



Case study

Clinical implications of *Paracoccus yeii* bacteremia in a patient with decompensated cirrhosis



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ARTICLE INFO

Article history:

Received 1 September 2016

Received in revised form 17 November 2016

Accepted 17 November 2016

Available online xxx

Keywords:

Paracoccus yeii

Bacteremia

Decompensated cirrhosis

Gram negative

MALDI-TOF

ABSTRACT

Infections in patients with cirrhosis are common among those who develop variceal hemorrhage. Prophylactic antimicrobial treatment with third generation cephalosporins is recommended in patients with advanced cirrhosis and gastrointestinal hemorrhage. However no infectious source is identified in up to 50% of patients with cirrhosis and clinical sepsis. We report the first case of *Paracoccus yeii* bacteremia in a patient with decompensated cirrhosis who presented with variceal hemorrhage. This rare gram negative organism that occurs naturally in the soil has been difficult to isolate until recent technological advances and may not be susceptible to third generation cephalosporins. Our case reinforces the challenges in isolating rare infections in patients with cirrhosis, the need to consider uncommon organisms in infected but culture negative patients with cirrhosis, and the importance of optimizing antimicrobials to reduce the incidence of drug resistant organisms.

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Introduction

Infections are common in patients with cirrhosis and have been found in up to 66% of patients with variceal hemorrhage [1]. Prophylactic treatment with third generation cephalosporins is recommended in patients with advanced cirrhosis and gastrointestinal bleeding to cover for the predominant causative gut flora organisms [2,3]. Treatment is recommended even if no causative organism is identified as up to 50% of patients with cirrhosis and clinical sepsis have negative cultures [4]. Identifying appropriate antimicrobials can be challenging without a causative organism, and the empiric use of broad spectrum antimicrobials contributes to multidrug resistant organisms. We report the first known case of *Paracoccus yeii* bacteremia in a patient with decompensated cirrhosis who presented with variceal hemorrhage. This rare gram negative organism may not be susceptible to third generation cephalosporins. This finding may have implications for the management of infected but culture negative patients with cirrhosis.

Case

A 42 year old gentleman with decompensated cirrhosis from genotype 1a (G1a) hepatitis C (HCV) had been treated with 24 weeks of ledipasvir and sofosbuvir which ended 4.5 months earlier. He had been recently treated with ciprofloxacin for *Klebsiella pneumoniae* bacteremia of unknown source. His comorbidities included proliferative glomerulonephritis and chronic lymphedema. The patient presented with new onset jaundice (total bilirubin 23 mg/dL, direct bilirubin 18 mg/dL, alkaline phosphatase 99 U/L, alanine aminotransferase 31 U/L, aspartate aminotransferase 86 U/L) that peaked to total bilirubin 44 mg/dL and direct bilirubin 31 mg/dL. Model for End-Stage Liver Disease (MELD) score on admission was 27. Given the report of subjective fevers in the setting of recently treated *K. pneumoniae* bacteremia of unknown source, admission blood and urine cultures were obtained but were without growth. Diagnostic paracentesis was attempted but the patient had minimal ascites. Molecular studies revealed HCV relapse (HCV viral load = 4.44 log IU/mL) without NS5b resistance (insufficient sample for NS5a) and undetectable hepatitis B (HBV) and adenovirus. There was no serologic evidence of acute infection with hepatitis E, cytomegalovirus (CMV), or Epstein Barr virus (EBV). Liver biopsy demonstrated cirrhosis with moderate chronic inflammation, focal severe neutrophilic infiltrates with cholestasis, and ductular proliferation. Magnetic

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resonance imaging (MRI) and magnetic resonance cholangiopancreatography (MRCP) showed no cholangitis or abscess. Although drug induced liver injury from ciprofloxacin was clinically suspected, two sets of blood cultures were obtained daily due to concern for infection and lack of clinical improvement.

The patient elected discharge but was readmitted within 24 hours with hematemesis from variceal hemorrhage and portal hypertensive gastropathy. Empiric treatment for undifferentiated septic shock including spontaneous bacterial peritonitis prophylaxis were ceftriaxone 2 g IV every 24 hours, metronidazole 500 mg IV every 8 hours, and vancomycin 2 g IV every 12 hours. Diagnostic paracentesis was again attempted but the patient had minimal ascites. Given the lack of clinical improvement and the finding of bowel edema and severe colitis on computer tomography, infectious disease was consulted. It was recommended to adjust antimicrobials to piperacillin-tazobactam 3.375 mg every 6 hours, metronidazole 500 mg IV every 8 hours, and vancomycin 125 mg PO every 6 hours to cover for gut flora including *Clostridium difficile* until it could be ruled out.

