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**Listeria monocytogenes-Associated Biliary Tract Infections: A Study of 12 Consecutive Cases and Review**

Caroline Charlier, MD, PhD, Cindy Fevre, PhD, Laetitia Travier, PhD, Benoît Cazenave, MD, Hélène Bracq-Dieye, Juliette Podevin, MD, Daher Assomany, MD, Lydie Guilbert, MD, Céline Bossard, MD, Françoise Carpentier, MD, Valérie Cales, MD, Alexandre Leclercq, MSc, and Marc Lecuit MD, PhD

**Abstract:** At present, little is known regarding Listeria monocytogenes-associated biliary tract infection, a rare form of listeriosis. In this article, we will study 12 culture-proven cases reported to the French National Reference Center for Listeria from 1996 to 2013 and review the 8 previously published cases.

Twenty cases were studied: 17 cholecystitis, 2 cholangitis, and 1 biliary cyst infection. Half were men with a median age of 69 years (32–85). Comorbidities were present in 80%, including cirrhosis, rheumatoid arthritis, and diabetes. Five patients received immunosuppressive therapy, including corticosteroids and anti-tumor necrosis factor biotherapies. Half were afibrile. Blood cultures were positive in 60% (3/5). Gallbladder histological lesions were analyzed in 3 patients and evidenced acute, chronic, or necrotic exacerbation of chronic infection. Genoserogroup of the 12 available strains were Ib (n = 6), IIb (n = 5), and Ia (n = 1). Their survival in the bile was not enhanced when compared with isolates from other listeriosis cases. Adverse outcome was reported in 33% (5/15): 3 deaths, 1 recurrence; 75% of the patients with adverse outcome received inadequate antimicrobial therapy ($P = 0.033$).

Biliary tract listeriosis is a severe infection associated with high mortality in patients not treated with appropriate therapy. This study provides medical relevance to in vitro and animal studies that had shown Listeria monocytogenes ability to survive in bile and induce overt biliary infections.

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**Abbreviations:** BHI = brain heart infusion, CNS = central nervous system, Lm = Listeria monocytogenes, MIC = minimal inhibitory concentration, MLST = multilocus sequence typing, MN = maternal–neonatal, NRCL = National Reference Center for Listeria, S = septicemia.

**INTRODUCTION**

A severe foodborne infection that mostly occurs in immunocompromised patients is Listeria monocytogenes (Lm) that is a facultative intracellular Gram-positive bacterium responsible for listeriosis. Three main forms are described: septicemia (S), central nervous system (CNS), and maternal–neonatal (MN) infections. Aside from these typical presentations, localized infections are also reported, mostly as a consequence of a subclinical bacterial systemic dissemination. They include endocarditis, osteoarticular, and cutaneous infections as well as biliary tract infections, which have only been reported as isolated case reports, although Lm is well known to colonize the gut and survive in the bile.

We undertook a comprehensive retrospective survey over a 17-year period to review all the cases referred to the national surveillance system of listeriosis in France since it has been established. Twelve cases were identified and analyzed. In addition, the 8 previously published case reports were reviewed. This study reveals that among biliary tract infections, those associated with Lm tend to exhibit specific features, with a higher frequency of comorbidities, of concomitant bacteremia and of adverse outcome, which are reported in 80%, 60%, and 33% of cases, respectively. Lm-associated biliary tract infections should be considered in the occurrence of biliary tract infection in immunocompromised patients. Their diagnosis requires a clinical and microbiological workup, and treatment is based on a specific amoxicillin-based antibiotic regimen to which Lm is sensitive, and which is, otherwise, not recommended as a first-line therapy for biliary tract infections.

