Lactobacillus Bacteremia in Febrile Neutropenic Patients in a Cancer Hospital

Empirical antibiotic therapy for patients with febrile neutropenia has resulted in a decrease in the number of cases of bacteremia caused by enteric gram-negative bacilli. However, gram-positive organisms have emerged as a major cause of bacteremia in this population. We report the occurrence of a microaerophilic, gram-positive rod, Lactobacillus casei, that caused bacteremia among a significant number of febrile neutropenic patients who were receiving antimicrobials active against this organism.

We reviewed the charts of 22 patients admitted to the H. Lee Moffitt Cancer Center and Research Institute in Tampa, Florida, between January 1988 and June 1996. There were nine males and 13 females; the mean age was 45.2 years (range, 17–69 years). L. casei was isolated from the blood of all patients and from the urine of one; the organisms were cultured on both blood agar incubated at 35°C in room air and chocolate agar incubated at 35°C in a 5% CO2 environment. Species identification was performed by use of the Vitek ANI identification system (bioMérieux Vitek, Hazelwood, MO).

Multiple species, notably Escherichia coli, Staphylococcus epidermidis, or Candida species, were also recovered from the blood of 14 study subjects. Lactobacillus bacteremia occurred in 22 patients with 10 types of tumors.

A test for independent proportions indicated that bacteremia was significantly more frequent (9 [6.01%] of 162) among patients with acute myelogenous leukemia (AML) than among all others in the hospital registry (13 [0.1%] of 9,047; t = 4.1, P = .0001). The underlying malignancy most frequently complicated by bacteremia was AML (9 [5.4%] of 168), followed by all other leukemias (11 [4.4%] of 250) and, rarely, breast cancer (5 [0.33%] of 1,535).

The distribution of probable risk factors for lactobacillemia was as follows: neutropenia, 91% of patients (20 of 22); both mucositis and neutropenia, 36.4% (8 of 22); and vancomycin therapy, 95.5% (21 of 22). Antibiotics frequently used before lactobacillus bacteremia occurred included vancomycin (95.5% of patients), ceftazidime (63.8%), tobramycin (63.8%), metronidazole (59.1%), aztreonam (45.5%), acyclovir (45.5%), and flucnazole (40.9%). Use of the latter two drugs reflects the extent of mucositis present in these patients. Survival rates were higher among those receiving antibiotics appropriate for lactobacillus infection than other antibiotics (10 [66.7%] of 15 vs. 2 [28.6%] of 7, respectively), but this result was not statistically significant (P = .084) for our relatively small sample.

Four antibiotics known to be active against Lactobacillus and used after diagnosis in the present study were clindamycin (54.5% of patients), penicillin (27.3%), erythromycin (27.3%), at least two of the foregoing drugs (40.9%), and ampicillin, none. Nearly one-third (31.8%) of the patients were not treated with any antibiotic effective against Lactobacillus.

L. casei is found in the normal flora on mucosal surfaces but may cause serious infection in immunosuppressed patients. Clinical syndromes associated with L. casei infection include endocarditis [1, 2], sepsis [3–6], pneumonia [7], meningitis [4], mediastinitis [8], liver abscess [9], endometritis [6], amnionitis [5], and urinary tract infection [4]. Risk factors for bacteremia include neutropenia, prior surgery, malignancy, diabetes, and prior therapy with antimicrobials inactive against Lactobacillus [5]. Empirical antibiotics such as cephalosporins, aminoglycosides, and vancomycin are frequently used to treat febrile neutropenia but do not eradicate Lactobacillus [5]. Patel et al. [4] reported that the use of vancomycin in liver transplant recipients promoted colonization of the gastrointestinal tract and may constitute a contributing factor in the development of lactobacillemia. Lactobacillus species are usually susceptible to penicillins [1], ampicillin [2], clindamycin [4, 5], and erythromycin [5]. Antibiotics that are not commonly used for empirical therapy for febrile neutropenia. Bayer et al. [3] reported that a synergistic effect existed in vitro when penicillin or ampicillin and gentamicin/streptomycin were used in the treatment of lactobacillemia. Vancomycin, used either alone or in combination with gentamicin or streptomycin, did not have antimicrobial activity against Lactobacillus plantarum or L. casei. In another study L. casei or Lactobacillus acidophilus was effectively controlled by the use of gentamicin alone [2].

