JOURNAL OF CLINICAL MICROBIOLOGY, Aug. 1996, p. 1908–1913 Vol. 34, No. 8
0095-1137/96/$04.00+0

Clinical and Microbiological Characteristics of *Flavobacterium indologenes* Infections Associated with Indwelling Devices

PO-REN HSUEH,[1] LEE-JENE TENG,[2] SHEN-WU HO,[2] WEI-CHUAN HSIEH,[3] AND KWEN-TAY LUH[1]*

Departments of Laboratory Medicine[1] and Internal Medicine,[3] National Taiwan University Hospital, and School of Medical Technology, College of Medicine, National Taiwan University,[2] Taipei, Taiwan, Republic of China

Received 24 January 1996/Returned for modification 26 April 1996/Accepted 8 May 1996

Clinical infections caused by *Flavobacterium indologenes* have never been documented. Thirteen isolates derived from seven patients with indwelling device-associated *F. indologenes* infections were identified from 1 April through 30 November 1995. The antimicrobial susceptibilities to 20 antimicrobial agents of the isolates, the cellular fatty acid chromatograms for the isolates, and the random amplified polymorphic DNA (RAPD) patterns generated by arbitrarily primed PCR of the isolates were studied. The antibiotypes and RAPD patterns differed among the isolates recovered from different patients. However, both antibiotypes and RAPD patterns were identical among the five isolates from one patient with multiple episodes of central venous catheter-associated bacteremia within a 1.5-month period and between the two isolates from another patient suffering from two episodes of catheter-related bacteriuria at an interval of 14 days. It is documented that the recurrent infections in each of these two patients were caused by a single *F. indologenes* clone, respectively. Identical antibiotypes and RAPD patterns were also demonstrated between two isolates from a patient with ventilator-associated pneumonia, one recovered from an endotracheal aspirate and the other derived from a blood specimen 10 days later, indicating the invasive nature of *F. indologenes*. Two cellular fatty acid chromatograms were identified among these isolates. All of the isolates showed in vitro resistance to cephalothin, cefotaxime, ceftriaxone, moxalactam, aztreonam, aminoglycosides, erythromycin, clindamycin, vancomycin, and teicoplanin. *F. indologenes* should be included as an etiologic agent of infections associated with the use of indwelling devices.

Infections associated with indwelling devices continue to have a major impact on clinical practice. It is estimated that the number of intravascular devices, urinary catheters, endotracheal tubes, and other temporary or permanent devices implanted each year in the United States probably ranges into the millions (5, 6). The National Nosocomial Infection Surveillance system of the Centers for Diseases Control and Prevention (CDC) found that intravascular catheter-related bacteremias accounted for 82% of all nosocomial bacteremias surveyed in National Nosocomial Infection Surveillance system hospitals from September 1984 through July 1986 (5). Most frequently, gram-positive cocci, especially *Staphylococcus epidermidis*, are isolated from infections associated with the use of intravascular devices (5, 12), and gram-negative bacilli or *Candida* species are most often recovered from infections related to the use of endotracheal tubes or urinary catheters (6, 28). Indwelling device-associated infections caused by *Flavobacterium indologenes* are a distinct rarity and, to our knowledge, have not been reported in the literature.

F. indologenes, previously assigned as one of the *Flavobacterium* species CDC group IIb, was later designated in 1983 by Yabuuchi et al. (32). In 1990, this organism was further clearly differentiated from *Flavobacterium gleum* by DNA-DNA homology data and eight phenotypic characteristics (10, 31). Strains of *Flavobacterium* species CDC group IIb have been reported to be implicated in intravascular device-related bacteremias and meningitis; however, clinical infections caused by *F. indologenes* organisms have never been documented (22, 23). In this report, we describe seven patients with *F. indologenes* infections associated with the use of indwelling devices. Thirteen isolates recovered from these patients were studied by analyzing their in vitro susceptibilities to 20 antimicrobial agents, cellular fatty acid analysis, and molecular epidemiological typing.

MATERIALS AND METHODS

Clinical characteristics. From 1 April through 30 November 1995 seven patients with *F. indologenes* infections associated with the use of indwelling devices in the National Taiwan University Hospital were identified. Relevant information on the clinical presentations of these patients were collected. These data included the underlying diseases, associated conditions (the use of indwelling devices and chemotherapy), clinical syndromes, day of in-hospital positive culture for *F. indologenes*, other sites of isolation of this organism, antimicrobial therapy after culture results were available, and outcome.

Bacterial isolates. Thirteen isolates of *F. indologenes* recovered from the seven patients with indwelling device-associated infections were collected. These were identified by conventional methods as described previously (25) and were confirmed with the API 20NE system (BioMerieux, Marcy-I'Etoile, France) and the Vitek GNI system (Vitek System; BioMerieux Vitek, Hazelwood, Mo.). Additional tests used to differentiate between *F. indologenes* and *F. gleum*, including growth at 41°C, esculin hydrolysis within 4 h and after 24 h of incubation, acid production from D-xylose and L-arabinose, and the presence of urease, were performed in accord with the methods described by Yabuuchi et al. (31).

