Case Report
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급성담관염 및 총담관 결석에서 진단된 *Lactococcus garvieae* 균혈증 1례

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Acute Cholangitis with Common Bile Duct Stone Caused by *Lactococcus garvieae*: A Case Report

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Lactococcus garvieae is a Gram-positive cocci that has been known to be a fish pathogen, and considered as a low virulence organism rarely associated with human infection. We report a case of acute cholangitis with common bile duct (CBD) stone and bacteremia by *L. garvieae* bacteremia in a 70-year-old male. The patient presented with epigastric pain and was diagnosed with two CBD stones. Blood culture obtained prior to empiric antimicrobial therapy with ceftizoxime sodium showed growth with *Escherichia coli* and *L. garvieae*. The bacteria were confirmed by matrix-assisted desorption/ionization time-of-flight mass spectrometry. Initial attempt at endoscopic biliary drainage failed, and the patient underwent percutaneous transhepatic biliary drainage and subsequent stone removal. He occasionally ingested raw fish and had a history of gastric ulcer with acid suppression therapy, which could be possible risk factors for *L. garvieae* infection. This is the first case of *L. garvieae* bacteremia in acute cholangitis.

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INTRODUCTION

Lactococcus garvieae is a member of *Lactococcus* species, Gram-positive, catalase-negative, facultative anaerobic cocci.[1] *L. garvieae* was first discovered in rainbow trout raised in fish farms in Japan in the 1950s. In 1981, it was isolated as a causative agent of bovine mastitis, and in 1983, based on genetic analysis, it was named *Streptococcus garvieae*, and in 1985, it was classified as a new genus *Lactoccoccus*.[2] *Lactococcus* species have been recognized as low virulence organisms that cause opportunistic infections in humans.[3] In recent years, steadily increasing number of cases associated with *L. garvieae* human infections are being reported.[4] This is a case report with literature review in which *L. garvieae* bacteremia was identified in a patient with acute

cholangitis and common bile duct (CBD) stone.

CASE

A 70-year-old male visited the emergency room of our institution with severe epigastric pain that had begun occurred five hours prior. He had been diagnosed with essential hypertension, diabetes mellitus, paroxysmal atrial fibrillation, hyperthyroidism, and gastric ulcer. The patient was a farmer by occupation, living in Changnyeong, Gyeongsangnam-do, Republic of Korea. He occasionally ingested raw saltwater fish frequently for several decades.

Physical examination on admission showed severe tenderness in the epigastrium and right upper quadrant. There was no Murphy's sign and rebound tenderness. The patient had normal lung sounds and no heart murmurs. The vital signs were as follows: body temperature of 37.8℃, heart rate of 60/min, respiratory rate of 16/min and blood pressure of 110/60 mmHg.

The laboratory tests performed in the emergency room were as follows: white cell count 9,800 /mm^3, polymorphoneutrophil count 8,418 /mm^3, hemoglobin 7.4 g/dL, erythrocyte sedimentation rate 36 mm/hr, aspartate transferase 202 IU/L, alanine transaminase 53 IU/L, alkaline phosphatase 159 IU/L, gamma glutamyl peptidase 533 U/L, total bilirubin 2.1 mg/dL, direct bilirubin 2.0 mg/dL, C-reactive protein 37 mg/L (range, <5.0 mg/L), and procalcitonin 1.84 ng/mL (range, <0.5 ng/mL).

Abdominal computed tomography showed two CBD stones with intrahepatic and extrahepatic bile duct dilatations (Fig. 1).

The patient was diagnosed as acute cholangitis with CBD stone. After obtaining two pairs of blood cultures using BACT/ALERT® Culture Media (bioMérieux, Durham, NC, USA) in the emergency room, empiric antimicrobial therapy with 2 grams of intravenous ceftizoxime sodium (Epocelin®; Donga-ST, Anseong, Korea) every 12 hours was started. After obtaining informed consent, endoscopic retrograde cholangiopancreatography was attempted, but the major duodenal papilla was in far distal part of the duodenal second portion and there was a large juxtapapillary diverticulum. Deep bile duct cannulation could not be done. Therefore, percutaneous transhepatic biliary drainage (PTBD) was performed. The patient showed improvement in symptoms and laboratory findings after intravenous antimicrobial therapy and biliary drainage.

