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CASE REPORT

A Patient of Spontaneous Bacterial Peritonitis in Hepatitis C Cirrhosis Caused by *Gordonia terrae*: A Case Report

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Background: *Gordonia terrae* is an opportunistic pathogen that rarely causes clinical infections. Here, we first report a case of spontaneous bacterial peritonitis in patients with hepatitis C cirrhosis caused by *Gordonia terrea*.

Case Presentation: A 71-year-old male patient was diagnosed with spontaneous bacteria peritonitis secondary to hepatitis C cirrhosis. The result of bacterial culture in ascites was positive, and the pathogenic bacteria was preliminarily identified as the *Gordonia* genus by matrix-assisted laser desorption ionization–time of flight mass spectrometry. After 16S rRNA sequencing analysis, it was determined to be the *Gordonia terrea*. Symptoms relieved after treatment with ceftazidime.

Conclusion: This case indicates that the clinical infections caused by *Gordonia terrea* should be brought to the forefront. Accurate and rapid bacterial identification results are highly beneficial to the diagnosis and therapeutic regime.

Keywords: spontaneous bacterial peritonitis, rare pathogen, *Gordonia terrae*, identification

Introduction

Gordonia terrea (*G. terrea*) is a gram-positive coccobacillus that is rare in clinical practice. *G. terrae* is characterized as an aerobic, non-dynamic, positive modified Ziehl-Neelsen staining bacteria. Due to time-consuming cultivation and strict nutritional requirements, it is prone to be misidentified as *Rhodococcus or Nocardia* genus.[1,2] In addition, it is probably failed to recognize as pathogen instead of contamination from the environment. In our study, we first report a case of spontaneous bacterial peritonitis (SBP) in patients with hepatitis C cirrhosis caused by *G. terrea*. It was preliminarily identified as *Gordonia* genus by matrix- assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS), and further definitely identified as the *G. terrea* through 16S rRNA gene sequencing analysis.

Case Presentation

General Condition and Case History

A 71-year-old male patient was admitted on February 6, 2023, due to swelling of both lower limbs and abdominal distension for more than 20 days (Figure 1). The patient was hospitalized for liver preservation and symptomatic treatment with a diagnosis of hepatitis C cirrhosis in 2017. In May 2022, the patient rehospitalized for spontaneous bacterial peritonitis. During hospitalization, no pathogenic bacteria were found in ascites culture, and the patient relieved after ceftriaxone treatment. With a history of hypertension up to 160/80 mmHg for 8 years, he took antihypertensive drugs regularly, and the blood pressure could be controlled within a normal range. The patient had suffered diarrhea in the past 8 months without significant weight loss. The results of the physical examination after admission displayed as follows: body temperature 36.5°C, pulse 75 beats/min, respiratory rate 18 beats/min, blood pressure 123/67 mmHg. The patient revealed clear consciousness, dark complexion, facial telangiectasia, and no yellowing of sclera and skin. Liver palm and spider nevus were clearly discernible. The patient exhibited abdominal distention, scattered light tenderness, and rebound pain in the whole