**PATIENTS AND METHODS**

**Data Collection**

Surveillance of human listeriosis in France is based on both mandatory reporting of cases to the Institut de Veille Sanitaire, France, since 1999 and voluntary submission of Lm.
strains to the National Reference Center for Listeria (NRCL). The exhaustiveness of this reporting is estimated above 87%. We studied all listeriosis cases declared between January 1999 and March 2013 with mention of “cholecystitis,” “cholangitis,” “liver,” or “bile duct.” In addition, all patients with similar clinical data and for whom isolates were sent to the NRCL between 1996 and 1999, before the mandatory reporting era, were also included. Clinicians and microbiologists were contacted, and medical charts were directly analyzed according to a preestablished checklist. An appropriate local ethical committee (Comité de Protection des Personnes Ile de France 8) considered the study as observational and hence exempted to the Institutional Review Board approval, according to the French legislation.

**Review of the Literature**

We searched the PubMed database for reports published between January 1966 and June 2013, using the terms “Listeria,” “listeriosis,” “cholecystitis,” “cholangitis,” “liver,” and “bile” without language restriction.

**Case Definition**

A case was defined as a person from whom Lm was isolated from the biliary tract. Infections were classified as cholecystitis, cholangitis, or biliary tract cyst infection. Liver abscesses without bile tract infection were excluded. Diagnosis of concurrent septicemia was based on a positive blood culture.

**L monocytogenes Typing**

Listeria isolates referred to the NRCL were identified with API Listeria (BioMérieux, Marcy l’Etoile, France), serotyped until January 2005, and then typed by multiplex polymerase chain reaction (PCR) genoserogrouping. PCR serogroups correspond to the 4 major serovars that cause human disease. Isolates were characterized by multilocus sequence typing (MLST) similar to the 745 other strains received in the NRCL, as previously described.

**Bile Resistance Assays**

Forty-two isolates were tested: 10 from biliary tract infection referred to the NRCL, the EGD bile susceptible, the LO28 bile-resistant reference strains, and 30 clinical isolates referred to the NRCL, the EGD, the LO28 Lm reference strains, and the 30 clinical isolates described above. Cultures were performed in BHI broth at 37°C upon shaking. Aliquot of BHI overnight liquid cultures (1:20) was added to fresh BHI medium. Exponential cultures were diluted in BHI medium, BHI with pork bile, at pH 5 and 7, to an optical density (OD600nm) of 0.06 in 100 μl. 96-well poly (vinyl chloride) microtiter plates (Falcon; Becton Dickinson Labware, Oxnard, CA). Biofilms were allowed to grow for 24 hours at 37°C. Unbound cells were removed by microplate inversion and tapping on absorbent paper. Microplates were washed in water and adherent cells were stained with crystal violet for 20 minutes. Excess stain was removed by 3 washes in water. Quantification of bound cells was performed by adding acetone–ethanol (20:80) and dissolved crystal violet was measured at OD595 nm. Each biomass was standardized relative to EGD reference strain, and Mann–Whitney test was used to compare each group.

**Histopathological Analyses**

Eight-micrometer-thick sections of paraffin-embedded tissue specimens were stained with hematoxylin eosin. Lm was labeled by immunohistochemistry using a polyclonal rabbit antiserum that detects Lm serotype 4b (Listeria O V/VI antiserum Seiken kit; Denka Seiken Co, Tokyo, Japan) and a goat anti-rabbit antibody coupled to peroxidase (EnVision+, Dako, Glostrup, Denmark), followed by hematoxylin counterstaining. Images were captured on a AxioImager A2 microscope (Zeiss) equipped with an AxioCam IcC 1 digital camera (Zeiss) and the AxioVision 4.8 software (Zeiss).

