SAGE Open Medical Case Reports
Volume 9: 1–5

DOI: 10.1177/2050313X211055292
journals.sagepub.com/home/sco
SAGE

A case of Methicillin-sensitive *Staphylococcus aureus* infective endocarditis that rapidly changed prognosis in a patient with cirrhosis: An atypical case with literature review

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Abstract

Bacterial infections represent a major cause of mortality and morbidity in patients with cirrhosis that can alter the clinical course of compensated cirrhosis. The most common infections are spontaneous bacterial peritonitis by gram-negative organisms, urinary-tract infection, and pneumonia. In this case report, we raise the question of considering infections in the prognosis scoring in this patient group.

Keywords

Gastroenterology/hepatology

Date received: 13 July 2021; accepted: 6 October 2021

Introduction

Model for end-stage liver disease (MELD) and the Child–Pugh scores[1,2] are the most frequently used prognostic models in clinical practice for patients with cirrhosis. Serum sodium, international normalized ratio (INR), bilirubin, creatinine, albumin, encephalopathy, ascites, and requirement for dialysis are the variables that determine these scores. Bacterial infections account for 50% of deaths in patients with liver cirrhosis (LC). Early diagnosis of infection is difficult due to non-specific manifestation and sometimes resembles liver failure. 26%–44% of patients die within 1 month of infection onset and another one-third within 1 year.[3] Serum biomarker like procalcitonin can be used to rule out asymptomatic infections. Acute kidney injury is a strong predictor of death in these patients. A bacterial infection can trigger rapid deterioration of liver function and is one of the most common causes of liver failure. The most widespread infections are spontaneous bacterial peritonitis (SBP) and pneumonia. Infective endocarditis, although rare, is also associated with significantly higher mortality. We urge our readers to consider infections when patients of LC present with acute kidney injury or decompensation. Here, we present a case of Methicillin-sensitive *Staphylococcus aureus* (MSSA) bacteremia in a patient who presented with SBP.

Case description

A 63-year-old male with history of alcoholic cirrhosis, without any significant valve disorder, and without history of drug abuse (MELD score of 13 as of a month ago) presented to the hospital with abdominal pain for the past 3 weeks. He had no prior history of ascites and never underwent a paracentesis. He had multiple admissions in the past for alcohol withdrawal with the most recent hospitalization 3 weeks ago. On examination, he was cachectic, icteric, and had a holosystolic murmur which was heard best at the apex with radiation to the axilla. His abdomen was diffusely tender and distended. There were erythematous, purpuric macules, and papules scattered diffusely on hands, legs, and feet bilaterally (Figure 1).

Admission labs were white blood cell count of 16.8 k/uL, hemoglobin of 10 g/dl, platelets of 292 k/uL, prothrombin time 27.8 s, sodium of 125 mEq/L, potassium of 4.8 mmol/L,

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urea of 54 mg/dL, creatinine 3.3 mg/dL, bilirubin 9.1 mg/dL, alanine transaminase (ALT) of 24 U/L, aspartate transaminase (AST) of 76 U/L, alkaline phosphatase of 93 U/L, lactic acid dehydrogenase (LDH) 829 U/L, total protein of 7.4 g/dL, albumin of 2.6 g/dL, and INR of 2.3. One month ago, labs were essentially normal, except for a bilirubin of 4.4 mg/dL, and hemoglobin of 10.5 g/dL. His current MELD score was 38 points. Paracentesis was performed on the ascitic fluid which showed a cell count of 2000 cells/mm^3 with neutrophilic predominance with polymorphonuclear cell count PMN of 700 cells/mm^3. The admission lab values are mentioned in Table 1.

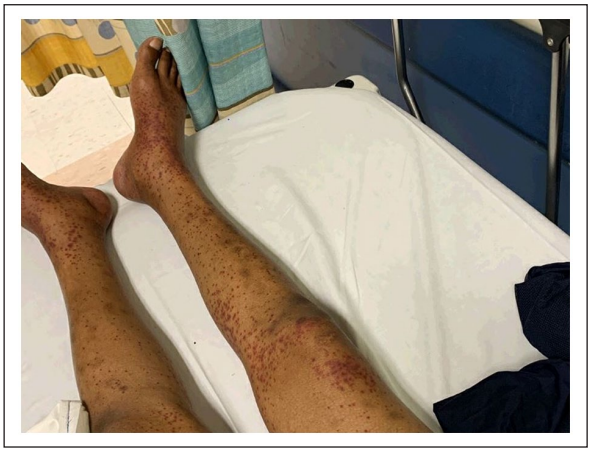

Figure 1. Erythematous macules and papules scattered in both legs.