Antimicrobial susceptibility testing. The MICs of 20 antimicrobial agents for the 13 isolates of *F. indologenes* were determined by the agar dilution method described by the National Committee for Clinical Laboratory Standards (16). The following antimicrobial agents were obtained as standard reference powders of known potency for laboratory use: cephalothin, clindamycin, erythromycin, gentamicin, netilmicin, amikacin, trimethoprim-sulfamethoxazole, and vancomycin, from Sigma Chemical Co. (St. Louis, Mo.); piperacillin and minocycline, from Lederle Laboratories (Pearl River, N.Y.); cefotaxime, from Hoechst AG (Frankfurt, Germany); ceftriaxone, from Roche Laboratories (Nutley, N.J.);

* Corresponding author. Mailing address: Department of Laboratory Medicine, National Taiwan University Hospital, No. 7, Chung-Shan South Rd., Taipei, Taiwan, Republic of China. Phone: 886-2-3562150. Fax: 886-2-3224263.

TABLE 1. Clinical features of seven patients with indwelling device-related infections caused by *F. indologenes*

Patient no.	Age (yr)/sex[a]	Underlying disease(s)[b]	Associated infection(s)	Indwelling device(s)[c]	Isolate(s)	Source	Date of isolation (mo/day)
1	28/M	Burn (82% TBSA)	Wound infection, bacteremias	CVCs	A1	CVC	9/13
					A2	Blood	9/25
					A3	Blood	10/5
					A4	Blood	11/2
					A5	CVC	11/2
2	61/M	CVA	Urinary tract infections	UC	B1	Urine	9/18
					B2	Urine	10/2
3	69/M	AML	Pneumonia	ET	C1	Sputum	8/28
					C2	Blood	9/8
4	69/M	AML, neutropenia	Bacteremia	PAC	D	Blood	11/8
5	59/F	MM, neutropenia	Bacteremia	PAC	E	Blood	9/12
6	5/F	Neuroblastoma	Bacteremia	HC	F	Blood	9/11
7	1/F	Hepatoblastoma	Bacteremia	PAC	G	Blood	4/26

[a] M, male; F, female.
[b] TBSA, total body surface area; CVA, cerebrovascular accident; AML, acute myelogenous leukemia; MM, multiple myeloma.
[c] CVCs, central venous catheters; UC, urinary catheter; ET, endotracheal tube; PAC, Port-A-Cath; HC, Hickman catheter.

ceftazidime, from Glaxo Operations, Ltd. (Greenford, England); cefoperazone, from Pfizer Inc. (New York, N.Y.); moxalactam, from Shionogi Pharmaceutical Co. Ltd. (Osaka, Japan); aztreonam, from Bristol-Mayers Squibb Laboratories (New York, N.Y.); imipenem, from Merck Sharp & Dohme (West Point, Pa.); ofloxacin, from Daiichi Pharmaceutical Co. Ltd. (Tokyo, Japan); ciprofloxacin, from Bayer Co. (Leverkusen, Germany); and teicoplanin, from Marion Merrill Dow (Kansas City, Mo.). The drugs were incorporated into agar in serial twofold concentrations from 0.03 to 128 μg/ml. The MIC of each antibiotic was defined as the lowest concentration which inhibited visible growth of the organism. *Staphylococcus aureus* ATCC 29213, *Escherichia coli* ATCC 25922, and *Pseudomonas aeruginosa* ATCC 27853 were used as control strains in each set of tests. The percentage of isolates susceptible to these antimicrobial agents was determined by applying the susceptibility breakpoints used for *Pseudomonas* species (16).

Cellular fatty acid analysis. The isolates used for cellular fatty acid analysis were incubated on Trypticase soy agar which was not supplemented with blood (BBL Microbiology System, Cockeysville, Md.) at 35°C for 24 h in ambient air. Harvest and lysis of cells, saponification, methylation of fatty acids, and extraction of fatty acid methyl esters were performed according to the manufacturer's instructions (13). Fatty acid methyl esters were analyzed by gas-liquid chromatography (GLC) with the Microbial Identification System (Microbial ID Inc., Newark, Del.) with a Hewlett-Packard model 5890A instrument (Hewlett-Packard, Avondale Division, Avondale, Pa.) equipped with a fused-silica capillary column (25 m in length by 0.2 mm in internal diameter) and a flame ionization detector. The conditions for GLC were those recommended in the operational manual of the Microbial Identification System (13). Cellular fatty acids were identified by comparing the retention times with those of authentic standards (Hewlett-Packard).