**RESULTS**

**Clinical Cohort**

A retrospective analysis of all cases declared to the NRCL was performed as described in the “Patients and Methods” section. Among the 3231 human cases for which a clinical Lm strain was collected between January 1996 and March 2013, 12 involved patients with biliary tract infections (hereafter named the French cohort), representing 0.37% of the infections reported during the study period. They included 9 cholecystitis (75%), 2 cholangitis (17%), and 1 biliary cyst infection (8%) that is listed in Table 1. Eight additional cases were identified in the literature; all were cholecystitis and are also listed in Table 1. The patients from the French cohort and those previously reported were analyzed together to identify the main characteristics of Lm-associated biliary tract infections.
| Reference | Patient No. | Type of Infection | Age at Diagnosis, Sex, Underlying Disease | Geno-Serogroup, MLST Type (Serootyping) | Blood Cultures | Gallstone (+/-/NA | Histopathology | IHC for Lm | Treatment | Surgery | Antibiotics | Outcome |
|-----------|-------------|-------------------|------------------------------------------|----------------------------------------|----------------|------------------|----------------|-------------|-----------|---------|-------------|---------|
| This study | 1           | Cholecystitis     | 80-year-old woman Chronic adrenal insufficiency | IVb, CC6                               | Not performed | +, acute cholecystitis (see Figure 4A–C) | Yes            | Surgery Amoxicillin 6 g/d, 7 d + Gentamicin, 2 d | Surgery | Amoxicillin 6 g/d, 7 d + Gentamicin, 2 d | Cure (3 mo) |
| This study | 2           | Cholecystitis     | 49-year-old man Diabetes Alcoholic cirrhosis | IVb, CC6                               | Not performed | +, necrotic exacerbation of chronic cholecystitis (see Figure 4D–F) | Yes            | Surgery | Amoxicillin clavulanate 3 g/d + Nebcin, 2 d | Surgery | Recurrence requiring 6 wk amoxicillin and 2 percutaneous drainages with cure (2 y) |
| This study | 3           | Cholecystitis and perforated peptic ulcer | 71-year-old man Alcoholic cirrhosis Obesity | IVb, CC240                             | Not performed | +, chronic cholecystitis (see Figure 4G–I) | Yes            | Surgery Amoxicillin clavulanate 3 g/d + Nebcin, 2 d | Surgery | Amoxicillin clavulanate 3 g/d + Nebcin, 2 d | Lost for follow-up |
| This study | 4           | Cholecystitis     | 85-year-old woman Rheumatoid arthritis treated by corticosteroids, methotrexate, and infliximab | IIb, CC224                             | Negative      | –, acute cholecystitis | No             | Surgery | Amoxicillin 3 g/d, 10 d | Surgery | Amoxicillin 3 g/d, 10 d | Cure (1 mo) |
| This study | 5           | Cholecystitis     | 36-year-old man | IVb, CC6                               | Not performed | +, NA | NA | Surgery No antibiotic | Surgery | No antibiotic | Lost for follow-up |
| This study | 6           | Cholecystitis     | 77-year-old man Prosthetic aortic valve | IIb, CC3                                | Not performed | +, acute cholecystitis | NA | Surgery No antibiotic | Surgery | No antibiotic | Cure (2 y) |
| This study | 7           | Cholecystitis     | 82-year-old woman Rheumatoid arthritis Dementia Hypothyroidism Diabetes mellitus | IIa, CC7                                | Not performed | +, acute cholecystitis | NA | Surgery Piperacillin-tazobactam 12 g/d, 1 wk | Surgery | Piperacillin-tazobactam 12 g/d, 1 wk | Cure (2 y) |
| This study | 8           | Cholecystitis     | 78-year-old woman Atrial fibrillation Breast cancer Chronic lymphoid leukemia | IIb, CC5 truncated InLA                | Not performed | +, chronic cholecystitis | NA | Surgery No antibiotic | Surgery | No antibiotic | Cure (2 mo) |
| This study | 9           | Cholecystitis     | 68-year-old woman Hypertension | IIb, CC5                                | Positive | +, NA | NA | Surgery Amoxicillin 6 g/d, 3 wk | Surgery | Amoxicillin 6 g/d, 3 wk | Cure (10 y) |

