

CASE REPORT



Breaking Bad: a case of *Lactobacillus* bacteremia and liver abscess

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ABSTRACT

We present a case of a 46-year-old Hispanic male with a past medical history significant for uncontrolled diabetes presenting with abdominal pain, nausea and vomiting and found to have *Lactobacillus* bacteremia and liver abscess. A PubMed and Clinical Key literature review of the other known cases of *Lactobacillus* liver abscess was performed. Through examination of previous case reports, the patient presented in this paper, and the associated risk factors of *Lactobacillus* liver abscess it is likely that the incidence of this rare condition will increase and would therefore be prudent to further study *Lactobacillus* as a pathogenic bacteria so that its complications may be better treated and prevented.

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1. Introduction

The human intestinal lumen contains millions of living organisms that help in absorption of nutrients and production of organic compounds including vitamin K. *Lactobacillus* is an anaerobic, acid-producing, gram-positive rod, widely known as a group of probiotic bacteria. It is generally regarded as one of the ‘good’ bacteria. They are part of the normal flora of the oral cavity, GI, and the female GU tract. There are many species of *Lactobacillus* identified, four of which are clinically used as probiotics; *L. acidophilus*, *L. bulgaricus*, *L. reuteri*, and *L. rhamnosus* GG. Amongst these species, *L. acidophilus* is the dominant bowel bacteria. Generally, *Lactobacillus* preparations are used to maintain and restore the normal intestinal bacterial flora. They do so by producing lactic acid and hence creating an acidic environment unfavorable for the growth of other pathogens such as bacteria and fungi. They also produce lactases, lipases, and proteases that may aid in digestion. Because of their role as probiotics, *Lactobacillus* preparations have been used, and have shown efficacy, in treatment and prevention of antibiotic-associated diarrhea, acute gastroenteritis in children, atopic dermatitis in infants, constipation, inflammatory bowel disease, and nonalcoholic fatty liver disease[1].

Lactobacillus, despite their many beneficial roles in humans, do have the potential to translocate out of their normal environment and cause serious illness in the right patient and under the appropriate circumstances. *Lactobacillus* bacteremia, sepsis, and endocarditis have been reported in a number of cases in the past [2,3]. These severe infections have occurred in patients with underlying diseases such as uncontrolled diabetes mellitus, valvular heart disease, immunocompromised

(HIV, chronic steroids, chemotherapy), short bowel syndrome, and hematologic malignancies [4–6]. Some associated risk factors include dental procedures, use of total parenteral nutrition, IV drug abuse, abdominal surgery, and excessive dairy product consumption or probiotic use [7–9].

Although rare, *Lactobacillus* liver abscess has been reported in a total of 9 case reports in the literature [9–17]. Review of literature was done using keywords ‘*Lactobacillus*’ ‘liver abscess’ ‘bacteremia’, through PubMed and MeSH databases with no restrictions for date range. In each of those cases, there were many of the aforementioned risk factors above and comorbidities associated with the presentation of *Lactobacillus* bacteremia and liver abscess. We present a case of *Lactobacillus* bacteremia and liver abscess in a 46-year-old male with past medical history significant for newly diagnosed uncontrolled diabetes. With the epidemic of diabetes mellitus in the US, this case underscores the need to consider ‘good’ *Lactobacillus* as a potential pathogen in this patient population.

2. Case presentation

We present a case of a 46-year-old Hispanic male with a past medical history of newly diagnosed uncontrolled diabetes (hemoglobin A1c 9.9%) who comes in with a three-week history of worsening generalized abdominal pain and body aches associated with persistent fevers, nausea, and vomiting. In addition, he has had a decreased appetite for the last three weeks as well as an unintentional 50-pound weight loss over the last two years. He is originally from Mexico; however, he had not traveled out of the US for 10 years. He lives alone and

