician ($n = 27$). Hospital charts were reviewed for confirmation of the isolation report as well as for primary and secondary diagnoses, surgical procedures, admission date, date of first *P. maltophilia* isolation, date of discharge or death, source and method of specimen procurement, whether *P. maltophilia* was isolated as a pure culture or as part of a mixed culture, other organisms isolated if mixed culture, and isolate-specific therapy for the *P. maltophilia* isolate.

Microbiologic data. *P. maltophilia* isolates were identified by the Analytical Profile Index procedure (API 20-E; Analytab Products, Plainview, N.Y.) supplemented by oxidase and DNase testing. Antimicrobial susceptibility testing was performed by standardized methods (1, 25).

Statistical analysis. Evaluation of risk factors related to the death of patients was achieved by performing discriminant function analysis (15). Evaluation of mean age as it related to outcome was made by using a two-tailed *t* test (3).

RESULTS

During the 4-year study, 99 nosocomial cases were identified; only 2 patients had community acquired *P. maltophilia* isolates. The overall rate of nosocomial *P. maltophilia* isolation was 10.1 per 10,000 discharges (annual range, 7.1 [1981] to 14.1 [1984]). Pulmonary isolates were the most

* Corresponding author.
† Present address: The Fairfax Hospital, Falls Church, VA 22046.
‡ Address for reprints: 3299 Woodburn Rd., Suite 220, Annandale, VA 22003.

TABLE 1. Crude mortality and frequency of *P. maltophilia* isolation at the University of Virginia from 1981 to 1984

Yr	% Mortality for all patients	No. of patients (% mortality) with isolate(s) from the following source:				
		Bacteremia	Pulmonary	Urine	Wound	Other[a]
1981	41.2	4	6	0	4	3
1982	45.8	3	16	1	3	1
1983	45.5	4	13	2	3	0
1984	38.9	1	26	3	4	2
Overall	43.2	(33)	(59)	(0)	(21.4)	(0)

[a] Includes one isolate each from the following sources: labial cyst, peritoneal fluid, peritoneal dialysate, amniotic fluid, ear drainage, and eye drainage.

frequent (62% of patients), followed by wound sites (14% of patients) and bacteremias (12% of patients) (Table 1). The crude mortality rate was 43.2% (annual range, 39 to 46%). No case clustering was noted during the study period.

Age group. The distribution frequency and outcome by age are shown in Table 2. Of the 12 cases occurring in patients less than 1 year of age, 10 occurred in patients born prematurely, one patient had congenital heart disease, and one patient had a congenital urethral stricture (urine isolate). All of the four patients in this age group who died were born prematurely and had *P. maltophilia* sputum isolates (three with mixed culture, one with pure culture). None of the four deaths were attributed to *P. maltophilia*.

Underlying disease. The frequency distribution of underlying diagnoses among the 99 patients showed that 23 patients had a primary diagnosis of malignancy; 12 of these patients died. There was no histologic predominance noted among deaths of patients with a *P. maltophilia* isolate. Furthermore, 23 patients had a tracheostomy (19 of the 23 had a pulmonary source for the *P. maltophilia* isolate; 11 of them died). Thirteen patients in all had a primary diagnosis of atherosclerotic cardiovascular disease, 11 patients had a primary diagnosis of acute renal failure, and 10 patients had been admitted with multiple trauma.

Mixed-culture cases. Of the 99 patients, 36 demonstrated *P. maltophilia* isolates in pure culture and 63 demonstrated the isolate as part of a mixed bacterial culture (Table 3). Thirty-one percent of patients with pure-culture *P. maltophilia* isolates died, compared with 51% of patients with mixed-culture isolates. Among the 63 patients with mixed-culture results, *Enterobacter* species was the most frequent additional isolate (14 patients), followed by *Pseudomonas aeruginosa* (12 patients), *Staphylococcus aureus* (10 patients), *Escherichia coli* (8 patients), *Candida* species (7 patients), *Klebsiella* species (7 patients), and *Acinetobacter* species (4 patients).

Bacteremia cases. Of the 12 cases of nosocomial *P. maltophilia* bacteremia, 8 were documented by pure culture (two deaths) and 4 had a polymicrobial bloodstream infection (two deaths).