(Continued)
| Reference | Patient No. | Type of Infection | Age at Diagnosis, Sex, Underlying Disease | Geno-Serogroup, MLST Type (Serotyping) | Blood Cultures | Gallstone (+/−/NA) Histopathology | IHC for Lm | Treatment | Surgery | Antibiotics | Outcome |
|-----------|------------|-------------------|------------------------------------------|--------------------------------------|---------------|---------------------------------|-----------|----------|---------|-------------|---------|
| This study | 10         | Cholecystitis and cholangitis | 62-year-old man End-stage renal insufficiency Hepatorenal polycystic disease Prosthetic aortic tube | IIb, CC2 | Not performed +, chronic cholecystitis | NA | Surgery Ceftriaxone, 7 d + Metronidazole, 7 d | Death (septic shock) |
| This study | 11         | Cholangitis       | 32-year-old man HCV related and alcoholic cirrhosis Liver transplantation 1 wk before Lm angiocholitis under corticosteroids and tacrolimus | IVb, CC1 | Positive −, NA | NA | No surgery Imipenem Amikacin Vancomycin (posology and duration NA) | Cure (3 mo) |
| This study | 12         | Infected biliary tract cyst | 72-year-old man Biliary tract cyst | IIb, CC59 | Not performed +, purulent necrosis | NA | 2 echographic drainages Amoxicillin clavulanate 6d, 24 d then Amoxicillin, 2 mo | Death (septic shock) |
| Medoff et al16 | N = 1       | Cholecystitis     | 60-year-old woman | ND, (1a) | Not performed | NA, NA | NA | Surgery Penicillin, 10 wk | Cure |
| Gordon and Singer17 | N = 1       | Cholecystitis | 76-year-old woman HTA Myocardial infarction Hysterectomy | ND | Not performed | NA, acute necrotic | NA | Surgery Ampicillin, 7 d + Gentamicin + Metronidazole | Cure |
| Allerberger et al18 | N = 2       | Cholecystitis     | 71-year-old woman Liver steatosis | NA, (1/2c) | Not performed +, chronic | NA | Surgery Amoxicillin, 4 d | Cure |
| Allerberger et al18 | N = 2       | Cholecystitis | 57-year-old man Alcoholism Liver steatosis | NA, (4b) | Not performed +, acute necrotic | NA | Surgery None | Cure |
| Gluck et al19 | N = 1       | Cholecystitis     | 60-year-old woman Rheumatoid arthritis treated by prednisolone and infliximab | NA | Positive | NA, NA | NA | Surgery Ceftriaxone + Gentamicin + Metronidazole | Death (brain hemorrhage and multiorgan failure) |
| Wagner and Allerberger20 | N = 1       | Cholecystitis | 54-year-old man None | NA, (1/2a) | Not performed | NA, NA | NA | NA | NA |
Epidemiology

Ten patients were men (50%) and their median age was 69 years (range 32–85). Comorbidities are detailed in Table 1: 16 patients (80%) had 1 to 4 associated comorbidities (16/20), which included cirrhosis, hypertension, and rheumatoid arthritis (n = 4, each), diabetes (n = 3), aortic patch tube (n = 2), obesity, end-stage renal insufficiency, liver transplantation, chronic adrenal insufficiency, myocardial infarction, dementia, hypothyroidism, chronic obstructive pulmonary disease, chronic lymphoid leukemia, and breast cancer (n = 1, each). Five patients were receiving immunosuppressive drugs at the time of *Lm*-associated biliary tract infections, namely, corticosteroids (n = 4), infliximab plus methotrexate (2/17, 12%, one of them with additional ciclosporin), etanercept, tacrolimus, and fludarabin (n = 1, each). Cholecystolithiasis was reported in 88% of the patients with cholecystitis (14/16).

Clinical Features

Median time from first symptom to hospitalization was 2 days (range 0–60, n = 12) with all but 2 patients hospitalized within the first week of symptoms. Median duration of hospitalization was 11 days (range 1–96, n = 18). Fever was reported in 50% of the cases (10/20, range 38–40°C). Abdominal pain was reported in 88% of cases (15/17). Previous or concomitant diarrhea and vomiting were observed in 11% (2/18). Gastric ulcer was concomitantly diagnosed in 2 other patients (2/18, 11%). Jaundice was noted in only 1 case with cirrhosis (1/18, 6%). None of these cases arose in the context of neurolisteriosis or pregnancy-associated listeriosis.