Lactobacillus becomes a potential pathogen in patients with cancer when empirical antibiotics used to treat episodes of febrile neutropenia lack activity against this organism. Capnocytophaga infection, also seen in febrile neutropenic patients with mucositis, similarly requires therapy with penicillin or clindamycin [10]. The widespread use of third-generation cephalosporins, aminoglycosides, and vancomycin as empirical therapy for febrile neutropenia facilitates the development of lactobacillus infections. Once discovered and treated promptly, however, lactobacillus bacteremia readily responds to treatment with penicillin, clindamycin, or erythromycin in combination with gentamicin.

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References
Clostridium difficile Colitis: A Possible Cause of Unexplained Elevation of Serum Alkaline Phosphatase Levels in Patients with AIDS

Most elevations in serum levels of alkaline phosphatase (AP) in patients with AIDS result from hepatobiliary disorders, but unexplained elevations are also encountered [1, 2]. We describe marked elevations in serum levels of AP secondary to Clostridium difficile colitis in a patient with AIDS.

A 58-year-old male with AIDS presented to the hospital with a fever (temperature, 103°F). His medical history was notable for chronic diarrhea secondary to duodenal microsporidiosis, which was treated unsuccessfully with metronidazole. Findings on physical examination were unrevealing. The WBC count was 5,600/μL, and the AP level was 1,100 U/L. Levels of transaminases, bilirubin, albumin, γ-glutamyl transeptidase (GGTP), and 5’ nucleotidase (5’NT) were normal, as was the prothrombin time. Radiological studies, including a bone scan, did not show any abnormalities, and multiple blood cultures were negative. The patient’s temperature normalized over 48 hours, and he was discharged.

Five days later, he was readmitted with fever, chills, and vomiting; the chronic diarrhea persisted. Physical examination revealed a temperature of 99.6°F, a normal abdomen, and blood in his stools. The WBC count was 4,200/μL with 34% neutrophils and 47% band forms. The AP level was 1,850 U/L; levels of liver transaminases remained normal. Plain abdominal films showed a dilated colon with thumbprinting; an ultrasonogram revealed a normal liver and biliary tree with moderate ascites; an abdominal CT scan showed colitis, pneumatosis, and ascites (figure 1). Sigmoidoscopy demonstrated the presence of yellow plaques; pseudomembranous colitis was confirmed by examination of biopsy specimens and the results of a C. difficile toxin assay (titer, 1:1,000). The fever cleared with metronidazole therapy, the AP level decreased to 611 U/L, and repeated abdominal CT scan showed regression of the colonic inflammation previously evident and resolution of the ascites.

The patient received metronidazole for 14 days, and 1 week after the drug was discontinued, his fever recurred (temperature, 102°F). The chronic diarrhea was still present and unchanged in nature. The WBC count was 3,800/μL with 34% band forms, and the AP level had risen to 1,050 U/L. Empirical treatment with antibiotics was given but discontinued after blood cultures were found to be negative and the fever resolved. On repeated testing, the AP level was 2,140 U/L, the GGTP level remained normal, and the 5’NT level was 17 IU/L (normal, < 10 IU/L). A repeated C. difficile toxin assay was positive at a titer of 1:100. Treatment with vancomycin (125 mg po q.i.d.) was initiated and gradually tapered over 2 months. The patient remained afebrile, and the AP level declined to 136 U/L. After completion of therapy and at a 6-month follow-up evaluation, the serum levels of AP and GGTP remained normal. The chronic diarrhea subsequently resolved fol-

Figure 1. Axial CT images obtained with both oral and intravenous contrast media show extensive colonic wall thickening due to Clostridium difficile colitis in a patient with AIDS. a: At the level of the right kidney, both the ascending (black arrow) and the descending (white arrow) colon show wall thickening and submucosal edema. b: Thickening of the sigmoid colon is present with intraluminal stranding (black arrow) and pneumatosis (white arrow). Also note the presence of ascites (FL).