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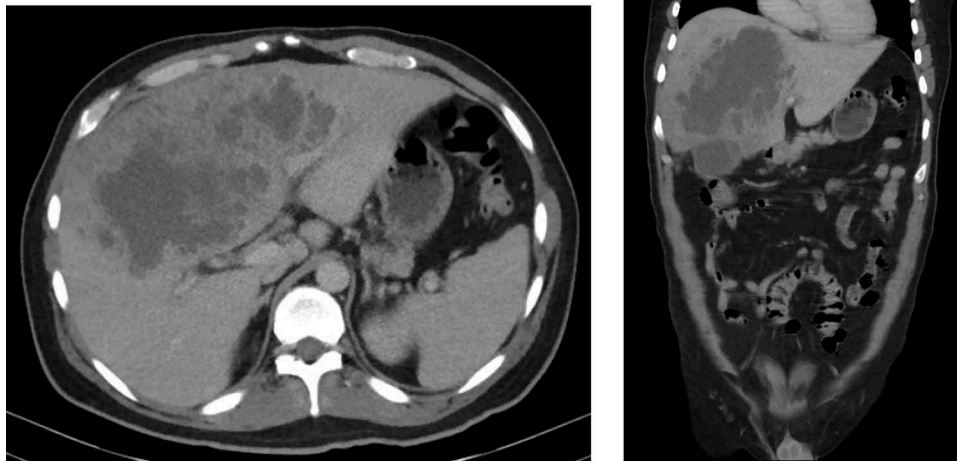


Figure 1. CT abdomen and pelvis, axial/coronal view, day of admission: large multiloculated complex cystic lesion predominantly involving the right lobe of the liver measuring 16 cm and most likely representing multiple contiguous abscesses.



Figure 2. CT abdomen and pelvis, axial view, 21 days after admission.

works as a carpenter. He denies any use of tobacco, alcohol, sexually transmitted diseases, or illicit drug use.

On admission, vitals were as follows: temperature 38.6°C (101.5°F), heart rate 103, respiratory rate 16, 97% oxygen saturation on room air. Physical exam was significant for the presence of a thin looking, malnourished male, BMI 20.7. Cardiovascular exam was significant for tachycardia. Pulmonary examination revealed decreased breath sounds bilaterally and right lower lobe rales. Abdominal examination was positive for a tender abdomen to moderate palpation localized to the epigastric and right upper-quadrant region. No splenomegaly, and unable to assess hepatomegaly due to significant pain on palpation or percussion.

Laboratory studies revealed the following: complete blood count (CBC) was significant for leukocytosis $16.2 \times 10^3 \mu\text{L}$ and hemoglobin 11.9 g/dL. Comprehensive metabolic panel (CMP) was significant for sodium 123 mEq/L, chloride 84 mEq/L, albumin 2.9, total bilirubin 2.2 mg/dL (0.8 direct, 1.4 indirect), alkaline phosphatase 349 IU/L, ALT/AST 104/92 IU/L, glucose 304 mg/dL. Lactic acid 2.0 mmol/L.

Due to concern for an intra-abdominal pathology a CT abdomen and pelvis with contrast (Figure 1) and abdominal ultrasound were performed which revealed the following:

Abdominal ultrasound showed evidence of a diffusely heterogenous liver with multiple areas of hyperechogenicity involving the right and left lobes measuring $12.9 \times 16.4 \times 11.1$ cm. The gallbladder was distended with gallstones and a thickened gallbladder wall.

The patient was admitted to the hospital for further management of a suspected large multiloculated liver abscess. Diagnostic considerations at this time included a pyogenic abscess versus invasive amoebic abscess, and we subsequently started a combination of ampicillin-sulbactam and metronidazole. Stool studies for ova and parasites, *Clostridium difficile*, *Cryptosporidium* antigen, fecal leukocytes, stool culture, and *Giardia* antigen were negative. Serologies for *Entamoeba histolytica*, *Echinococcus*, hepatitis, HIV, interferon gamma assay were all unrevealing. Blood cultures revealed the growth of a *Lactobacillus* species. Exact speciation was never obtained by our hospital lab.

After stabilization, the patient was sent to interventional radiology for CT guided percutaneous abscess aspiration and drainage involving the largest loculation. This resulted in significant drainage output, 80 to 120 mL per day of a thick, milky, purulent fluid. Gram stain and culture from the aspirate also grew *Lactobacillus* species; however, the exact strain was never identified. MRCP was performed to evaluate for common bile duct dilation and ascending biliary infection, which was unremarkable. Echocardiogram was performed and revealed no valvular vegetations.