Laboratory Characteristics

Transaminases blood levels ranged from <1N to 6N (n = 15), and median aspartate amino transferase and alanine amino transferase were 73 and 49 UI/mL, respectively. Total bilirubin blood level was normal in 93% of cases (13/14). Median leukocyte count was 1221/mm³ (range 432–3690, n = 10), including 3 patients below 1000/mm³. Median hemoglobin blood level was 14 g/dL (n = 15), and median platelet count was 189,500/mm³ (n = 14) including 3 patients below 100,000/mm³. Median C-reactive protein blood level was 125 mg/L (range 11–300, n = 8).

Microbiological Features

Diagnosis was confirmed by bile or gallbladder swab culture in all the cases. *Lm* was never suspected before culture results and was the only recovered pathogen in all cases. Blood cultures were performed in only 5/18 patients, 4 of them had temperature >38°C; they were positive in 3 (60%). Further microbiological analyses were performed on the 12 French isolates. Antimicrobial sensitivity was unremarkable when compared with a large panel of more than 4000 clinical strains.23

Genoserogrouping

French strains were collected from patients originating from various geographical origins, at various times (1996, 1997, 1998, twice in 1999, 2000, 2003, 2008, 2009, twice in 2010, and 2013). They belonged to 3 major genoserogroups:
IVb (n = 6/12), IIb (n = 5/112), and Ila (n = 1/12), and matched the overall distribution of human clinical isolates in France during the same period (data not shown).

**MLST**
The strains were identified as belonging to 9 distinct clonal complexes (CCs), without any CC associated with biliary tract strains (Figure 1).

**InlA Surface Expression**
Among the 12 strains of the French cohort, 1 exhibited a truncated form of InlA, confirmed by sequencing (data not shown).

**Bile Survival Assays**
MICs were similar for Lm biliary tract isolates and from S and CNS (20%, \( P > 0.05 \)) (Figure 2).

**Biofilm Assays**
No difference in biofilm ability among strains was observed with or without pork bile at pH 7 reflecting the gallbladder conditions. In the presence of pork bile, at pH 5 reflecting duodenal conditions, bile tract isolates had significantly lower biofilm ability than those from S, CNS, and MN infections (\( P = 0.001 \)) (Figure 3).

**Histology**
Gall bladder histopathology was analyzed and anti-Lm immunoenzymatic labeling was performed in 3 patients for whom gallbladder samples were available (Table 1). Cholecystitis with cholecystolithiasis was confirmed in all the cases (Figure 4). Patient 1 had acute cholecystitis with edematous congestive transmural inflammation (Figure 4A), polymorphonuclear cells infiltrate (Figure 4B), and focal mucosal ulceration. Patient 2 had necrotic exacerbation of
chronic cholecystitis (Figure 4D), with necrosis of the mucosa and muscularis (Figure 4D and E), necrotic luminal tissue debris, and inflammatory fibrosis in the serosal coat. An aspect evocative of chronic cholecystitis was observed in Patient 3, with a diffuse mucosal-based infiltrate of mononuclear cells (Figure 4G and H). Such patterns of acute, chronic, and necrotic exacerbations of chronic infection mirror those reported in classical cholecystitises. The presence of Lm was confirmed in 3 cases (Figure 4C, F, and I). Bacteria were located in the gallbladder lumen, sometimes as aggregates (Figure 4C and I), or within tissue fragments in necrotic cholecystitis (Figure 4F).