RAPD assay. All isolates were cultured in brain heart infusion broth (Difco Laboratories, Detroit, Mich.) for 18 to 24 h at 35°C in ambient air. Extraction of bacterial DNA was performed with a commercial kit (Puregene; Gentra Systems, Inc., Minneapolis, Minn.). The random amplified polymorphic DNA (RAPD) assays, generated by arbitrarily primed PCR, were performed with the following two arbitrary oligonucleotide primers obtained from OPERON Technologies, Inc. (Alameda, Calif.): OPA-10 (5′-GTGATCGCAG-3′) and OPB-15 (5′-GGAGGGTGTT-3′). The amplification reactions were done in a final volume of 25 μl containing 10 mM Tris-HCl (pH 8.3); 50 mM KCl; 2 mM $MgCl_2$; 100 μM (each) dATP, dCTP, dGTP, and dTTP; 5 pM primer, 0.5 U of *Taq* DNA polymerase (Perkin-Elmer Cetus, Norwalk, Conn.); and 1 μl of bacterial DNA extract. The PCR conditions consisted of 40 cycles for 1 min at 94°C, 1 min at 35°C, and 2 min at 72°C and a final extension for 5 min at 72°C. The samples were overlaid with 10 μl of mineral oil and were amplified in a thermocycler (PTC-100; MJ Research Inc., Watertown, Mass.). The amplification products were analyzed by electrophoresis in a 1.4% agarose gel and were detected by staining with ethidium bromide.

Definitions. Patients with intravascular device-associated infections caused by *F. indologenes* were defined as those with a body temperature of >38.3°C and malaise, chills, or tachypnea with no obvious identifiable source of infection except for exit-site or tunnel infection. Moreover, cultures of at least two blood samples (obtained through the central catheter or from a peripheral source) were positive for *F. indologenes* or culture of one blood sample and culture of one catheter tip or exit-site sample were positive for the same organism (5, 12). Infection related to the use of indwelling urinary catheters was characterized as the development of bacteriuria and pyuria during the period of catheterization (28). Ventilator-associated pneumonia was defined in accord with the statement of Salata et al. (21). Neutropenia was defined as a leukocyte count of $<4 \times 10^9$/liter. Antibiotic therapy was considered to be appropriate if the drugs chosen proved to be active against the isolate on the basis of the results of susceptibility testing.

Antibiotypes were considered identical if the MICs of all antimicrobial agents tested were identical or within a 1-dilution discrepancy. RAPD patterns were considered identical if every band was shared. Isolates were defined as the same strain or originating from a single clone if they had identical antibiotypes and RAPD patterns.

RESULTS

Characterization of patients. The clinical characteristics of the seven patients with indwelling device-associated infections are provided in Table 1.

(i) Patient 1. A previously healthy 28-year-old man was transferred to the hospital because of a third-degree burn, which occurred 2 days before, covering 82% of his body surface. He experienced profound wound sepsis, intractable ventilator-related pneumonia, and an unstable hemodynamic status during his 2-month hospital stay. A central venous catheter was removed on the sixth hospital day because of the suspicion of intravascular catheter-related infection. A culture (isolate A1) of the catheter tip for bacteria yielded abundant *F. indologenes* organisms. This organism was subsequently recovered from the patient's blood specimens on hospital days 7 (isolate was not collected), 14 (isolate was not collected), 18 (isolate A2 and an *Acinetobacter baumannii* isolate), 28 (isolate A3), and 56 (isolate A4). Another two central venous catheters were inserted on the 7th and 56th hospital days. The long interval between these two catheter implantations was due to the lack of an appropriate site of access on the extensively lesioned skin. Cultures of both of these two catheter tips yielded *F. indologenes* (one is isolate A5 and the other isolate was not collected). The patient was treated with multiple antimicrobial agents, including broad-spectrum cephalosporins, imipenem,

TABLE 2. In vitro susceptibilities of the 13 *F. indologenes* isolates

Antimicrobial agent	MIC (μg/ml) for the indicated isolate[a]												
	A1	A2	A3	A4	A5	B1	B2	C1	C2	D	E	F	G
Beta-lactams													
Piperacillin	128	128	128	128	128	>128	>128	64	128	2	4	64	2
Cephalothin	>128	>128	>128	>128	>128	>128	>128	>128	>128	>128	>128	>128	>128
Cefotaxime	>128	>128	>128	>128	>128	>128	>128	>128	>128	64	32	>128	64
Cefoperazone	>128	>128	>128	>128	>128	>128	>128	128	128	8	8	128	8
Ceftriaxone	>128	>128	>128	>128	>128	>128	>128	>128	>128	32	32	>128	32
Ceftazidime	32	32	64	32	32	8	8	8	8	2	8	16	2
Moxalactam	128	128	128	128	64	>128	>128	128	128	128	64	64	64
Aztreonam	>128	>128	>128	>128	>128	>128	>128	>128	>128	>128	>128	>128	>128
Imipenem	>128	>128	>128	>128	>128	>128	>128	1	1	64	64	>128	32
Aminoglycosides													
Gentamicin	>128	>128	>128	>128	>128	>128	>128	16	16	>128	>128	>128	128
Netilmicin	>128	>128	>128	>128	>128	>128	>128	16	16	>128	>128	>128	>128
Amikacin	>128	>128	>128	>128	>128	>128	>128	>128	>128	>128	>128	>128	64
Fluoroquinolones													
Ofloxacin	64	64	64	64	32	8	8	64	32	64	2	64	4
Ciprofloxacin	128	128	128	128	128	4	4	128	128	64	1	64	2
Others													
Erythromycin	>128	>128	>128	>128	>128	>128	>128	>128	>128	>128	>128	>128	64
Clindamycin	4	4	4	4	4	4	4	4	4	4	4	128	4
Minocycline	8	16	8	8	8	4	4	4	4	8	8	8	2
SXT[b]	16	16	8	16	16	16	8	8	16	32	1	1	0.5
Vancomycin	16	16	16	16	16	16	16	16	16	16	16	16	16
Teicoplanin	32	32	16	32	32	32	32	32	32	64	32	32	32