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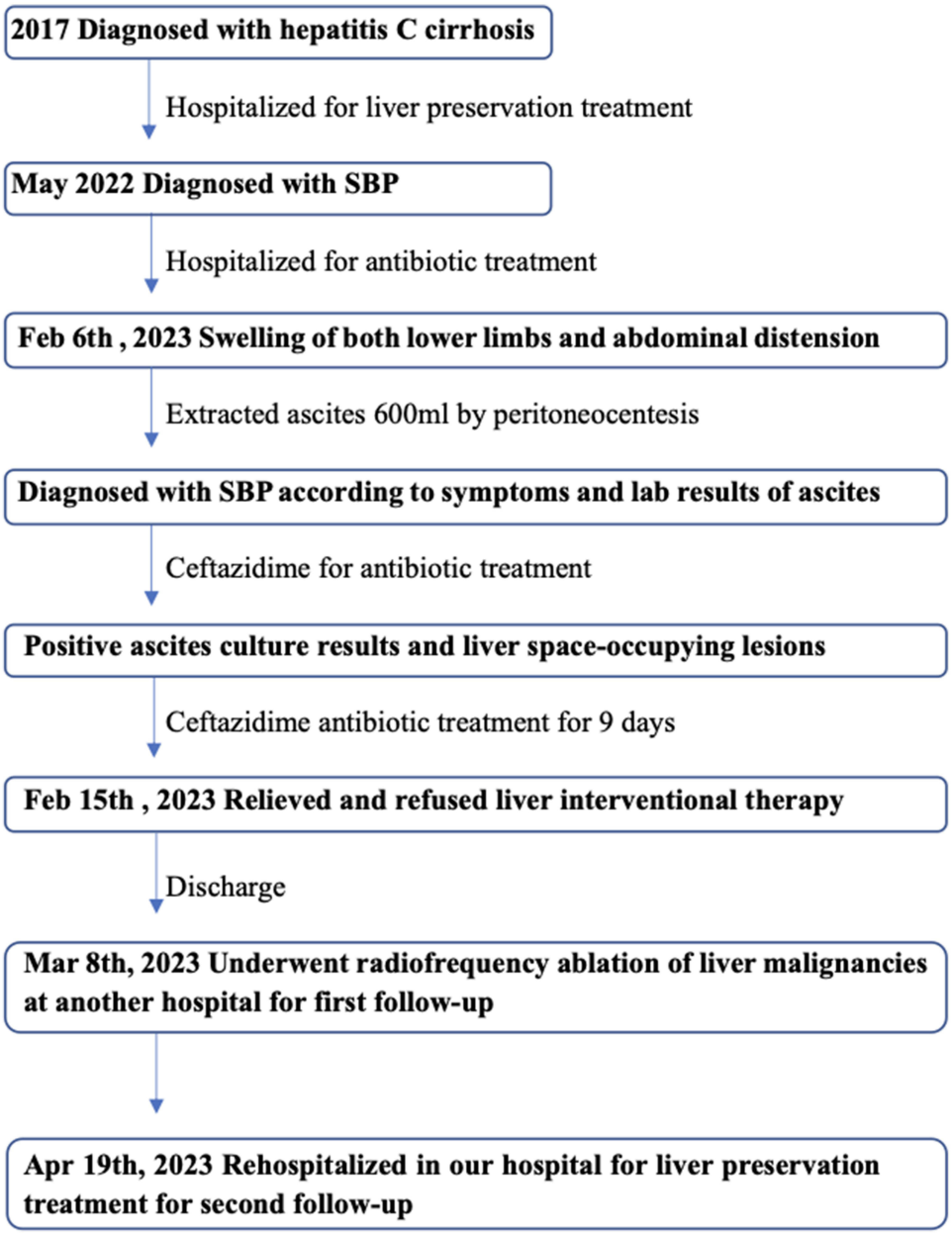

Figure 1 Flow chart of the development process and outcome of the case.
Abbreviation: SBP, spontaneous bacteria peritonitis.

abdomen. There was no muscle tension, no touch under the ribs of the liver and spleen and no percussion pain in the liver area of the patient. The patient presented with edema in both lower limbs, positive shifting dullness, and negative Murphy's sign.

Imaging and Clinical Laboratory Examination

Full abdominal contrast-enhanced computed tomography (CT) indicated liver cirrhosis, splenomegaly, ascites and esophageal gastric varices. Contrast-enhanced magnetic resonance (MR) revealed nodule in the right lobe of the liver, which was unable to rule out malignancy. Ultrasonography indicated bilateral renal cysts. The main laboratory examination results were presented as below: total protein 54.5 g/L, albumin 24.7 g/L, alanine aminotransferase 40 U/L, aspartate aminotransferase 59 U/L, total bilirubin 24.1 μmol/L, indirect bilirubin 17.3 μmol/L, direct bilirubin 6.8 μmol/L, C-reactive protein (CRP) 14.4 mg/L, D-dimer 2760 μg/L, platelet count 66×10^9/L, alpha fetoprotein 15.08 ng/mL, carbohydrate antigen 19-9 (CA199) 49.30 U/mL, hepatitis C virus antibody 13.95 S/CO. Routine urinalysis results

showed elevated red cell and white cell counts, and 24-hour proteinuria was 3.63 g. 600 mL of light yellow and slightly turbid ascites was extracted through peritoneocentesis. Routine examination of ascites presented yellow and translucent appearance, positive Rivalta test, white blood cell 276×10^6/L, polymorphonuclear cell 143 $\times10^6$/L. The ascites samples were delivered to the clinical laboratory for bacterial culture.