### DISCUSSION

Here, we have studied the detailed features of Lm-associated biliary tract infections in a cohort of 20 cases, that includes 12 new consecutive cases declared in France over the last 17 years and 8 previously published reports. Important conclusions can be drawn from this study. First, Lm-associated biliary tract infection is a genuine clinical entity. It mostly involves older patients with comorbidities and is associated with a much higher mortality rate than other biliary tract infections (15% vs 3%, P < 0.03). The nonprescription of amoxicillin/ampicillin or other effective antibiotics such as ampicillin/sublactam, piperacillin/tazobactam, or carbapenems might be associated with poor outcome: death or recurrence of infection (P = 0.03). These conclusions have important implications for clinicians: the identification of Lm in a bile sample should lead to the swift prescription of amoxicillin/ampicillin, which should be maintained beyond the perioperative period, in contrast to current guidelines for the management of community-acquired biliary tract infections that recommend discontinuation of antibiotics within 24 hours after cholecystectomy in the absence of infection outside the gallbladder wall. Among the first-line drugs recommended in uncomplicated community-acquired cholecystitis, third-generation cephalosporins should not be used because of their intrinsic lack of activity, whereas carbapenems and piperacillin/tazobactam both display bactericidal activity toward Lm. Perioperative bacteriological sampling is not systematically recommended and the absence of fever reported in most cases does not lead to the prescription of blood cultures: this likely leads to an underestimation of the actual burden of biliary tract infections associated with Lm. The main limitation of the study is its retrospective nature, because of the rarity of the disease.

Lm is known to colonize the gut and Lm asymptomatic fecal carriage has been documented in 1% to 12% of healthy individuals. Bile exhibits antimicrobial activities, given its ability to interact with membrane lipids and damage bacterial membranes. Lm, as many other enteric pathogens, has evolved to survive in the bile and in the proximal region of the small intestine where bile is released. The occurrence of biliary tract infections associated with Lm is therefore not surprising. Indeed, all Lm strains express a bile salt hydrolase encoded by bsh that detoxifies bile by deconjugating glycine/taurine from bile salts. Lm is also able to accumulate solutes such as betaine and carnitine, thereby enhancing its resistance to stress conditions, and the osmolyte transporters OpuC, BetL, and Gbu involved in their uptake play a major role in Lm tolerance to the bile. An active bile exclusion system called BiIE is also implicated in Lm survival in bile. All these systems are transcriptionally regulated by PrfA, Lm master virulence gene regulator, and are functionally active at the low pH of the proximal small intestine. Other genes and metabolic pathways implicated in amino acid synthesis, purine metabolism, and biotin uptake have been more recently identified in Lm and may be involved in resistance to bile stress in gallbladder neutral pH conditions.

Consistent with these in vitro data, Lm is able to colonize the gall bladder after both oral and intravenous challenge in a mouse model of infection. It can survive...
and multiply extracellularly in the mouse gallbladder lumen, be released via the biliary tract in the intestinal lumen, and induce overt cholecystitis. These experimental findings match those observed in the present cohort of patients with Lm-associated biliary tract infection (Figure 4) and are therefore relevant to the human situation. Indeed, as observed in the mouse, Lm was consistently found extracellularly in the gallbladder of the patients (Figure 4). Moreover, 1 of the clinical strains expresses a truncated and, therefore, nonfunctional form of InlA unable to mediate Lm internalization, further illustrating that Lm-associated biliary tract infection does not result from epithelial invasion, a finding that is also de facto observed in the mouse model of biliary tract infection, InlA being not functional in the mouse.

Survival in bile in vivo and the ability to induce biliary tract infection is likely a general property of Lm for several reasons. First, the isolates responsible for Lm-associated biliary tract infection do not belong to specific clonal complexes but reflect the diversity of the strains isolated from patients with listeriosis. Second, biliary tract infection isolates do not have increased survival in bile-containing medium. They do not either exhibit enhanced biofilm-producing ability, including in a bile-rich environment.