Blood cultures collected the day before discharge of the previous admission flagged as “positive” after 5 days of incubation in the aerobic bottle (BacTec Plus Aerobic/F), but no organisms were seen upon Gram stain. However, after two days of incubation, small mucoid colonies of oxidase positive Gram negative coccobacilli were seen growing on Chocolate agar only. The team was notified and antimicrobials were adjusted to only piperacillin-tazobactam 4.5 g every 6 hours. The organism was very slow growing, and initial attempts at identification were unsuccessful. After an additional two days of incubation, an identification of *Paracoccus yeeii* was made by Matrix Assisted Laser Desorption Ionization Time of Flight Mass Spectrometry (MALDI-TOF MS; Vitek MS) with a match of 99.9% to the Vitek MS IVD unclaimed database. Identification was confirmed by sequencing of the first 500 bp of the 16S gene. Upon speciation, the patient was switched to ceftazidime 1 g every 12 hours to cover for *P. yeeii* as well as concern for a hospital acquired pneumonia. The patient completed a 2 week treatment course of gram negative antimicrobial coverage with two beta lactam agents and had clinical improvement with no other culture growth of *P. yeeii*. Unfortunately, the patient developed end-stage liver disease and eventually succumbed to death due to septic shock from *Citrobacter freundii* pneumonia.

Discussion

To our knowledge, this is the first reported case of *P. yeeii* in a patient with cirrhosis. Patients with decompensated cirrhosis are at high risk of infection from immune dysregulation, a heightened inflammatory response, altered gut flora, and bowel translocation. However, no causative organism is found in up to 50% of patients with decompensated cirrhosis presenting with clinical sepsis. This case of bacteremia with a rare gram negative organism is instructive regarding optimal diagnosis and treatment of infection in patients with decompensated cirrhosis who have an unclear source of infection as they have an extremely high risk of morbidity and mortality.

P. yeeii is an aerobic gram negative coccobacillus that has been isolated in soil and marine sediment, and has been rarely reported as infections in humans. *P. yeeii* has been identified in the past through commonly available biochemical tests, and this case demonstrates the utility of MALDI-TOF MS for the identification of this infrequently encountered organism [5,6]. The few reported cases of *P. yeeii* to date have entailed peritonitis among peritoneal dialysis patients [5,7], myocarditis in a heart transplant patient [8], corneal graft infection [9], and heart failure with bullous skin

lesions [10]. All cases identified *P. yeeii* through culture of affected tissues. Only 2 cases, including ours, have been associated with bacteremia and ours is the first case of a patient with cirrhosis. The source of bacteremia in our case remains unclear, but it is plausible that the patient's lymphedema and bowel edema could be sources for this environmentally found organism. Over the previous year, the patient had several episodes of bacteremia thought to be from bowel translocation including Group G β -hemolytic streptococci, *Streptococcus mitis/oralis*, *Citrobacter braakii*, and *Enterococcus faecium* (the patient was not on chronic antimicrobials). The challenges in isolating *P. yeeii* suggest that it is underdiagnosed. MALDI-TOF may help with rapid diagnosis and guide appropriate treatment when initial cultures in patients with decompensated cirrhosis and clinical sepsis are negative.

It is recommended that patients with advanced cirrhosis who develop gastrointestinal bleeding be treated empirically with third generation cephalosporins [2,4]. However, this case illustrates that uncommon gram negative organisms may not necessarily be covered with third generation cephalosporins. Although we did not have antimicrobial susceptibilities performed in our case, the existing literature on *P. yeeii* suggests that the organism is susceptible to fluoroquinolones and beta-lactams though higher minimum inhibitory concentrations (MICs) were reported with third generation cephalosporins [5].

This case reinforces the challenges in isolating rare infections in patients with cirrhosis. In the absence of obvious infectious sources in a patient with decompensated cirrhosis, consideration should be given to uncommon gram negative organisms. Collaboration with infectious disease specialists and microbiologists is warranted in these cases to isolate infectious organisms and to identify appropriate antimicrobials promptly.

Funding source

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

None.

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