[a] Isolates A1, A2, A3, A4, and A5 were *F. indologenes* isolates from patient 1; isolates B1 and B2 were from patient 2; isolates C1 and C2 were from patient 3; and isolates D, E, F, and G, from patients 4, 5, 6, and 7, respectively.
[b] SXT, trimethoprim-sulfamethoxazole.

ciprofloxacin, aminoglycosides, and vancomycin, which were later proved to be effective against all of the isolates except the *F. indologenes* isolates cultured from his various clinical specimens during hospitalization. He died on the 64th hospital day.

(ii) Patient 2. A 61-year-old man was admitted to the hospital because of a cerebrovascular accident. On the fourth day, he developed a fever (temperature, 38°C) and pyuria associated with the implantation of a urinary catheter for urinary incontinence. A culture of urine from the catheter grew *F. indologenes* organisms. He was treated with ceftazidime and amikacin. The fever subsided on the second day of treatment. Another event of fever and chills occurred 14 days after the previous episode, and the same antimicrobial agents were administered. Three days later, the symptoms disappeared, and a culture of urine from the indwelling urinary catheter yielded the same organism.

(iii) Patient 3. A 69-year-old man diagnosed with acute myelogenous leukemia was admitted for maintenance chemotherapy. He had had a Hickman catheter in place for 2 months. Ten days after the start of chemotherapy, he presented with a fever (temperature, 39°C) and dyspnea and then developed respiratory distress necessitating ventilator support. His peripheral leukocyte count was 0.5×10^9/liter. Empiric therapy with piperacillin and amikacin was initiated. Bacterial culture of an endotracheal aspirate grew *F. indologenes* and *Acinetobacter baumanii* isolates, but the culture of blood collected simultaneously was negative. A chest X ray taken 8 days later showed a consolidation in the right lower lung consistent with the diagnosis of pneumonia. A subsequent culture of blood drawn 10 days after the previous blood culture was positive for *F. indologenes*. The patient defervesced 10 days after changing piperacillin to ceftazidime and is continuing amikacin use.

(iv) Patients 4, 5, 6, and 7. Patients 4 through 7 all had underlying hematologic malignancies and received chemotherapy during their hospital stays. In patients 4, 5, and 7, a Port-A-Cath was used for access for intravenous chemotherapy. A Hickman catheter was implanted in patient 6. Intravascular catheter-associated infections caused by *F. indologenes* isolates were diagnosed within 7 to 10 days after the initiation of chemotherapy in all four patients, and two of them (patients 4 and 5) were in the neutropenic stage. They were all treated with antimicrobial agents with in vitro activity against the infecting *F. indologenes* isolates, and the patients' clinical symptoms disappeared 3 days later. All catheters remained in place during the hospital days. Follow-up cultures of blood drawn from these patients were negative for *F. indologenes.*

Bacterial isolates. All of the isolates were oxidase-positive, glucose-nonfermenting, and gram-negative rods. Growth on sheep blood agar revealed within 24 h of incubation smooth, circular, yellow-pigmented colonies 1 to 2 mm in diameter. The biochemical profiles produced by the API 20NE system and Vitek GNI card showed with a probability of >99% that the organism was *F. indologenes*. All of these isolates failed to grow at 41°C, did not produce acid from D-xylose and L-arabinose, and were negative for esculin hydrolysis within 4 h of incubation but positive after 24 h of incubation, indicating that the characteristics of these isolates were in agreement with those of *F. indologenes.*

Susceptibility testing. The results of testing of the susceptibilities of the isolates to 20 antimicrobial agents are provided in Table 2. The antibiotypes of the isolates from different patients varied. However, the different isolates from patients 1, 2, and 3 had identical antibiotypes, respectively. All isolates were uniformly resistant to cephalothin, cefotaxime, ceftriax-