The ability of Lm to survive in bile has several clinical consequences. First, asymptomatic Lm bile colonization could be nonpathogenic per se, but serve as a reservoir reinoculating the proximal small intestine where Lm crosses the intestinal barrier. It could also constitute the reservoir that feeds long-term fecal shedding, reported in up to 12% of patients. This would facilitate dissemination and have major public health implications, as described for Salmonella enterica serovar Typhi. Although not formally demonstrated in humans, this sequence of events has been observed in mice, where bioluminescence studies have shown the release of viable Lm in the bile during gallbladder contractions and their expulsion in the digestive tract. From the gut, they could reinfect the host and disseminate into the environment. Finally, obstructing lithiasis in the context of preexisting Lm bile colonization is the most probable trigger of overt Lm cholangitis/cholecystitis, as described in other typical biliary tract infections.

The lower positivity rate of blood cultures compared with the bile cultures mirrored previously published data on bile tract infections.

Microbiological examination of the bile/gallbladder and blood cultures are far from being routinely performed in patients with listeriosis.

**FIGURE 3.** Biofilm formation in 12 French isolates and in 30 strains selected at random among isolates received in 2012 from the National Reference Center for Listeria from patients with septicemia (S), central nervous system (CNS), and maternal–neonatal (MN) infections. P values were determined as compared to S, CNS, and MN isolates (Mann–Whitney test). BHI = brain heart infusion, BTI = bile tract infections.
cholecystectomized patient with cholecystitis, and Lm-associated biliary tract infection, although certainly rare, therefore likely remains largely undetected in the clinical practice. Furthermore, piperacillin/tazobactam is routinely used in the United States to treat patients with biliary infections and may explain the rare isolation of Listeria. In a review compiling 211 cases of cholecystectomy (including 34 urgent and 177 elective surgeries), diphteroid-like rods compatible with Lm were evidenced in at least 3 cases, yet no further characterization was performed. As culture-based pathogens detection could be lowered by preoperative prophylaxis (http://www.sages.org/publication/id/06/), more recent studies using PCR tools have

FIGURE 4. (A–C) Gallbladder sections from 3 patients with acute cholecystitis (Patient 1), (D–F) necrotic exacerbation of chronic cholecystitis (Patient 2), and (G–I) chronic cholecystitis (Patient 3). Lm was genoserotyped as IVb in the 3 cases. In acute cholecystitis, HE staining revealed edematous congestive transmural inflammation (A; arrow), polymorphonuclear cells infiltrate (B; arrow), and focal mucosal ulceration (B; arrowhead). Lm was seen in the lumen as aggregates and individual bacteria (C). In the necrotic exacerbation of chronic infection, necrosis involved the mucosa and the muscularis (D, F), with necrotic luminal tissue debris and inflammatory fibrosis in the serosal coat. Lm was located in the lumen and in necrotic tissues lining the lumen (F). In chronic cholecystitis, diffuse mucosal-based infiltrate of mononucleate cells was observed (G, H; arrow). Lm was observed inside the lumen (I). Scale bars: HE staining, 100 μm; IHC staining, 2 μm. HE = hematoxylin-eosin, IHC = immunohistochemistry, L = lumen, P = peritoneal cavity.
also been performed to identify pathogens involved in cholecystitis. Neither Lemos et al., in a Brazilian study involving 84 patients who had not receive preoperative antibiotic prophylaxis, nor Lee et al., in a Korean study performed on bile tract samples from 156 patients, evidenced any Lm.

Lm biliary tract infection should be considered as a genuine although rare cause of cholecystitis. In contrast, the occurrence of transient and asymptomatic Lm bile colonization could be frequent although this remains to be established in the context of prospective studies.

In conclusion, the results from this study validate in human the experimental data that had been obtained in the mouse and provide strong evidence that the presence of Lm in the bile should be taken into account by clinicians. Lm-associated biliary tract infection requires a specific treatment based on surgery and the prescription of amoxicillin. Lm survival in the bile and chronic colonization in the biliary tract is not only a cause of morbidity and mortality. The biliary tract also likely constitutes a reservoir that favors Lm long-term fecal carriage and transmission.

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