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Fatal Case of *Listeria innocua* Bacteremia

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***Listeria innocua* is widespread in the environment and in food. This species has to date never been described in association with human disease. We report a case of fatal bacteremia caused by *L. innocua* in a 62-year-old patient.**

CASE REPORT

A 62-year-old woman was admitted to the hospital with a 3-day history of right-upper-quadrant abdominal pain. Her past medical history included hypertension, asthma, gout, and osteoarthritis. At the time of admission to the emergency service, physical examination revealed features of severe septic shock with hypotension (blood pressure, 83/45 mmHg), tachycardia (120 beats/min), and extreme weakness. Her temperature was 39.9°C with jaundice. Because of rapid deterioration of her neurological condition, she was transferred to the intensive care unit for continuous ventilation and hemodynamic support. A blood test at admission showed a leukocyte count of 9.5×10^9/liter, a hemoglobin level of 9.1 g/dl, a platelet count of 22,000/mm^3, a creatinine level of 198 μmol/liter (normal, 50 to 130 μmol/liter), and a serum C-reactive protein level of 210 mg/liter (normal, <5 mg/liter). Hepatic results showed widespread disturbance: bilirubin, 89 μmol/liter (normal, 5 to 30 μmol/liter); aspartate aminotransferase, 257 IU/liter (normal, <38 IU/liter); alanine aminotransferase, 143 IU/liter (normal, <40 IU/liter); and gammaglutamyl transpeptidase, 641 IU/liter (normal, 5 to 40 IU/liter). Pancreatic enzymes were normal. Arterial blood gases revealed severe metabolic acidosis. An abdominal ultrasonographic examination yielded a 20-mm bile duct stone and an 11-mm gallstone. A diagnosis of cholangitis with severe septic shock was established. Two blood cultures were taken, and empirical antimicrobial therapy with intravenous cefotaxime and ornidazole was initiated. The patient's condition deteriorated rapidly with the appearance of signs of hepatocellular insufficiency and disseminated intravascular coagulation. A surgical intervention was decided on and showed cholangitis with hepatic duct necrosis. Postoperative hours were complicated with the persistence of severe hepatic failure, coagulation troubles, and multiple-organ dysfunction, and the patient died 40 h after admission. Blood cultures became positive 2 days after her death with small gram-positive rods.

Blood cultures taken at the time of admission were incubated in the automated BacT/ALERT system (Biomerieux, Marcy l'Etoile, France). Of the samples in the two sets of bottles, both those in bottles maintained under aerobic conditions became positive after 4 days of incubation with small, gram-positive rods with a coryneform appearance. After 24 h of incubation, the colonies were small, white, and nonhemolytic on sheep blood agar plates. Among the positive reactions were catalase production, rapid esculin hydrolysis, and production of acid from glucose, maltose, and lactose. With the use of the Api Coryne system (Biomerieux), the numerical profile 2170164 was obtained, which in the API Plus version 2.0 database corresponds to a "good identification" of *Listeria monocytogenes* and/or *L. innocua.* In order to differentiate between the two species, the following tests were used: evaluation of acid production from D-xylose, L-rhamnose, D-mannitol, and alpha-methyl-D-mannoside by using the Api 50 CH system (Biomerieux); a CAMP test using beta-hemolysin-producing *Staphylococcus aureus* (ATCC 25923); and a rapid slide test using the *L. monocytogenes* polyvalent antiserum (Difco). Results are shown in Table 1. In consideration of the origin of the strain (blood culture), the severity of the disease (septic shock), and the biochemical characteristics of the isolate, presumptive identification of *L. monocytogenes* was given, and the strain was sent to the national *Listeria* reference laboratory (Pasteur Institute, Paris, France) for definitive identification and serotyping. The isolate was, surprisingly, identified as *L. innocua* serovar 6a. An Api *Listeria* system test (Biomerieux) was rapidly performed. The profile obtained (7510) identified the isolate as *L. innocua* with 99.6% probability. A sequence analysis of the 16S rRNA gene was finally done using the MicroSeq 500 16S rDNA bacteria sequencing kit with an automated DNA sequencer (ABI PRISM 310 sequencer), both from Perkin-Elmer Applied Biosystems (Courtabeuf, France). The sequence obtained (523 bp) was compared to all bacterial sequences available from the GenBank database by using the BLAST program (National Center for Biotechnology Information). The analysis showed 100% identity between the isolate and four published *L. innocua* sequences (GenBank accessionno. AL596173, AL596172, AL596170, and AL596164) and 99.62% similarity between the isolate and *L. monocytogenes* (GenBank accession no. AL591983).