Isolates Culture and Identification

The ascites was injected into aerobic and anaerobic bottles (BD, USA), which were matched with BACTEC ™ FX40 automatic blood culture instrument (BD, USA). No suspicious bacteria were found in the direct smear of ascites sample after Gram staining. The aerobic bottle reported positive alarm prompt after 64 hours cultivation. The culture fluid was inoculated to Columbia blood agar and MacConkey agar plate (Yancheng, China), and placed the plates into a 35°C, 5% CO_2 incubator. Meanwhile, smear staining and microscopic examination were conducted, and the results showed gram-positive coccobacillus (Figure 2A), negative for acid fast staining (Figure 2C), and partially positive for modified Ziehl-Neelsen staining (Figure 2D). Wright-Giemsa staining was conducted for a better observation (Figure 2B). Scattered pinpoint-shaped colonies emerged on the blood agar plate after 24 hours of cultivation (Figure 3A), and small white colonies appeared after 48 hours (Figure 3B). After 72 hours, dry, wrinkled, and protruding colonies were formed, which were light brown with irregular edges (Figure 3C). After 120 hours, the colonies gradually turned dark brown (Figure 3D). No bacterial growth was observed on MacConkey agar plate. MALDI-TOF MS was applied to the bacterial identification. The detections were carried out twice by Clin -ToF II MALDI (BIOYONG, China) according to reference version (version 3.6.2) of the bacteria bank. The twice results suggested

