JOURNAL OF CLINICAL MICROBIOLOGY, Oct. 1988, p. 2213–2215
0095-1137/88/102213-03$02.00/0

Vol. 26, No. 10

# Dysgonic Fermenter 3 Bacteremia in a Neutropenic Patient with Acute Lymphocytic Leukemia

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Received 5 April 1988/Accepted 14 June 1988

**Persistent dysgonic fermenter 3 bacteremia occurred in a granulocytopenic leukemic patient on broad-spectrum antibiotic therapy. This is the first reported case of bacteremia with this fastidious gram-negative rod. Characteristic microbiology and antibiotic susceptibility testing are reviewed. Trimethoprim-sulfamethoxazole therapy eliminated the bacteremia.**

The first reported case of dysgonic fermenter 3 (DF-3) associated with clinical infection, diarrhea in an immunodeficient host, was recently published (4). We describe a case of bacteremia in a leukemic patient with a perianal defect.

A 24-year-old male with relapsed acute lymphocytic leukemia received vigorous chemotherapy and spinal irradiation, leaving him profoundly neutropenic for 6 weeks preceding his presentation with an unusual bacteremia. During this period, he had episodes of polymicrobial bacteremias (*Escherichia coli, Klebsiella pneumoniae, Clostridium tertium, Enterococcus* spp., and *Pseudomonas aeruginosa*) and persistent problems with decubitus ulcers, stool incontinence, and an anal fissure. He remained on various broad-spectrum antimicrobial regimens for most of his neutropenic course. Five weeks into his granulocytopenic course, after a 3-week hiatus of fevers, he developed low-grade temperatures (100 to 101°F [37.8 to 39.3°C]), a worsened decubitus ulcer, two blood-oozing anal fissures, persistent watery incontinent stool, and mental status changes. His antibiotic regimen at this time included imipenem, 1 g every 6 h; tobramycin, 100 mg every 8 h; clindamycin, 500 mg every 6 h; and ketoconazole. Pertinent physical examination revealed a II/VI systolic flow murmur, a nontender abdomen with active bowel sounds, prominent splenomegaly, poor anal sphincter tone, a large perianal decubitus ulcer appearing contiguous with rectal mucosa, and two anal fissures; no fluctuance or mass was palpable.

Laboratory data showed a leukocyte count of 100/mm$^3$ (100% lymphocytes), hematocrit of 22 g/100 ml, and a platelet count of 16,000/mm$^3$. Stool for enteric bacterial pathogens, *Campylobacter* species, ova and parasites, and *Clostridium difficile* toxin were repeatedly negative. Pelvic computerized tomography did not suggest a perirectal abscess; an echocardiogram showed normal heart valves. On day 3 of incubation, multiple aerobic and anaerobic blood culture bottles were determined to be positive radiometrically (BACTEC 460, 6B and 7D bottles; Johnston Laboratories, Inc.). Gram stain of the blood culture revealed a coccobacillary gram-negative rod (Fig. 1). For 8 consecutive days, the patient had a persistent bacteremia despite imipenem, tobramycin, vancomycin, and clindamycin. At this time, intravenous trimethoprim-sulfamethoxazole (160 mg of trimethoprim every 6 h) was initiated; within 24 h, blood cultures were sterile and remained so until the patient's demise 5 days later with systemic aspergillosis. Autopsy was unrevealing of acute bacterial infection including multiple-tissue Gram stains and postmortem cultures of spleen, lung, endocardium, kidneys, brain, and bone marrow, although a perirectal defect was noted.

Subculture of anaerobic and aerobic blood culture vials yielded pinpoint whitish grey colonies on chocolate and blood agar (GIBCO Laboratories) at 24 h which somewhat coalesced after 48 h of growth at 35°C (Fig. 2). No growth was noted on MacConkey agar (Walter Reed Army Medical Center [WRAMC]). A distinctive aromatic, sweet, sialagogic odor was produced by this isolate. As part of the evaluation, this organism was grown on brain heart infusion agar (WRAMC) with X and V factors. Growth was noted around X and XV (Fig. 3), suggesting a growth factor dependency for heme. This nonmotile organism was catalase and oxidase negative; fermented glucose, maltose, sucrose, and lactose but not xylose; did not produce indole or reduce nitrate; hydrolyzed esculin; and produced acid on the slant and in the butt of triple sugar iron agar. Due to the fastidious nature of the organism, fermentation reactions were obtained by the rapid sugar method and by supplementing conventional media (WRAMC) with 1 to 2 drops of rabbit sera per 3 ml of media. The gram-negative rod was identified as Centers for

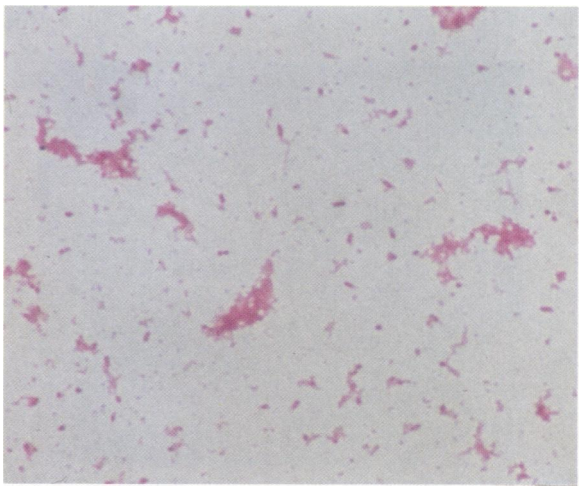

FIG. 1. Gram stain; blood culture of DF-3 (×500).