Patient was empirically started on Piperacillin and Tazobactam. Patient blood culture revealed gram-positive cocci in clusters and 750 mg of Vancomycin was added 2 days later (given high suspicion of healthcare-associated infection which is defined as infections that develop in less than 48 h after admission or previous exposure to healthcare setting in the preceding 90–180 days).[4] Final culture was positive for MSSA. Paracentesis fluid culture revealed MSSA as well. Echocardiogram showed vegetation on the mitral valve 17 mm × 4 mm (Figure 2(a)). Antibiotics were changed to cefazolin. The patient was not a candidate for surgery in spite of embolic events due to a high Mayo

Table 1. Lab values on admission.

Lab (units)	Reference range	Absolute value
White blood cell count ($\times 10^3$)	3.8–10.5	16.8
Absolute neutrophil count ($\times 10^3$)	1.8–7.4	87.3
Absolute lymphocyte count ($\times 10^3$)	1.0–3.3	5.1
Hemoglobin (g/dL)	11.5–15.5	10.1
Mean corpuscular volume (fL)	80.0–100.0	98.6
Platelet count ($\times 10^3$/uL)	150–400	292
Sodium (mmol/L)	135–145	125
Potassium (mmol/L)	3.5–5.3	5.4
Chloride (mmol/L)	98–107	94
Carbon dioxide—serum (mmol/L)	22–31	18
Blood urea nitrogen (mg/dL)	7–23	54
Creatinine (mg/dL)	0.5–1.3	3.3
Glucose—serum (mg/dL)	70–99	91
Calcium (mg/dL)	8.4–10.5	7.6
Protein total—serum (g/dL)	6.0–8.3	7.4
Albumin (g/dL)	3.3–5.0	2.6
Total bilirubin (mg/dL)	0.2–1.2	9.1
Alkaline phosphatase (U/L)	40–120	93
Aspartate aminotransferase (U/L)	4–32	76
Alanine aminotransferase (U/L)	4–33	24
pH—arterial	7.32–7.43	7.34
Lactate (arterial) (mmol/L)	0.5–2.0	4.8
Prothrombin time: (s) INR: PTT: (s)	10.2–12. 0.8–1.1 25–33	27.8 (H) 2.3 (H) 42.8 (H)
Fibrinogen: (mg/dL)	324–571	174 (L)
Lactate dehydrogenase (U/L)	135–225	829
Procalcitonin (ng/mL)	0.02–0.10	0.36
High-sensitivity troponin (ng/L)	<6–14	6
Creatine kinase, serum (U/L)	30–200	2
Creatine kinase-MB (units/L)	0–6.7	28.2
Serum pro-brain natriuretic peptide (pg/mL)	0–300	2790

INR: international normalized ratio; PTT: prothrombin time.

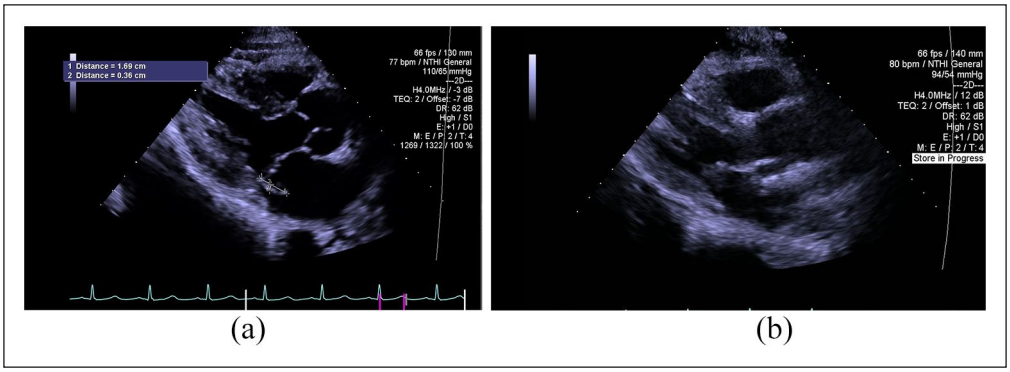

Figure 2. Parasternal long axis view of the echocardiogram showing (a) vegetation on the mitral valve and (b) clearance of the vegetation.