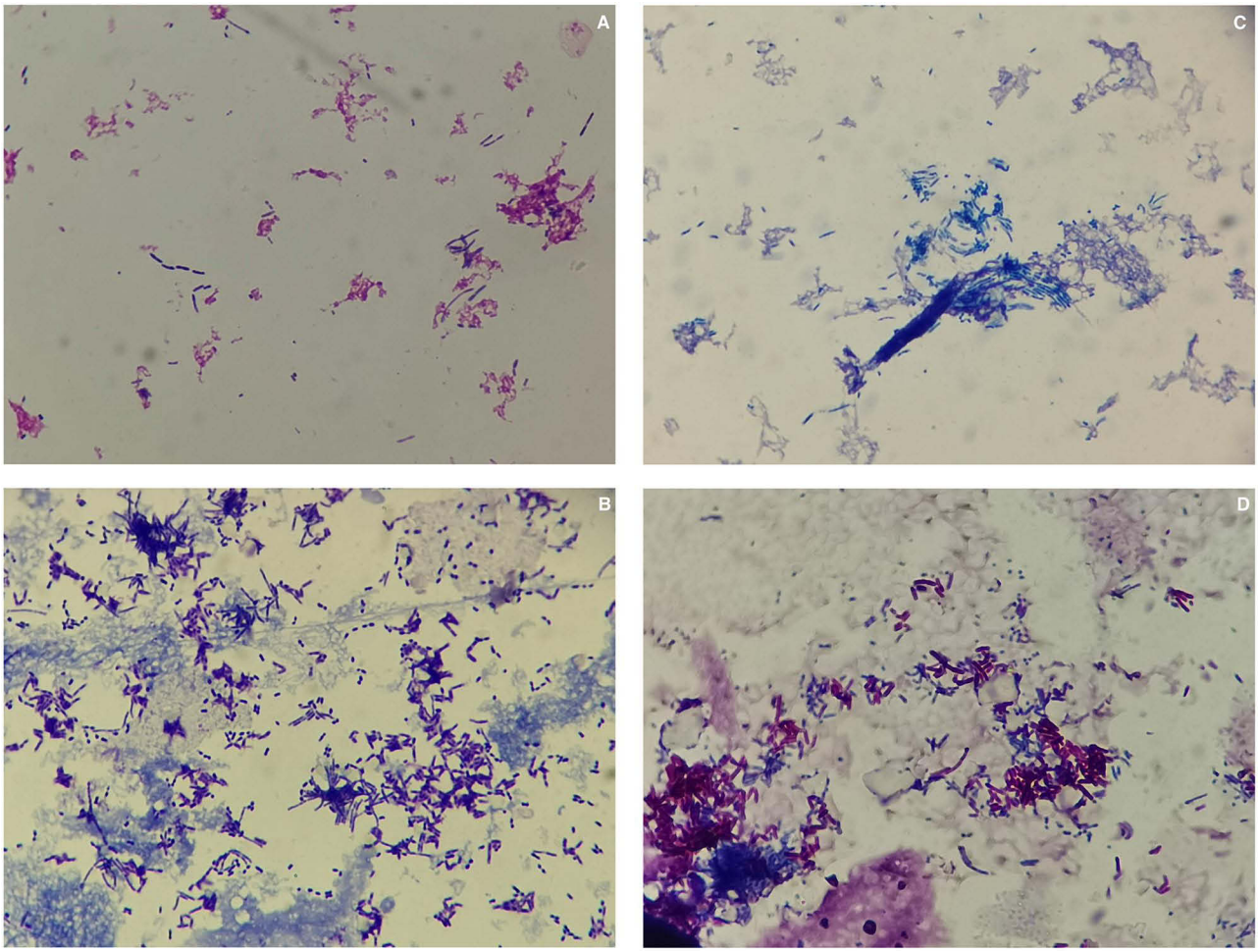

Figure 2 Microscopic morphological characteristics of smear staining (magnification: 1000×): Gram staining (**A**), Wright-Giemsa staining (**B**), Ziehl-Neelsen staining (**C**), modified Ziehl-Neelsen staining (**D**).

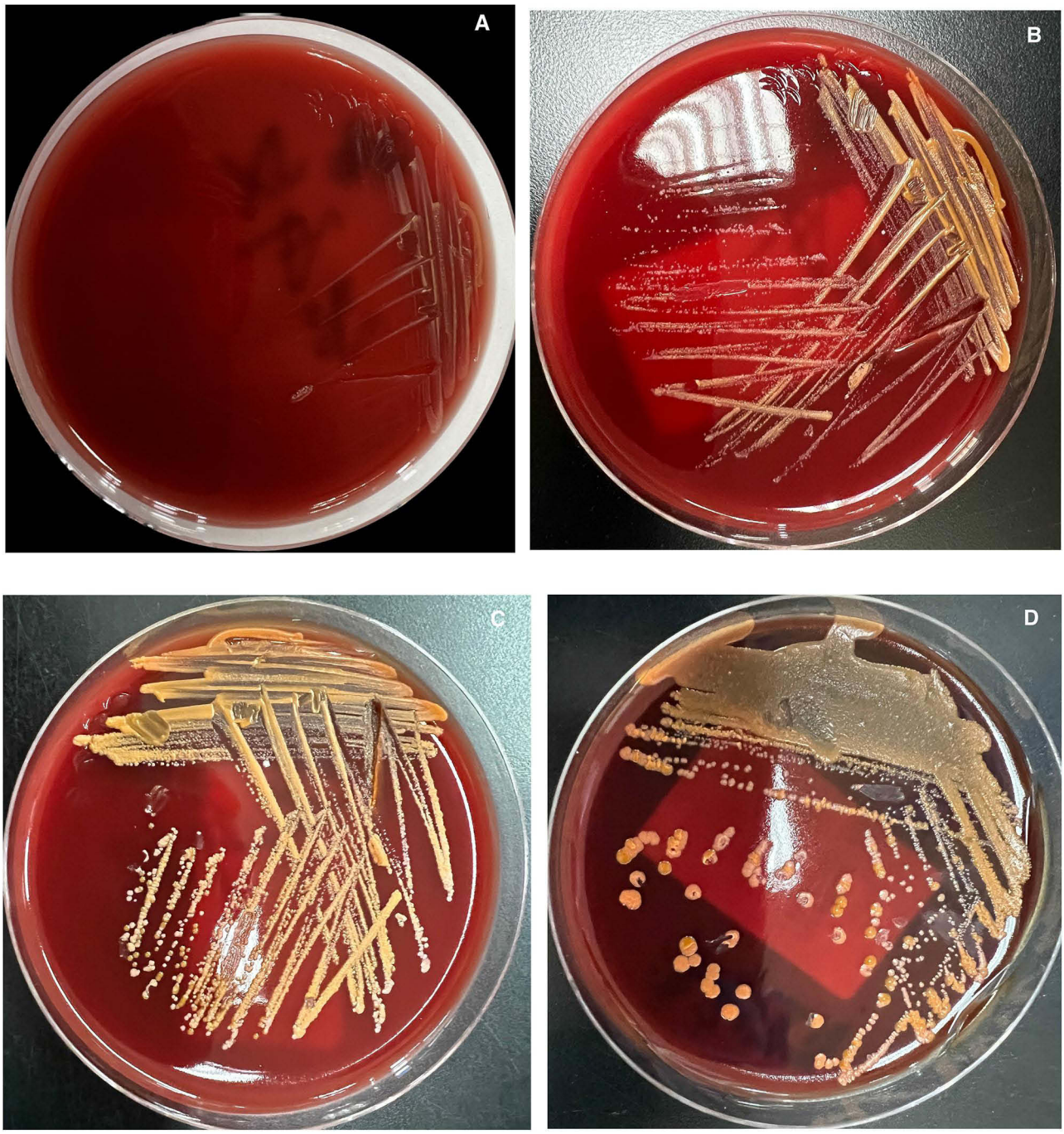

Figure 3 Different incubation time of the colony growth characteristics of *G. terrae* subculture on Columbia blood agar:24h (**A**), 48h (**B**), 72h (**C**), 120h (**D**).