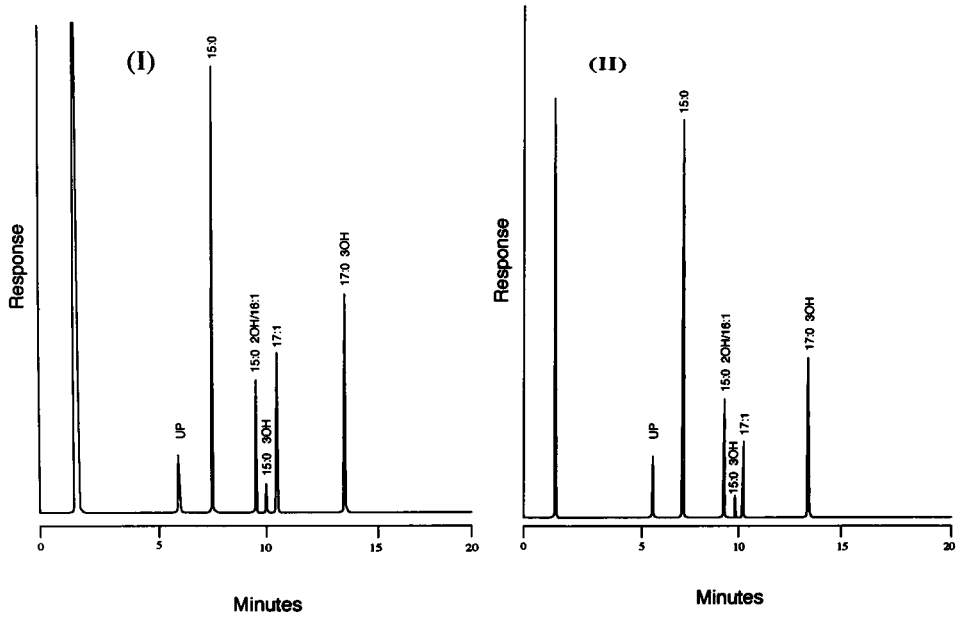

FIG. 1. Gas chromatograms of esterified fatty acids for *F. indologenes* isolates. Pattern I was found for isolates A1 to A5, D, and F, and pattern II was found for isolates of B1, B2, C1, C2, E, and G. The designation of the fatty acid peaks refers to the number of carbon atoms and the number of double bonds. The 2OH and 3OH refer to a hydroxyl group at carbon atoms 2 and 3, respectively. UP, unknown peak (Microbial Identification System; Microbial ID Inc.).

one, moxalactam, aztreonam, aminoglycosides, erythromycin, clindamycin, vancomycin, and teicoplanin. Susceptibilities to piperacillin, cefoperazone, ceftazidime, imipenem, quinolones, minocycline, and trimethoprim-sulfamethoxazole were variable.

Cellular fatty acid chromatograms. Results of GLC analysis of esterified cellular fatty acids for these isolates were characterized by the presence of four major and two minor peaks (Fig. 1). Two cellular fatty acid patterns (pattern I and pattern II) were identified among these isolates. Isolates with pattern I chromatograms contained more heptadecenoic acid ($C_{17:1}$) than 2-hydroxyl-pentadecanoic acid/hexadecenoic acid ($C_{15:0}$ 2OH/$C_{16:1}$). However, isolates with pattern II chromatograms had more 2-hydroxyl-pentadecanoic/hexadecenoic acid ($C_{15:0}$ 2OH/$C_{16:1}$) than heptadecenoic acid ($C_{17:1}$). The chromatograms of the five isolates derived from patient 1 were similar, and those of two isolates each from patients 2 and 3, respectively, were similar.

RAPD patterns. Arbitrarily primed PCR revealed that the isolates recovered from the seven different patients had seven different RAPD patterns (Fig. 2). The five isolates (isolates A1 to A5) from patient 1 had identical fingerprints which could be easily differentiated from those of the other isolates. This was also true of the two isolates from patient 2 (isolates B1 and B2) and the two isolates from patient 3 (isolates C1 and C2).

DISCUSSION

Flavobacteria, unlike species of staphylococci (especially *S. epidermidis*), which are the most common member of the skin flora associated with catheter-related bacteremias (5, 12, 29), are not normally present in the human microflora (25). However, these organisms as well as certain gram-negative bacteria can thrive in aqueous environments and can cause intravascular device-related bacteremias, wound sepsis, and ventilator-associated pneumonia by virtue of their ability to contaminate and persist in fluid-containing apparatuses (2, 7, 9, 18, 22, 23). An outbreak of indwelling arterial catheter-related nosocomial bacteremias has been reported previously (23). The production of a biofilm by these bacteria not only allows the maintenance of the organisms on a specific surface but also challenges the action of antimicrobial agents (5).

RAPD analysis has been extensively applied for epidemiological typing and taxonomic study of clinical isolates (3, 30). No previous reports have described the use of this technique to type clinical isolates of *F. indologenes*. The critical step of this application depends on the choice of primers (30). In the present study, only 2 of the 40 arbitrary primers (OPA-01 to OPA-20 and OPB-01 to OPB-20) tested had a good ability to discriminate among the isolates from different patients. In the present study, the RAPD patterns of the isolates recovered from different patients within an 8-month period differed markedly, indicating that they were clonally unrelated. The identical RAPD patterns of five isolates from patient 1 leads to the conclusion that the multiple episodes of bacteremia were caused by the same strain, which remained in the catheter during the period of implantation (at least 1.5 months), and were not due to reinfection with different clones of *F. indologenes*. This is not always the case for other bacteria (12). Patient 1 represents, to our knowledge, the first clinical description of recurrent catheter-related bacteremia caused by a single *F. indologenes* clone and demonstrates the capability of long-term colonization of intravascular devices with this organism.