surgical risk of 40% mortality within 7 days. His kidney function continued to deteriorate. Urine studies showed UNa of 79 mEq/L, U creatinine of 50.2 mg/dL, and FENa of 4.1%. Patient had a daily electrocardiography (EKG) which did not show an AV block. No persistent fever or bacteremia was noted. He had hepatorenal syndrome (HRS) for which he was initially started on octreotide, midodrine, albumin without response, and eventually needed hemodialysis. He was discharged to rehab with long-term intravenous antibiotics for a total of 6 weeks. Patient's repeat echocardiogram showed improvement in valve function with clearance of vegetation (Figure 2(b)). Even with the clearance of infection, patient's clinical course continued to deteriorate with multiple admissions for refractory symptomatic ascites, hepatic hydrothorax, recurrent pleural effusion, acute liver failure and encephalopathy. He was not a candidate for transplantation due to active alcohol abuse within last 6 months. He underwent placement of palliative peritoneal drainage catheter and transferred to tertiary care for transjugular intrahepatic portosystemic shunt (TIPS). The improved survival seen in patients with HRS from TIPS made us refer him for the same.[5] Other factor affecting success from TIPS is pre-TIPS bilirubin which was 2.6 mg/dL in his case.

Discussion

Bacterial infections are frequent and pose a serious concern among patients with LC as they further deteriorate liver function. Infection increases mortality by four-fold: 30% of infected patients die within 1 month and another 30% die within 1 year.[6] Most frequent infections are SBP by gram-negative organisms, urinary-tract infection (UTI),[7–9] and pneumonia. Multiple studies have been done on patients with liver cirrhosis (LC) hospitalized for infection to study the consequences of infections on liver function and patient survival. One such study by Merli et al.[10] showed that an MELD score of more than 15 is an independent predictor of infection, and higher scores correlate with higher mortality rates. Infections worsen liver function in 62% of the patients. Another study by Khan et al.[11] noticed an 8% increase in mortality rate with every one point rise in MELD score above 22 in patients of LC with infection. The specificity to predict poor outcome was higher in MELD score compared to the Child–Pugh score. The multicenter study by Borzio et al.[8] showed that infections are associated with decompensation of LC. The inpatient hospital mortality was higher in infected than non-infected patients, 15% versus 7% ($p < 0.05$). Obstein et al.[12] found that higher MELD scores were independently associated with higher risk for SBP. A sequential study by Caly and Strauss[9] indicated that mortality is 30% for patients with infections compared to 5% for those without infection. SBP and Pneumonia are the most severe infections with a mortality rate of 35% and 40%, respectively. Another study by Juntermanns et al.[13] concluded that higher MELD score is associated with higher mortality in case of sepsis.

The severity of infection in LC is attributed to the state of immune dysfunction. Porto systemic shunting prevents clearing of the bacteria. Nearly all components of systemic immune response are significantly impaired in cirrhosis. Decrease in phagocytic activity, reduction in serum albumin, complements and protein C activities with impaired opsonic activities are seen both in ascitic and serum fluid. Bacterial translocation, migration of gut bacteria through systemic circulation via mesenteric lymph nodes and portal vein has compromising effects in cirrhosis. This is enhanced in decompensated stages. The triad of fever, abdominal pain, and worsening ascites may not be present in all cases of SBP. However, recognition of SBP from ascitic fluid neutrophil count in asymptomatic patients and treatment with broad-spectrum antibiotics have demonstrated improvement in mortality. Other infections do not have such markers in asymptomatic patients, but can be considered when cirrhotic patients present with sudden decompensation or a new kidney injury. Through our case report, we want to emphasize the importance of early detection and treatment of infection to improve prognosis in patients. Prevention of infections can improve outcome in patients awaiting transplant. Suggestions have been made to the use of procalcitonin and C-reactive protein (CRP) in ruling in and ruling out infection.[14]

SBP is usually caused by gram-negative organism and gram-positive streptococci. Gram-positive *Staphylococcus aureus* are rare causes. If point of care gram stain of ascitic fluid could have been done and proper antibiotics were initiated early enough, our patient's prognosis might have been better. Guo et al.[15] remark in their retrospective study that there are differences in precipitating factors and prognosis with gram-positive and gram-negative organisms in SBP.

Infective endocarditis is a rare but serious infection. Studies by Garg et al.,[16] Pérez De Isla et al.,[17] and Fernández Guerrero et al.[18] concluded that infective endocarditis in cirrhosis had higher inpatient mortality and acute kidney injury (AKI) (31.8% vs 28.5%), $p < 0.001$ as compared to no cirrhosis. While the demographics and causative organism remain the same in cirrhotic versus non-cirrhotic in endocarditis, prognosis is poor. Hence, early diagnosis in imperative for survival.