the strain pertained to the *G. terrae* (confidence value: 48%) and *G. rubripertinota* (confidence value: 46%). The sample was also sent to Beijing Genomics institution (BGI) (Wuhan) for 16S rRNA gene sequencing analysis, and the primers sequence were as follows: 27 F (5′-AGAGTTTGATCCTGGCTCAG-3′) and 1492R (5′-TACGGCTACCTTGTTACGACTT-3′). The coverage length was 1369 bp. After Blast alignment, the sequencing comparison results indicated that the strain had the highest homology (100%) with the *G. terrae* RL-JC02 (GenBank: CP049836.1).

Treatment and Follow-Up

Considering the liver cirrhosis history accompanied by the symptoms of peritonitis, ascites testing results and elevated CRP supported the preliminary clinical diagnosis of spontaneous bacterial peritonitis.[3] After ascites extraction on the second day of

admission, ceftazidime was given for empirical therapy. Ceftazidime was given with a dose of 2g with an interval of 12h, along with intravenous administration of albumin and diuretic treatment with furosemide spironolactone. Based on the staining results, it was suggested to select antibiotics against gram-positive bacteria such as vancomycin. However, considering the history of chronic kidney disease and the relief of peritonitis symptoms, the physician preferred to use ceftazidime continuously. The therapy period of ceftazidime lasted for 9 days. After treatment, abdominal tenderness and distension were relieved, ascites decreased, and lower limb edema alleviated. According to the contrast-enhanced MR results, it was recommended to accept surgical and interventional treatment for focal space-occupying hepatic lesions. Unfortunately, the patient refused further treatment and requested discharge. One month after discharge, we conducted the first telephone follow-up, and he represented that he underwent radiofrequency ablation of liver malignancies in another hospital on March 8th, 2023. Through the second telephone follow-up on April 19th, 2023, we learned that the patient rehospitalized in our hospital and sought for liver preservation treatment.

Discussion

In 1971, the *Gordonia spp*. was first described by *Tsukamura*[4] and officially designated as *Gordonia* in 1997. It belongs to the bacterial domain, phylum *Actinomycetota*, class *Actinobacteria*, order *Actinomycetales*, suborder *Corynebacterineae*, and family *Gordoniaceae*.[5] At present, the *Gordonia spp*. includes over 40 species, among which *G. bronchialis, G. aichiensis, G. rubropertincta, G. sputi*, and *G. terrae* are related to human diseases.[6,7] Currently, 17 bacteriophages have been subsumed in GenBank.[8] The *Gordonia spp*. is ubiquitous in the natural environment, which can be isolated from water and soil. The application value of *Gordonia spp*. is mainly embodied in biotechnology and biodegradability on pollutants.[9] As an opportunistic pathogen, *Gordonia* infection is rare in clinical practices.[10,11] The patients with immunocompromised or immunosuppressive therapy may suffer the infection with *Gordonia*. Due to the slow-growing prosperity and high requirements for culture, identification of the *G. terrae* poses significant complexity. The conventional identification methods of *G. terrae* mainly include culture, biochemical methods and experiments.[12] The utilization of conventional laboratory identification methods can provide clues and tacks for the identification of *G. terrae*, but it can still to be mistakenly identified as *Corynebacterium, Rhodococcus, Actinomyces* or *Mycobacterium*.[13–15] Identification with *Mycobacterium* can be achieved by modified Ziehl-Neelsen staining. *G. terrae* is positive, while *Mycobacterium* presents modified Ziehl-Neelsen staining negative. Aerial hyphae can be used as a key point to distinguish *G. terrae* from *Nocardia. Nocardia* can produce aerial hyphae, while *G. terrae* fails to produce aerial hyphae.[16,17] Given the slow growth of *G. terrae*, multiple staining methods and extended plate incubation time contribute to improve detection rates and avoid omission. Conventional methods usually have some limitations. With the extensive development of MALDI-TOF MS in clinical microbiology laboratory, it has provided great help for the identification of *G. terrae*. The MALDI-TOF MS for bacterial identification holds the characteristics of rapidness and convenience, but obtaining a definite identification result still relies on whole gene sequencing technology. Especially for the identification of some rare bacteria, the performance of MALDI-TOF MS is less than satisfactory. Through gene phenotype 16S rRNA sequencing analysis, the confirmation of *G. terrae* can be achieved. However, most clinical microbiology laboratories are unable to carry out this technology and need to be sent to testing institution, which is often a time-consuming detection.