A wide variety of gram-positive and gram-negative bacteria may be implicated in recurrent cases of bacteriuria associated with the use of indwelling urinary catheters (28). However, only some of these strains, especially *E. coli* and *Providencia stuartii*, have been documented to have the ability to persist for weeks and months in the catheterized urinary tract (14, 27). For one patient in our study (patient 2), two isolates of *F. indologenes* were collected from urine specimens at an interval of 2 weeks. Although we could not culture the same organism from the urinary catheter, the identical RAPD patterns and

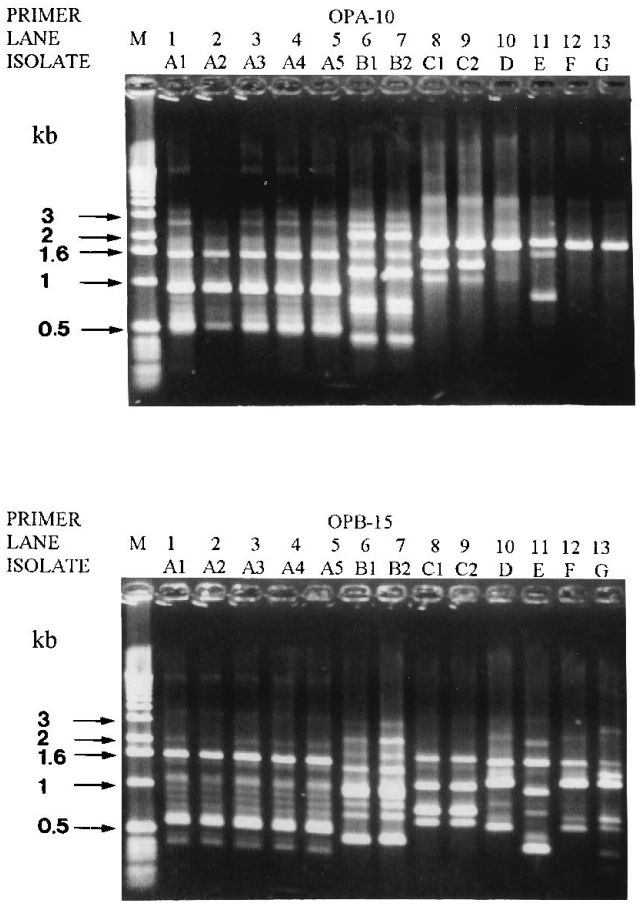

FIG. 2. RAPD patterns generated by arbitrarily primed PCR with two primers (primers OPA-10 and OPB-15) for 13 isolates of *F. indologenes*. Lanes: M, marker (1-kb ladder; Gibco BRL Products, Gaithersburg, Md.); *F. indologenes* isolates 1 to 5, A1, A2, A3, A4, and A5 from patient 1, respectively; 6 and 7, *F. indologenes* isolates B1 and B2 from patient 2, respectively; 8 and 9, *F. indologenes* isolates C1 and C2 from patient 3, respectively; 10 to 13, *F. indologenes* isolates D, E, F, and G from patients 4, 5, 6, and 7, respectively.

antibiotypes of these two isolates strongly suggest that both episodes of bacteriuria were caused by the same strain, which probably remained in the catheter at least during the interval between the two episodes. However, the possibility of reinfection by the same strain from an environmental source cannot be completely excluded. *F. indologenes* was recovered from an endotracheal aspirate from patient 3, who subsequently developed ventilator-associated pneumonia. The same strain was isolated from a blood culture 10 days later, indicating the invasive nature of *F. indologenes* isolates from pneumonic lesions into the bloodstream.

Analysis of the antimicrobial susceptibility test results provided some interesting points. First, all antimicrobial agents tested, including the broad-spectrum cephalosporins, aztreonam, aminoglycosides, and quinolones, routinely prescribed to treat infections caused by glucose-nonfermenting, gram-negative bacilli, had poor activities against isolates from our patients. In our study the degree of susceptibility of the *F. indologenes* isolates to these antimicrobial agents was quite similar to those of other flavobacterial species revealed in previous reports (1, 11, 19, 24, 26). This wide range of resistance presents a dilemma to clinicians in choosing the optimal antimicrobial agents for treating infections caused by this organism. The inappropriateness of the antimicrobial agents prescribed for patient 1 partly contributed to the persistence of this organism and the fatal outcome. Second, the antimicrobial susceptibilities of the isolates at a different intervals, ranging from weeks (patient 2 and 3) to months (patient 1), remained nearly identical, despite intervening therapy. Third, in addition to the RAPD patterns among the isolates, identical antibiotypes could provide a good prediction of strain relatedness.