Among the two pairs of blood culture samples requested to the microbiology lab, gram-negative bacilli and gram-positive cocci were confirmed after 9 hours and 47 minutes in the first aerobic medium, and gram-negative bacilli were confirmed in the second aerobic medium after 10 hours and 7 minutes. VITEK® MS (bioMérieux, Marcy l'Etoile, France), a fully automatic microbial

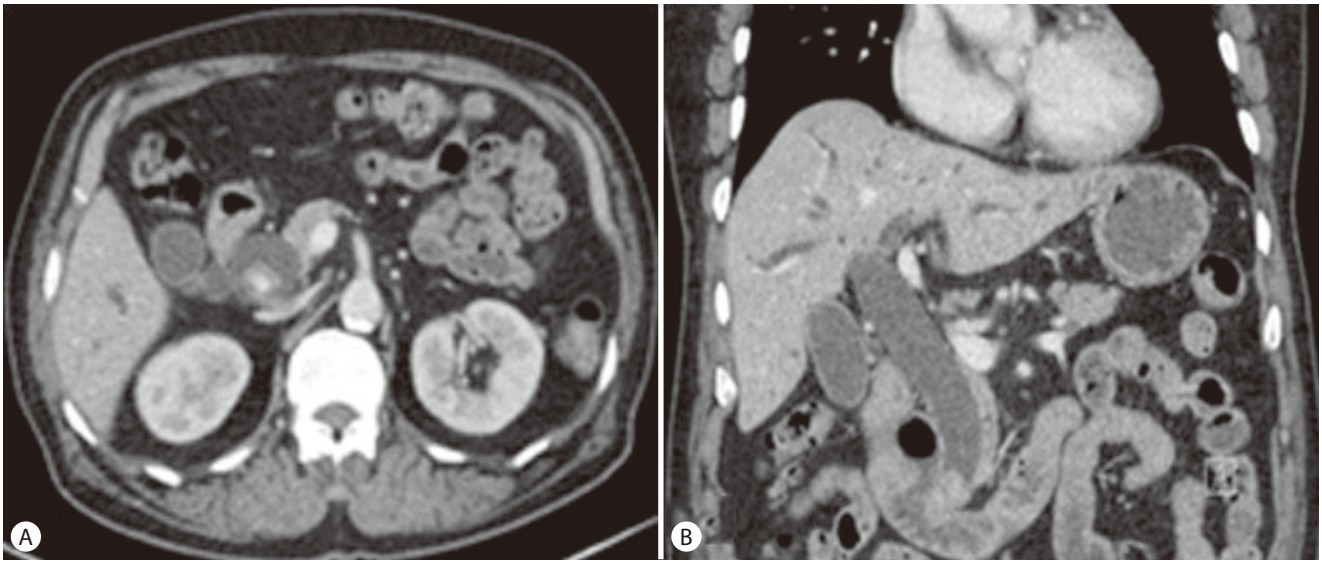

Fig. 1. Abdominal computed tomography findings. (A) Axial scan showed a hyperdense density inside dilated common bile duct. (B) Coronal scan showed a hyperdense density in the distal common bile duct and diffuse dilatation of intrahepatic and extrahepatic bile ducts.

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mass spectrometry identification equipment using the matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) method, identified the pathogens as *Escherichia coli* and *L. garvieae* with a high confidence value (99%). The samples were also analyzed with BACT/ALERT® VIRTUO® (bioMérieux, Durham, NC, USA) system, an automatic blood culture tester, and this confirmed the previous identification of *E. coli* and *L. garvieae*. In addition, bile culture was performed using bile fluid drained through the PTBD track. However, this was a culture test conducted after the use of systemic antibiotics, and the culture result was confirmed as no growth.

Because there are no specific breakpoints available for antimicrobial susceptibility and resistance for *L. garvieae*, 2 grams of intravenous ceftizoxime sodium (Epocelin®; Donga-ST) every 12 hours was maintained for the first 6 days, followed by 100 milligrams of oral cefditoren pivoxil (Meiact®; Boryung, Anseong, Korea) every 8 hours for 8 days, by referring to the minimum inhibitory concentration values of *E. coli* identified together after the consultation to the Department of Infectious Diseases.

The patient showed improvement in clinical course and laboratory results. CBD stones were removed through PTBD tract, and the patient was discharged on the eighth day from admission after confirming there were no residual CBD stones on PTBD cholangiography. He had no recurrent symptoms during follow-up at outpatient clinic, and PTBD catheter was removed 29 days after insertion.

DISCUSSION

L. garvieae is a non-motile Gram-positive cocci that produces alpha hemolysis in blood agar plate and is a major pathogen in fishes that causes fatal hemorrhagic sepsis.[5] The first case of human infection with *L. garvieae* was reported in 1991.[6] Since then, cases of infectious spondylodiscitis,[3] urinary tract infections,[5] acalculous cholecystitis,[7] meningitis,[8] endocarditis in native and prosthetic valves[9] have been reported. However, this bacterium had never been reported as a causative agent of acute cholangitis with CBD stone. To the best of our knowledge, this is the first case of acute cholangitis with CBD stone caused by *L. garvieae*.