TABLE 2. Nosocomial *P. maltophilia* isolates at the University of Virginia Hospital

Patient age (yr)	No. of patients with outcome:	
	Survival	Death
<1	8	4
1–19	3	0
20–39	13	2
40–59	10	8
60–79	18	28
≥80	4	1

Risk factors associated with fatal outcome for the 99 patients included the following: requirement for stay in any intensive care unit during hospitalization ($P = 0.0001$), age over 40 years ($P = 0.002$), and a pulmonary source for the *P. maltophilia* isolate ($P = 0.003$). The statistical model developed by discriminant function analysis demonstrated a sensitivity of 88% and a specificity of 80% for predicting a fatal outcome for patients. Evaluable factors which were found not to be statistically significant predictors of fatal outcome included the following: sex, length of hospitalization, blood or urine as the source of the *P. maltophilia* isolate, isolate-specific antibiotic therapy, and length of time from the date of isolation to the date of patient discharge or death (Table 3).

During the study period, *P. maltophilia* isolates demonstrated 100% susceptibility to trimethoprim-sulfamethoxazole. Sixty percent of the isolates were resistant to all aminoglycosides (amikacin, tobramycin, and gentamicin), 76% of the isolates were resistant to all semisynthetic penicillins (carbenicillin, ticarcillin, azlocillin, mezlocillin, and piperacillin), and 96% of the isolates were resistant to all cephalosporin antibiotics (cephalothin, cefamandole, cefoxitin, cefuroxime, cefotaxime, ceftriaxone, cefaperazone, and ceftazidime).

DISCUSSION

Several reports suggest that *P. maltophilia* is the second most frequent pseudomonad recovered from clinical material after *P. aeruginosa* (17, 28, 29). Early reports stressed that *P. maltophilia* was recovered in mixed culture and had limited human pathogenicity in the absence of underlying deficiencies in the immune function of a patient (12, 13, 28, 34). Evidence supporting this association with host immune defects derives from a recent report showing that 39 of 82 (48%) patients from whom *P. maltophilia* was isolated had a malignant lesion at the isolate site (23). Nagai suggested that an altered microenvironment owing to anaerobic glycolysis from tumor destruction could select for the emergence of certain organisms in situ (23). However, pathogenicity of this species in patients without malignancies has also been documented (10, 32, 37, 38) (Table 4).

This report appears to support the concept of the limited virulence of the organism, because patients from whom *P. maltophilia* was isolated as part of a mixed culture had a significantly greater likelihood of death (50%), compared with a 30% case-fatality ratio for patients from whom *P. maltophilia* was isolated in pure culture. Furthermore, among bacteremic cases, two of four (50%) patients with mixed culture died, compared with two of six (33%) patients with pure culture; however, these small numbers limit the strength of datum interpretation.

One striking characteristic of *P. maltophilia* is its resistance to most commonly used antimicrobial agents, including

TABLE 3. Clinical characteristics of *P. maltophilia* cases at the University of Virginia Hospital from 1981 to 1984

Case outcome	Mean age (yr)[a]	Sex (no. of patients)		Mean length of hospitalization (days)[b]	No. of isolates from culture type	
		Male	Female		Pure[c]	Mixed
Survival	43.0	36	20	53.5	25	31
Death	56.8	25	18	65.2	11	32

[a] Overall mean, 49.0 years. $P = 0.006$.
[b] Overall mean, 59.0 days.
[c] $P = 0.05$.

TABLE 4. Common-source *P. maltophilia* isolates from the hospital environment

Reservoir	No. of patients		Reference
	Colonized	Infected	
Chlorhexidine-cetramide disinfectant	63	7	37
EDTA anticoagulant in vacuum blood collection tubes	25	1 (fatality)	32
Transducer dome and calibration device	8	8 (1 fatality)	10
Cardiopulmonary bypass pump	1	1	38

those effective against *P. aeruginosa* (8, 21, 22, 36, 39–41). Additionally, inducible β-lactamases have been isolated and purified from *P. maltophilia* strains (30). All strains tested were susceptible to trimethoprim-sulfamethoxazole, but more than 75% were resistant to β-lactam agents, and 60% were resistant to all aminoglycosides. Contact isolation might be considered in certain settings to prevent cross transmission to patients with known host immune defects.

This report highlights several features of infection and colonization owing to *P. maltophilia*. First, the rate of nosocomial isolation has been increasing, and the 43% crude mortality rate indicates a high-risk group of patients. Second, the identified risk factors of intensive care unit hospitalization, age over 40 years, and pulmonary site for the *P. maltophilia* isolate are statistically significant predictors of fatal outcome. Third, the inherent resistance of the organism to several (or all) aminoglycoside and β-lactam antibiotics favors an epidemiologic niche which can be exploited effectively in modern hospitals. Finally, *P. maltophilia* should no longer be viewed as a harmless saprophyte in hospitalized patients.

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