Determination of the cellular fatty acid profiles of bacteria by GLC offers a useful alternative to traditional identification procedures and may provide a valuable tool for epidemiological studies (17). The cellular fatty acid compositions of flavobacteria, including *F. meningosepticum*, *F. odoratum*, *F. breve*, *Flavobacterium* species CDC group IIb, and *Flavobacterium*-like groups IIe, IIh, and IIf, have been studied by various chromatographic methods (4, 15, 25). In the present study, all of the isolates tested had the same cellular fatty acid compositions, which were in accord with those of *Flavobacterium* species CDC group IIb. However, two different chromatograms were identified among these isolates regarding the relative percentages of 2-hydroxyl-pentadecanoic acid/hexadecenoic acid ($C_{15:0}$ 2OH/$C_{16:1}$) and heptadecenoic acid ($C_{17:1}$) which were not found in previous studies. Isolates belonging to the same strain, as identified by identical antibiotypes and RAPD patterns, had the same chromatographic patterns. Nevertheless, the presence of identical chromatographic patterns among unrelated isolates suggests the inadequacy of this technique as a useful marker for epidemiological typing of flavobacteria.

It is generally accepted that indwelling devices should be removed if the clinical symptoms of indwelling device-related infection do not improve after appropriate antibiotic treatment (5, 8, 20). All but one of our patients (patient 1) were successfully treated with antibiotics with in vitro activity against *F. indologenes*, and the devices remained in place, indicating that indwelling device-related infections caused by *F. indologenes* do not always require removal of the devices.

In summary, *F. indologenes* should be included in the etiologic diagnosis of indwelling device-associated infections. For an immunocompromised host, the recovery of *F. indologenes* isolates from clinical specimens (especially blood, sputum, and urine) should alert clinicians to the possibility of persistent colonization of the implanted devices and the need for in vitro susceptibility testing to choose the optimal antimicrobial agents for treating this multiresistant organism.

REFERENCES

1. **Aber, R. C., C. Wennersten, and R. C. Moellering, Jr.** 1978. Antimicrobial susceptibility of flavobacteria. Antimicrob. Agents Chemother. **14:**483–487.
2. **Cabrera, H. A., and G. H. Davis.** 1961. Epidemic meningitis of the newborn caused by flavobacteria: epidemiology and bacteriology. Am. J. Dis. Child. **101:**289–295.
3. **Chatelut, M., J. L. Dournes, G. Chabanon, and N. Marty.** 1995. Epidemiological typing of *Stenotrophomonas* (*Xanthomonas*) *maltophilia* by PCR. J. Clin. Microbiol. **33:**912–914.
4. **Dees, S. B., C. W. Moss, D. G. Hollis, and R. E. Weaver.** 1986. Chemical characterization of *Flavobacterium odoratum*, *Flavobacterium breve*, and *Flavobacterium*-like groups IIe, IIh, and IIf. J. Clin. Microbiol. **23:**267–273.
5. **Dickinson, G. M., and A. L. Bisno.** 1989. Infections associated with indwelling devices: concepts of pathogenesis; infections associated with intravascular devices. Antimicrob. Agents Chemother. **33:**597–601.
6. **Dickinson, G. M., and A. L. Bisno.** 1989. Infections associated with indwelling devices: infections related to extravascular devices. Antimicrob. Agents Chemother. **33:**602–607.
7. **George, R. M., C. P. Cochran, and W. E. Wheeler.** 1961. Epidemic meningitis of the newborn caused by flavobacteria: clinical manifestation and treatment. Am. J. Dis. Child. **101:**296–304.
8. **Harvey, W. H., T. E. Pick, K. Reed, and R. I. Solenberger.** 1989. A prospective evaluation of the Port-A-Cath implantable venous access system in chronically ill adults and children. Surg. Gynecol. Obstet. **169:**495–500.
9. **Holmes, B.** 1987. Identification and distribution of *Flavobacterium meningo-*