For the first time, this case report presented a hepatitis C cirrhosis patient combined with SBP infected by *G. terrae* in the ascites. According to literature reported, diseases related to *G. terrae* infection are as follows: dialysis related peritonitis,[18–20] catheter-related bacteremia,[21,22] brain abscess and meningitis,[16,23] skin infections,[2] kidney abscess,[24] acute cholecystitis[14] etc. SBP is a common complication in patients with liver cirrhosis. A retrospective analysis showed that the mortality rate of cirrhosis combined with SBP was as high as 17.8%.[25] As the literature reported, about 40% of patients presented with elevated polymorphonuclear cell count in ascites and negative bacterial culture results, but treatment should still be considered as SBP.[26] Given the high mortality, the occurrence of SBP poses significant detriment to patients with liver cirrhosis and ascites,[27] and it is imperative to conduct empirical antibiotic therapy for suspected SBP.

There is currently no consensus on the principles for the use of antibiotics in the therapy of *Gordonia* infection. Due to the long identification time, the selection of antibiotics also brings great difficulties and challenges. Considering the differences in primary disease and infection symptoms comprehensively, empirical treatment tends to be diverse and individualized. The antibiotic susceptibility testing by *Mueller-Hinton* agar dilution suggested that penicillins and aminoglycosides were effective

against *Gordonia. spp*.[14] A patient with pacemaker-induced endocarditis by *Gordonia bronchialis* was sensitive to multiple antibiotics (amoxicillin-clavulanate, ceftriaxone, ciprofloxacin, imipenem, tobramycin, amikacin, linezolid and trimethoprim-sulfamethoxazole).[28] According to the literature reported, *G. terrea* was susceptible to penicillin, ampicillin, amikacin, erythromycin, ceftriaxone, imipenem, gentamicin and vancomycin using the E-test method, while ceftazidime showed resistance.[19] A literature integrated five *Gordonia* -infected cases, of which four cases chose vancomycin, cephalosporins or a combination as empirical treatment program.[29] A French study retrospectively analyzed the medication of antibiotics in 10 patients with *Gordonia*-caused bacteremia, and the results indicated that β-lactam monotherapy was supposed to be the preferred drug for empirical medication.[30] In our case report, ceftazidime was effective and symptoms alleviated. Ceftazidime is recommended as a first-line antibiotic for empirical therapy of community-acquired SBP. After gram-positive coccobacillus found, considering the history of chronic kidney disease and the relief of peritonitis symptoms, the physician preferred to use ceftazidime continuously. *Gordonia* -infected patients usually has a better prognosis through the combination of primary disease treatment and antibiotic use,[28,31] and even no antibiotic treatment.[32] Therefore, more experience in antimicrobial therapy should be gradually accumulated to provide more precise and individualized treatment strategies.

Limitations

In this case, the susceptibility testing was failed to carry out. As a rare pathogen, the susceptibility testing of *G. terrae* required special culture media, which was incapable to be carried out routinely in our microbiology laboratory, and the procurement needed a certain period. In addition, the patient's refusal to subsequent treatment also led to the inability to perform the susceptibility test.

Conclusion

Liver cirrhosis supervening with SBP maybe insinuates a vicious condition, hence intervention measures and antibiotic therapy brook no delay. Although *G. terrae* is considered as a rare pathogen causing human infections, it is still indispensable to enhance full recognition and emphasis of *G. terrae* both for clinical and laboratory settings. By combining multiple identification methods, the detection rate of *G. terrae* can be improved.

Data Sharing Statement

The study protocol on the current study is available from the corresponding author Dr. Xiaosong Qin.

Ethics Statement

The Committee of Ethics of the China medical university of Shengjing hospital reviewed and approved the study protocol (NO.2023PS1040K). The informed consent from the patient was obtained about the personal information and clinical data.

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Disclosure

The authors declare no conflicts of interest in this work.

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