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FIG. 2. DF-3 growth; chocolate agar plate at 48 h.

Disease Control group DF-3, the designator DF for dysgonic fermenter (poorly growing).

Antimicrobial susceptibility testing was performed by Kirby-Bauer disk diffusion, using enriched Mueller-Hinton agar (WRAMC). Tube macrodilution susceptibility testing (Mueller-Hinton broth with 5% Fildes enrichment) was also performed with selected antibiotics. In addition, bactericidal levels against the DF-3 isolate were determined. The results of this testing are shown in Table 1. National Committee for Clinical Laboratory Standards guidelines were used to interpret disk diffusion zone diameters (2). The zone diameters are reported for those antibiotics for which interpretive criteria have not been established that are applicable to this organism. Tube macrodilution testing supports the susceptibility of this isolate to trimethoprim-sulfamethoxazole and chloramphenicol as well as the interesting finding of resistance to imipenem (despite a 21-mm zone size on disk diffusion), correlating with the lack of clinical response to imipenem in our patient. Testing of this organism by chromogenic cephalosporin revealed no β-lactamase activity.

DF-3 has not been established as a human pathogen. The Centers for Disease Control have a collection of isolates from many sources, including 10 blood isolates (19% total isolates) (4). In our patient this resistant organism probably was selected for by prolonged broad-spectrum antibiotic use

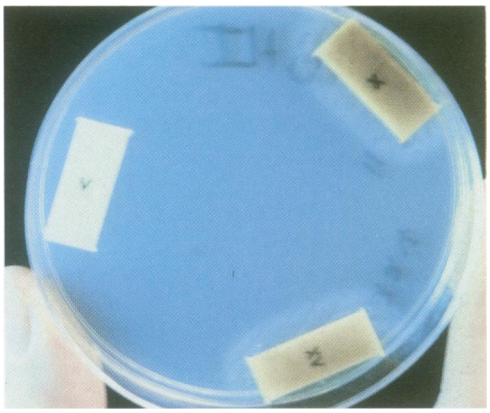

FIG. 3. DF-3 growth on brain heart infusion agar at 24 h with X and V factors.

TABLE 1. Antimicrobial susceptibility testing

| Antimicrobial agent | Disk diffusion[a]/ zone diam (mm) | Tube dilution (μg/ml) |
|---|---|---|
| Amikacin | R | |
| Ampicillin | 17.8 | MIC, 16; MBC, 16 |
| Cefoperazone | R | |
| Cefoxitin | I | |
| Ceftazidime | R | |
| Ceftizoxime | I | |
| Ceftriaxone | I | |
| Cefuroxime | R | |
| Cephalothin | R | |
| Chloramphenicol | S | MIC, 4; MBC, >128 |
| Clindamycin | R | |
| Ciprofloxacin | R | |
| Erythromycin | R | |
| Gentamicin | R | |
| Imipenem | S | MIC, 50; MBC, 50 |
| Methicillin | R | |
| Mezlocillin | I | |
| Penicillin | 14 | |
| Rifampin (5 μg) | 20.5 | |
| Tetracycline | R | |
| Tobramycin | R | |
| Trimethoprim-sulfamethoxazole | S | MIC, 0.12/2.37; MBC, 0.12/2.37 |
| Vancomycin | R | |

[a] S, Susceptible; I, intermediate; R, resistant.

and most likely populated his gatrointestinal tract. The absence of isolation of DF-3 from stool cultures was a function of the screening technique for routine enteric pathogen culture utilized in our laboratory and the fastidious growth requirements of the organism. A portal of entry into the patient's vascular system existed in multiple perianal defects. Predisposed to infection by a pronounced granulocytopenia, a subsequent bacteremia could be predicted. In a prospective evaluation of 581 cancer patients, 8% of acute lymphocytic leukemia patients developed perirectal or perianal abscesses and 65% of perirectal abscesses in this series progressed to gram-negative sepsis (3).

In contrast to the two reported DF-3 stool isolates (4), the DF-3 blood isolate was resistant to clindamycin and tetracycline and susceptible to chloramphenicol and trimethoprim-sulfamethoxazole (Table 1). Although Kirby-Bauer disk diffusion suggested a susceptibility to imipenem, this was not supported by an MIC and an MBC of 50 μg/ml, consistent with the clinical persistence of DF-3 bacteremia through imipenem therapy. The patient's low-grade fevers abated and his blood cultures remained sterile while he was on trimethoprim-sulfamethoxazole. Autopsy revealed no evidence of a disseminated bacterial process, suggesting a response of the DF-3 to therapy.

This case represents an infection in a severely immunocompromised host with a fastidious organism of unestablished pathogenicity. Microbiologic characteristics are reviewed, and some new antimicrobial susceptibility information is presented.

We are indebted to Scott Brown for technical assistance with the antimicrobial susceptibility testing.

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