Throughout his hospital stay, our patient underwent periodic IR guided catheter drainage and manipulations to drain the adjacent contiguous loculations in the liver. In addition, there was an interval development of a sub-diaphragmatic fluid collection, which required placement

of a second drain. Furthermore, a moderate right-sided pleural effusion was also noted. The patient underwent thoracentesis, and the fluid was consistent with an exudative effusion.

Three weeks after the admission, our patient was re-imaged one final time (Figure 2) which showed dramatic resolution of his liver abscess, as well as improvement in the subphrenic fluid collection and right-sided pleural effusion. The second drain that was placed for the subphrenic fluid collection was removed before discharge, and the original drain for the liver abscess was removed one week later. He was discharged home to complete a total of 5 weeks of antibiotics, the last 2 weeks with amoxicillin-clavulanate based on cultures and sensitivities (Appendix; Table 1).

3. Discussion

When evaluating a patient with a liver abscess, the most common etiology is a pyogenic liver abscess accounting for 48% of visceral abscesses and 13% of intra-abdominal abscesses overall [18]. It has similar risk factors to Lactobacillus liver abscess such as diabetes, hepatopancreaticobiliary, and intracolonic disease. Important microbiological causes of pyogenic liver abscess include gram-negative bacilli (*Escherichia coli*, *Klebsiella pneumoniae*) and streptococci [19]. Therefore, when presented with a patient with a liver abscess, a pyogenic liver abscess should be strongly considered and treated empirically covering the most common bacteria.

Cases of Lactobacillus bacteremia and liver abscess are extremely rare in the literature. This makes understanding the pathophysiology and etiologies of this rare infection that much more challenging. The known entities in the literature that predispose patients to this exceedingly rare infection include immunosuppression, uncontrolled diabetes, bacterial translocation, and use of probiotics.

Other case reports (Appendix; Table 2) have identified probiotics as the etiology for the development of Lactobacillus liver abscess [9,17]. The use of probiotics has become widespread over the past few decades. Although their mechanism of action remains incompletely understood, they are thought to improve intestinal function by maintaining the integrity of the epithelial and mucosal layers of the colon. They then enhance the mucous layer and strengthen the tight junctions of the intestinal epithelial mucosa. They are also thought to decrease apoptosis through production of protective cytokines (such as IL-10 and TGF- β) [20]. Our patient did not have a history of extensive probiotic intake or probiotic-rich foods such as yogurt and other dairy products, eliminating this as a factor in our case.

The only identified known risk factor for our patient was his diabetes, which combined with lack of health insurance presented as uncontrolled diabetes. Diabetes

mellitus is associated with two types of vascular disease. Non-occlusive microangiopathy, which is caused by increased vascular permeability and impaired autoregulation of blood flow involving the capillaries and arterioles. Macroangiopathy is associated with atherosclerotic lesions [21]. In addition, advanced glycation end products (AGEs) are responsible for glycosylation of basement membranes resulting in increased vascular permeability. Metabolic alterations in diabetes have also been reported to contribute in changes in endothelial cells. This is likely a factor in the higher susceptibility of diabetic patients to deadly complications of infectious diseases. This endothelial injury could be a possible route of bacterial translocation from normal flora to bacteremia and formation of liver abscess.

A PubMed and ClinicalKey review of the literature identified six cases (out of eight reported cases of Lactobacillus liver abscess) that occurred in diabetics. However, each of those reported cases had an additional underlying disease process, particularly involving the hepatobiliary system such as post-cholecystectomy, ERCP, cholangitis, and Mirizzi syndrome, or other intestinal pathology including Crohn's disease [10,12,14,16,17]. Our patient only had uncontrolled diabetes thus predisposing him to increased risk of endothelial injury and bacterial translocation. However, without any evidence of other underlying predisposing factors mentioned above, this is the first case of Lactobacillus liver abscess in which there was no identifiable inciting event.