septicum in clinical material. J. Appl. Bacteriol. **62:**29–41.
10. **Holmes, B., R. J. Owen, A. G. Steigerwalt, and D. J. Brenner.** 1984. *Flavobacterium gleum*, a new species found in human clinical specimens. Int. J. Syst. Bacteriol. **34:**21–25.
11. **Jorgensen, J. H., L. A. Maher, and A. W. Howell.** 1991. Activity of meropenem against antibiotic-resistant or infrequently encountered gram-negative bacilli. Antimicrob. Agents Chemother. **35:**2410–2414.
12. **Khatib, R., K. M. Riederer, J. A. Clark, S. Khatib, L. E. Briski, and F. M. Wilson.** 1995. Coagulase-negative staphylococci in multiple blood cultures: strain relatedness and determinants of same-strain bacteremia. J. Clin. Microbiol. **33:**816–820.
13. **Microbial ID Inc.** 1992. Microbial identification system operational manual, version 4. Microbial ID Inc., Newark, Del.
14. **Mobley, H. L. T., M. G. Chippendale, J. M. Tenney, R. A. Hull, and J. W. Warren.** 1987. Expression of type I fimbriae may be required for persistence of *E. coli* in the catheterized urinary tract. J. Clin. Microbiol. **25:**2253–2257.
15. **Moss, C. W., and S. B. Dees.** 1978. Cellular fatty acids of *Flavobacterium meningosepticum* and *Flavobacterium* species group IIb. J. Clin. Microbiol. **8:**772–774.
16. **National Committee for Clinical Laboratory Standards.** 1993. Methods for dilution antimicrobial susceptibility testing for bacteria that grow aerobically. Approved standard M7-A3. National Committee for Clinical Laboratory Standards, Villanova, Pa.
17. **Onderdonk, A. B., and M. Sasser.** 1995. Gas-liquid and high-performance liquid chromatographic methods for the identification of microorganisms, p. 123–129. *In* P. R. Murray, E. J. Baron, M. A. Pfaller, F. C. Tenover, and R. H. Yolken (ed), Manual of clinical microbiology, 6th ed. American Society for Microbiology, Washington, D.C.
18. **Pederson, M. M., E. Marso, and M. J. Pickett.** 1970. Nonfermentative bacilli associated with man. III. Pathogenicity and antibiotic susceptibility. Am. J. Clin. Pathol. **54:**178–192.
19. **Raimondi, A., F. F. Moosdeen, and J. D. Williams.** 1986. Antibiotic resistance pattern of *Flavobacterium meningosepticum*. Eur. J. Clin. Microbiol. Infect. Dis. **5:**461–463.
20. **Rizzari, C., G. Palamone, A. Corbetta, C. Uderzo, and E. F. Vigano.** 1992. Central venous catheter-related infections in pediatric hematology-oncology patients: role of home and hospital management. Pediatr. Hematol. Oncol. **9:**115–123.
21. **Salata, R. A., M. M. Lederman, and D. M. Shales.** 1987. Diagnosis of nosocomial pneumonia in intubated, intensive care unit patients. Am. Rev. Respir. Dis. **135:**426–432.
22. **Siegman-Igra, Y., D. Schwaqrtz, G. Soferman, and N. Konforki.** 1987. *Flavobacterium* group IIb bacteremia: report of a case and review of *Flavobacterium* infections. Med. Microbiol. Immunol. **176:**103–111.
23. **Stamm, W. E., J. J. Colella, R. L. Anderson, and R. E. Dixon.** 1975. Indwelling arterial catheter as a source of nosocomial bacteremia: an outbreak caused by *Flavobacterium* species. N. Engl. J. Med. **292:**1099–1102.
24. **Strandberg, D. A., J. H. Jorgensen, and D. J. Drutz.** 1983. Activity of aztreonam and new cephalosporins against infrequently isolated gram-negative bacilli. Antimicrob. Agents Chemother. **24:**282–286.
25. **von Graevenitz, A.** 1995. *Acinetobacter*, *Alcaligenes*, *Moraxella*, and other nonfermentative gram-negative bacteria, p. 520–532. *In* P. R. Murray, E. J. Baron, M. A. Pfaller, F. C. Tenover, and R. H. Yolken (ed), Manual of clinical microbiology, 6th ed. American Society for Microbiology, Washington, D.C.
26. **von Graevenitz, A., and M. Grehn.** 1977. Susceptibility studies on *Flavobacterium* II-b. FEMS Microbiol. Lett. **2:**289–292.
27. **Warren, J. W.** 1986. *Providencia stuartii*: a common cause of antibiotic-related bacteriuria in patients with long-term indwelling catheters. Rev. Infect. Dis. **8:**61–67.
28. **Warren, J. W., J. H. Jenney, J. M. Hoopes, H. L. Muncie, and W. C. Anthony.** 1982. A prospective microbiologic study of bacteriuria in patients with chronically indwelling urethral catheters. J. Infect. Dis. **146:**719–723.
29. **Wesenberg, F., H. Flaatten, and C. W. Janssen, Jr.** 1993. Central venous catheter with subcutaneous injection port (Port-A-Cath): 8 years clinical follow up with children. Pediatr. Hematol. Oncol. **10:**233–239.
30. **Williams, J. G. K., A. R. Kubelik, K. J. Livak, J. A. Rafalski, and S. V. Tingey.** 1990. DNA polymorphisms amplified by arbitrary primers are useful as genetic markers. Nucleic Acids Res. **18:**6531–6535.
31. **Yabuuchi, E., Y. Hashimoto, T. Ezaki, Y. Ido, and N. Takeuchi.** 1990. Genotypic and phenotypic differentiation of *Flavobacterium indologenes* Yabuuchi et al 1983 from *Flavobacterium gleum* Holmes et al 1984. Microbiol. Immunol. **34:**73–76.
32. **Yabuuchi, E., T. Kaneko, I. Yano, C. W. Moss, and N. Miyoshi.** 1983. *Sphingobacterium* gen. nov., *Sphingobacterium spiritivorum* comb. nov., *Sphingobacterium multivorum* comb. nov., *Sphingobacterium mizutae* sp. nov., and *Flavobacterium indologenes* sp. nov.: glucose-nonfermenting, gram-negative rods in CDC group IIk-2 and IIb. Int. J. Syst. Bacteriol. **33:**580–598.