LACTOBACILLEMIA: AN EMERGING CAUSE OF INFECTION IN BOTH THE IMMUNOCOMPROMISED AND THE IMMUNOCOMPETENT HOST

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The bacterium, lactobacillus, is found in the mucosal surfaces of the mouth and the gastrointestinal and genitourinary tracts. There have been increasing reports of the micro-organism being a cause of serious infection in immunocompromised individuals. This article reviews the clinical presentation, laboratory characteristics and treatment of patients with lactobacillemia. (*J Natl Med Assoc.* 2000;92:83–86.)

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Lactobacillus species are ubiquitous microorganisms colonizing the mucosal surfaces of the mouth, gastrointestinal tract, and genitourinary tract. This bacterium has increasingly been reported as a cause of serious infections in both the immunocompetent and the immunocompromised host.[1–9] The most common presentation of *Lactobacillus* infection has been bacterial endocarditis.[10–12] However, more recently, *Lactobacillus* bacteremia has been reported as a cause of septicemia.[1,2,6,9] This article reviews the clinical features, laboratory characteristics, and treatment of patients with lactobacillemia.

MICROBIOLOGY

Lactobacillus species are commensals of the human mucosal tissues, including oropharynx, vagina, and the gut. They are not part of the skin flora. They appear to be microaerophilic Gram-positive rods that do not form spores. *Lactobacillus* ferment glucose but do not produce catalase or oxidase. Gas chromatography reveals the characteristic single peak of lactic acid that *Lactobacillus* produce, hence their name. Microscopy shows that their morphology resembles members of other genera, including *Corynebacterium*, *Clostridium*, *Nocardia*, and *Streptococcus*. The lack of mobility and catalase negativity distinguish *Lactobacillus* from *Listeria*, and a negative hydrogen sulfide reaction distinguishes them from *Erysipelothrix*.

In much of the literature, complete species identification was not performed, but *L. casei*, *L. acidophilus*, and *L. leishmaniasis* were noted to produce disease.[2] Isolated lactobacillemia occurred in about 60%[1,2] and polymicrobial bacteremia in 22% to 60% of the patients. The most frequent concomitant organisms included *Enterococci*, *Pseudomonas aeruginosa*, *Klebsiella oxytoca*, *Alcaligenes* species, *Candida albicans*, *Streptococcus viridans*, Coagulase-negative staphylococci, *Candida krusei*, and *Torulopsis glabrata*.[1–3]

RISK FACTORS

The risk factors for the development of lactobacillemia appear to be predominantly immunocompromised conditions and include persistent prolonged neutropenia, the use of broad-spectrum

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antibiotics, especially vancomycin (which results in the persistence of resistant gastrointestinal flora) and other immunosuppressive conditions.[1,2,4,6,11]

Approximately, 40% of the patients reviewed had underlying malignancy, 75% had received previous antimicrobials, 38% had undergone previous surgery, 20% to 27% had diabetes mellitus or had received corticosteroids, and 5 patients had undergone organ transplantation.[1–3]

Selective bowel decontamination, which is used in some liver transplant recipients, and the use of invasive gastrointestinal or respiratory procedures have also been associated with *Lactobacillus* bacteremia.[9,13] In addition, abdominal surgical procedures, such as the placement of a Roux-en-Y loop, may play a role by altering the bowel flora resulting in subsequent *Lactobacillus* infection.[9,14] In cancer patients, it appears to be more common in patients with acute myelogenous leukemia (5.4%). Additionally, other risk factors in neutropenic patients include mucositis, neutropenia, and antibiotic therapy.[4,6]

CLINICAL FEATURES

Patients with *Lactobacillus* bacteremia in the absence of endocarditis may present with a wide range of clinical features ranging from being asymptomatic to a sepsis-like syndrome.

The average age was between 55 and 60 years with no gender predisposition. The average duration of hospitalization was 11 days, and the average duration of antibiotic treatment was 12 days.[1,3] Multiple portal of entries have been described, including the oropharynx, genitourinary tract, and the gastrointestinal tract.

Lactobacillus has been reported as a cause of endocarditis in over 41 patients.[15] This entity has occurred in both native and prosthetic valves and has involved both the mitral and aortic vales. The clinical presentation of *Lactobacillus* endocarditis is similar to that of other pathogenic bacteria without any classical clinical features. It appears that clinical cure can be achieved in most cases with valve replacement needed in only a small proportion of the cases. Treatment failure occurs when patients are not treated with a combination of penicillin and an aminoglycoside but with a beta lactam alone. Vancomycin and cephalosporins are not good options as these bacteria are intrinsically resistant to them.