Studies have shown that certain species such as *L. rhamnosus GG* is acid and bile stable which could explain the close association between hepatobiliary pathology and lactobacillus liver abscess [22]. With this knowledge, a hepatobiliary source was evaluated with both an MRCP and abdominal ultrasound. MRCP showed no evidence of choledocholithiasis and no common bile duct dilatation. Abdominal ultrasound showed 5 mm common bile duct dilatation, distended gallbladder and thickened gallbladder wall. Particularly, in regards to the abdominal ultrasound, there are radiographic signs of biliary pathology; however, it is unclear whether this was a primary pathology which led to seeding of the liver or secondary to the liver abscess causing the biliary abnormalities. This perhaps could have been better evaluated with repeat abdominal ultrasound and/or MRCP as the liver abscess resolved, however would be unlikely to change overall management.

Lactobacillus bacteremia is typically indicative of profound immunosuppression and carries an overall poor prognosis with associated 30% mortality [23]. Due to this association, our patient was extensively worked up for other immunosuppressive comorbidities including HIV, immunoglobulin deficiencies, steroid use, and workplace exposures, all of which came back negative. Given that our patient was relatively young with previous good functional capacity and did not

experience any complications or require surgical intervention during his hospitalization he was able to make a full recovery. In addition, upon this outpatient visit after completion of antibiotic course and removal of his percutaneous drainage, he remained asymptomatic and was able to return to work in full capacity, all of which point to an excellent prognosis going forward. Furthermore, with improved control of his diabetes, we expect this is highly unlikely to recur in the future.

Given the increasing prevalence of diabetes mellitus in the USA and use of probiotics, it is expected that more cases of *Lactobacillus* bacteremia and liver abscess would be reported in the future[24]. In regards to the use of probiotics, the prevalence is likely underestimated given the presence of probiotics in other common foods such as milk, yogurt, and other dairy products[25]. This is in addition to their application in medicine for increasingly common conditions such as antibiotic-associated diarrhea and inflammatory bowel disease. Furthermore, as patients are living longer and longer with diabetes and our ability to manage complications of uncontrolled diabetes improve the population of individuals at risk for *Lactobacillus* bacteremia will continue to increase. The same can be said for the increasing prevalence of other associated risk factors such as immunosuppression, hematological malignancies, and valvular disease. Therefore, the combination of increasing probiotic use and increasing population at risk for of *Lactobacillus* bacteremia the cases of *Lactobacillus* liver abscess should be expected to rise in the future. How quickly it would rise remains to be seen. It would therefore be of use to further study *Lactobacillus* for its virulence factors so that its pathogenesis may be better understood and its complications better prevented and treated.

Disclosure statement

No potential conflict of interest was reported by the authors.

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Appendix:

Table 1. Lactobacillus culture and sensitivities

Antimicrobial	MIC ($\mu\text{g/mL}$)
Ampicillin/sulbactam	0.06
Clindamycin	1
Imipenem	0.25
Meropenem	2
Metronidazole	>256
Penicillin	0.03

Table 2. Summary table of Lactobacillus bacteremia and liver abscess case reports:

Case	Risk factors	Species	Treatment	Reference
75-year-old male	Hepatocellular carcinoma status post intratumoral ethanol injection	<i>L. plantarum</i>	Antibiotics	Isobe, 1990
39-year-old male	Diabetes, chronic pancreatitis, choledochoduodenostomy	<i>L. acidophilus</i>	Antibiotics	Larvol, 1996
74-year-old female	Hypertension, excessive dairy consumption	<i>L. rhamnosus</i>	Percutaneous drainage plus antibiotics	Rautio, 1999
73-year-old female	Diabetes	<i>L. rhamnosus</i>	Surgical drainage plus antibiotics	Natario, 2003
27-year-old male	Crohn's disease, chronic steroids	<i>L. acidophilus</i>	Percutaneous drainage plus antibiotics	Cukovic-Cavka, 2006
51-year-old female	None	<i>L. paracasei</i>	Percutaneous drainage plus antibiotics	Burns, 2007
74-year-old male	Diabetes, Mirizzi syndrome	<i>L. rhamnosus</i>	Percutaneous drainage, cholecystectomy plus antibiotics	Chan, 2010
82-year-old female	Diabetes, cholecystectomy, probiotic use	Not identified	Percutaneous drainage plus antibiotics	Sherid, 2016