The route of human infection of *L. garvieae* is not yet well understood. Researchers have suggested that manipulation or consumption of contaminated raw fish, both saltwater and freshwater, and seafood is the most probable sources of infection.[3,4,5,7] Throughout the cases from *L. garvieae* human infection, the existence of different predisposing conditions and risk factors were noted. Such as an old age, cardiovascular diseases, and the presence of prosthetic valves or previous surgeries. In addition, anatomical or physiological alterations of the gastrointestinal tract, such as diverticulitis, colonic polyps, ulcers or the use of gastric acid suppressive therapy, are considered to be risk factors in the context of foodborne transmission of *L. garvieae*.[4] The patient in this case did not live near the sea nor had a seafood-manipulating occupation. but he occasionally ingested raw saltwater fish frequently before this presentation. And he had long standing lansoprazole and almagate treatment for his gastric ulcer, which could be possible risk factors for *L. garvieae* infection.

Penicillins and cephalosporins are both known to be effective in treatment of *L. garvieae* infections.[10] For our patient, ceftizoxime and cefditoren, third-generation cephalosporins, were administered sequentially for a total of 14 days and showed improvement in symptoms and clinical course.

Interestingly, *L. garvieae* has been found to be causing coinfection with *Klebsiella pneumoniae*, *Enterococcus* species and *E. coli*.[3,11,12] There was one case report for *L. garvieae* and *E. coli* coinfection in form of urinary tract infection.[12] But they were isolated in urine sample and no bacteremia was noted. Here we describe the unique case of *L. garvieae* and *E. coli* coinfection manifested as bacteremia.

Identification of *Lactococcus* species can be challenging because both *Lactococcus* and *Enterococcus* species share some similar phenotypical features. Hence, it can be easily misidentified as *Enterococcus* species.[9] Reliable methods for identification of *L. garvieae* include MALDI-TOF, 16S RNA PCR, API 32 strep kit and BD Automated Phoenix System.[9] In our institution, VITEK® MS (bioMérieux, Marcy l'Etoile, France), a fully automatic microbial mass spectrometry identification equipment using MALDI-TOF MS method and BACT/ALERT® VIRTUO® (bioMérieux, Durham, NC, USA) system, an automatic blood culture tester were used. They were helpful for identification of the organism but discordance among these tests can happen. Accurate

identification of the bacterium is necessary and can be achieved by genetic testing with 16S r-RNA and/or PCR testing. But they are costly and often not widely available.

In this case, *L. gavieae* was identified only in one pair of aerobic blood culture media. However, VITEK® MS (bioMérieux, Marcy l'Etoile, France) distinguished *L.gavieae* with a high confidence score. A previous study reported that the MALDI-TOF MS method was almost equivalent to genotypic identification methods such as 16S rRNA or PCR in identifying *Lactococcus* species.[13] Base on the study result, we concluded that *L. garvieae* is very likely to be the true pathogen in our case.

This is the first case in which *L. garvieae* was isolated from a patient with acute cholangitis with CBD stone, which will be helpful in the treatment of patients infected with *L. garvieae* in the future.

요 약

*Lactococcus garvieae*는 그람 양성 구균으로 해수 및 담수에 서식하는 어류의 병원균으로 알려져 있으며 인간 감염과 관련이 적은 낮은 독성균으로 알려져 있다. 저자들은 70세 남성에서 *L. garvieae* 균혈증을 동반한 총담관결석에 의한 급성담관염 1예를 보고한다. 환자는 급성 상복부 통증으로 본원 응급실로 내원하였고 실험실 혈액검사와 컴퓨터 단층 촬영으로 총담관결석을 동반한 급성담관염으로 진단되었다. 경험적 항생제를 투여하기전 혈액배양검사를 시행하였고 매트릭스 보조 레이저 탈착/이온화 비행시간형 질량분석법(MALDI-TOF MS)으로 *L. garvieae*와 *Escherichia coli* 균혈증이 확인되었다. 먼저 내시경적 담도 배액술을 시도하였으나 실패하여 경피경간담도 배액술을 시행하였고 이를 통해 담도 배액과 총담관결석을 제거하였다. 이후 환자는 양호한 임상 경과를 보여 퇴원하였다. 본 증례의 환자는 간혈적으로 생선회를 섭취한 바가 있었고 위궤양으로 인한 위산억제치료의 병력이 있었는데 *L. garvieae* 감염의 가능한 위험인자로 여겨진다. 본 증례는 급성담관염에서 *L. garvieae* 균혈증의 첫 사례로 향후 *L. garvieae* 감염 환자 치료에 유용할 것으로 기대된다.

국문 색인: 락토코커스 가비에; 담관염; 총담관석; 균혈증

Conflicts of Interest

Jimin Han is currently serving as an Associate Editor in Editorial Board of the *Korean Journal of Pancreas and Biliary Tract*; however, Jimin Han was not involved in the peer reviewer selection, evaluation, or decision process of this manuscript. June Seok Lee, Han Taek Jeong, June Hwa Bae, Ho Gak Kim, and Hyun Hee Kwon have no potential conflicts of interest.

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