Of the *Listeria* species, only *L. monocytogenes* is considered to be a significant human and animal pathogen, even though occasional human infections caused by *L. welshimeri*, *L. seeligeri*, and *L. ivanovii* have been reported (1, 3, 9). Widespread in the environment and in food, *L. innocua* is considered to be a nonpathogenic bacterium (1).

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TABLE 1. Biochemical and physiological characteristics of the isolate from the patient and available information for *L. innocua* and *L. monocytogenes*

Characteristic or test	Result[a] for:		
	Isolate	*L. monocytogenes*[b]	*L. innocua*[b]
Gram stain	Small gram-positive rods	Small gram-positive rods	Small gram-positive rods
Motility at:			
22°C	+	+	+
37°C	−	−	−
Beta-hemolysis	−	+	−
CAMP test with *S. aureus*	+	+	−
Hydrolysis of:			
Esculin	+	+	+
Hippurate	+	+	+
Acidification of:			
Glucose	+	+	+
D-Xylose	−	−	−
L-Rhamnose	+	+	V
Mannitol	−	−	−
α-Methyl-D-mannoside	+	+	+
Rapid slide test	+	NA	NA

[a] +, positive; −, negative; V, variable; NA, not available. The serovar associated with the isolate was 6a, those associated, with *L. monocytogenes* are 1/2a, 1/2b, 1/2c, 3a, 3b, 3c, 4a, 4b, 4ab, 4c, 4d, 4e, and 7, and those associated with *L. innocua* are 4ab, 6a, and 6b and an undesignated serovar.
[b] See reference 8.

On the microbiological side, the only phenotypic characteristic that classically distinguishes *L. monocytogenes* from *L. innocua* is hemolysis (4, 8). However, the hemolytic activity of *L. monocytogenes* may be weak, especially with low-producing strains, and questionable hemolytic reaction has been reported with some *L. innocua* strains when nonselective culture with brain heart infusion agar was used (5). Moreover, nonhemolytic *L. monocytogenes* strains have been recently described (2). The use of the CAMP test, proposed to enhance hemolytic activity of *L. monocytogenes*, does not always resolve the problem: ambiguous hemolysis has been noticed with several *L. monocytogenes* strains, even with the use of conventional sheep blood agar plates (6). Thus, distinguishing between *L. monocytogenes* and *L. innocua* on the basis of hemolytic activity is a risk. Rapid slide test with *Listeria* O polyvalent antiserum (recommended for a rapid identification of *L. monocytogenes*, since it is able to detect *Listeria* serovars 1, 4, 2, and 3) (Difco) should be avoided because of lack of specificity. Indeed, a distinct agglutination was noticed, although the strain was of serovar 6a, which was incompatible with *L. monocytogenes*. Since a few years ago, the Api *Listeria* system (Biomerieux) has provided a useful help for differentiating between *L. monocytogenes* and *L. innocua* on the basis of the absence of arylamidase (differentiation of *L. innocua* and *L. monocytogenes* [DIM] test) from the former (4). In our case, the Api *Listeria* system has given, easily and rapidly, the correct identification.

The clinical case reported here is unusual for several reasons. Bacteria encountered in cases of acute cholangitis are usually gram-negative rods such as *Escherichia coli* or *Klebsiella* spp. or sometimes gram-positive cocci (*Enterococcus* or *Streptococcus*), seldom anaerobes (7), and the initial antibiotherapy given was active against most of these species except *Enterococcus.* Gram-positive rods have never been reported. Most of these rods are susceptible to cefotaxime, except those of the genus *Listeria*, which are naturally resistant to this antibiotic. Second, among the *Listeria* species, only *L. monocytogenes* is widely known to be able to cause severe disease. *L. seeligeri* has been documented recently to have caused acute meningitis in an immunocompetent host (9). As for *L. innocua*, this is, to our knowledge, the first description of a human infection caused by this bacterium. Third, our patient was not known to be immunocompromised. Only inhaled corticoids taken to treat asthma could have led to some immunodeficiency. Thus, that *L. innocua* infection could lead to a fatal outcome was totally unexpected.

Finally, our report constitutes the first documentation of a case of bacteremia due to *L. innocua* and makes us keep in mind that, in blood cultures, the *Listeria* species encountered is not always *L. monocytogenes.*

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