SIGNS AND SYMPTOMS

Lactobacillus bacteremia include fever (60% to 100%), leukocytosis (22%), and rigors (23%). Unusual presentations include hypothermia and leukopenia.[2] Almost 18% to 22% of all the patients had no underlying immunocompromising condition at the time of lactobacillemia.[1,3]

Lactobacillemia has been reported to occur with other comorbid conditions such as pyelonephritis,[16] neutropenia following chemotherapy and cancer,[17–19] endometritis following dilation and curettage,[20] aortic graft infection,[21] and abscesses[22,23] Other clinical syndromes associated with *Lactobacillus* infection include sepsis, pneumonia, meningitis, and urinary tract infections.

The criteria used to define lactobacillemia, i.e., two sets of blood cultures positive for *Lactobacillus* or isolation of the organism from the blood and in another site of infection, suggests the presence of actual infection rather than contamination of blood cultures from skin flora or transient mucosal tissue-based bacteremia.[1] The fact that this organism has not been documented to cause intravenous catheter-associated infections also supports true infection.[1–3] In addition, Weinstein et al., did not find *Lactobacillus* to be a contaminant in the series of 500 cases with positive blood cultures,[24] and this lends further support to the fact that *Lactobacillus* bacteremia is a true infection when detected.

In addition, there has been no evidence to suggest that lactobacillus is a part of the normal skin flora and therefore one should consider this pathogen a true infection when isolated from blood cultures.

Lactobacillemia has also been reported to occur in patients with AIDS. These authors have reported four patients with lactobacillemia and AIDS; all these patients appeared to have been in the late stages of AIDS with CD4 counts less than 100 cells/mm^3. Concomitant polymicrobial infections such as Coagulase-negative staphylococci occurred in them as well.[7,25]

TREATMENT

The treatment of lactobacillemia should be guided by the clinical presentation and results of susceptibility testing because of the unusual antimicrobial susceptibility pattern associated with this organism.[9–10]

Several investigators have reported vancomycin

resistance with mean inhibitory concentrations (MICs) of more than 256 μg/mL. The frequent use of vancomycin therapy for patients in intensive care units and in neutropenic patients may account for the pathogenic characteristic of this organism in this patient population.[10,19,26] The mechanism of vancomycin resistance is not known.

It may involve diminished binding of the antibiotic to the cell wall as a result of altered peptide sequences, or the activity of vancomycin may be reduced by exclusion of its target sites by the target cell wall.[14]

Much of the early literature supported the use of a combination of penicillin or other beta lactam agents and an aminoglycoside in the treatment of lactobacillemia, especially when deep-seeded infection was suspected.[10,17] Bayer and his colleagues noted that the MICs of penicillin, ampicillin, and cephalothin for nine isolates were within achievable serum levels of these drugs; however, only 52% of mean bactericidal concentrations (MBCs) of these three antimicrobials were within the range of achievable serum levels. He also noted synergistic activity of penicillin and ampicillin with either streptomycin or gentamicin, but no synergy was noted between vancomycin and aminoglycosides.[10]

Of the parenteral cephalosporins, cephaloridine, cephazolin, and cefamandole were the most active inhibitory and bactericidal agents. Cefoxitin and cephalothin were not bacteriocidal at clinically attainable levels. These studies also demonstrated that the *Lactobacilleae* were generally resistant to metronidazole, norfloxacin, and ciprofloxacin, as well as trimethoprim sulfamethoxazole. The third generation cephalosporins appear to vary in their effectiveness against these isolates. Clindamycin, gentamicin, tobramycin, and chloramphenicol were almost 100% effective.[9,10,14,27]

These studies also showed that the MICs of penicillin and the MIC of ampicillin were in the range of 1 to 2 μg/mL. Thus, large intravenous doses of penicillin would be necessary to effectively inhibit *Lactobacillus.* The MICs of imipenem and erythromycin were low; however, these agents have been used to treat three patients with *Lactobacillus* bacteremia and prove to be a useful therapeutic alternative for patients with penicillin allergy, although further studies are indicated to confirm these data. Given the unusual and variable sensitivities reported in the literature, it is obvious that sensitivity testing is of utmost clinical importance.

CONCLUSION

Lactobacillus septicemia is becoming an increasingly important pathogen associated both in patients with immunocompromised as well as immunocompetent conditions. Identification and susceptibility testing of Gram-positive rods isolated from the blood stream of septic patients will aid in the diagnosis and management of this condition. *Lactobacillus* appears to be uniformly resistant to vancomycin and variably resistant to the cephalosporins and quinolones. Antimicrobials of choice include erythromycin, penicillin, clindamycin, aminoglycosides, and imipenem. Combination therapy should be the standard of care in endocarditis and possibly other deep-seated infections.

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