The North American Consortium for the Study of End-Stage Liver Disease[19] included 12 centers throughout North America showed that *Clostridium difficile* infections even though not as common as SBP, respiratory and UTI play an important role in determining the prognosis in these patients. The death rate for *C. difficile* infections was 41%. The index infections were healthcare-associated (56%) or nosocomial (20%). The death rate was the highest for respiratory (44%), bacteremia (38%) and *C. difficile* (41%) infections, and the lowest for urinary (21%) and skin (29%) infections or SBP (17%). The overall mortality of patients with infections was 25%, and patients who died had a higher MELD score at admission (25 ± 8 vs 19 ± 7, $p < 0.001$) and were more likely to have hepatic encephalopathy (HE), HRS, mechanical ventilation, and intensive care unit (ICU) stay during hospitalization (all $p < 0.0001$). 28% of the patients developed second infections during hospitalization.

The interplay of severity, type of infections, and higher MELD score are crucial to determine the prognosis. The response of infection is often unpredictable and exaggerated due to underlying immune dysfunction leading to ICU admission in these patients because of severe sepsis and septic shock.[20] Higher MELD score had better prognostic capacity than the Child–Turcotte–Pugh score and the Simplified Acute Physiology Score II.[21] Patients in ICU are prone to second infections due to the state of immune dysfunction, prolonged course and hospital stay, and presence of intravenous and intra-arterial catheter. Poor nutritional status, ongoing portal hypertension, related systemic hemodynamic changes, HE, and gastrointestinal bleeding contribute in prolonging the ICU course, thus adding to the risk of developing second infections. Second infections result in increased mortality in patients with LC.[19]

Severity of infections contributes to worse prognosis owing to precipitation of acute liver failure and ICU admission. Acute liver failure happens within the first week[22] which increases the Chronic Liver Failure-Sequential Organ Failure Assessment (CLIF-SOFA) or the Chronic Liver Failure-Organ Failure (CLIF-C OF) scores as evidenced by "CANONIC study." Even though liver transplantation is a definitive treatment of these patients, multiple organ failures delist them from transplant list.[23]

Acute kidney injury is a strong predictor of mortality (40%–50%).[3] Sort et al.[24] show early administration of albumin in patients with infection reduced incidence of renal impairment and death (22% vs 41% in control, $p < 0.03$). Navasa et al.[25] demonstrate the role of interleukin-6 and tumor necrosis factor in the development of acute kidney following splanchnic vasodilation. They emphasize persistence of acute kidney injury despite resolution of infection. In a study of 579 patients, Kimmann et al.[26] found that mortality continues to rise even after resolution of infection.

The response to infection is important predictor of survival in patients with LC. Healthcare-associated infections are often underestimated which are treated as community acquired infections that prove detrimental. A randomized control study performed by Merli et al.[27] showed that early intervention with broad spectrum antibiotics improved length of stay, mortality and morbidity in this population. Similar study by Ferrer et al.[28] showed early administration of antibiotics within an hour has improved impact on mortality.

Conclusion

Mortality and morbidity continue to increase even after resolution of infection in patients with cirrhosis. Some of them can be attributed to the persistence of inflammatory cascade even after resolution of infection. Cytokines lead to circulatory instability and irreversible deterioration. MELD score is a prognostic model used in healthcare settings to predict 3-month survival of patients with LC or liver failure secondary to various causes. It changes due to the dynamic nature of cirrhosis. Infections change the course of patients with LC and impact mortality; which are often underestimated by other established scores. The complex interplay of infections with the stage of liver disease determines the course in patients with LC. Based on our case report, we raise the question of considering the above and using it in the prognosis scoring in this patient group.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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References

1. Forman L. Predicting the prognosis of chronic liver disease: an evolution from child to MELD. *Hepatology* 2001; 33(2): 473–475.
2. Tsoris A and Marlar CA. *Use of the Child–Pugh score in liver disease*. Treasure Island, FL: StatPearls Publishing, 2021.
3. Bunchorntavakul C, Chamroonkul N and Chavalitdhamrong D. Bacterial infections in cirrhosis: a critical review and practical guidance. *World J Hepatol* 2016; 8(6): 307–321.
4. Fernández J, Acevedo J, Castro M, et al. Prevalence and risk factors of infections by multiresistant bacteria in cirrhosis: a prospective study. *Hepatology* 2012; 55(5): 1551–1561.
5. Brensing KA, Textor J, Perz J, et al. Long term outcome after transjugular intrahepatic portosystemic stent-shunt in non-transplant cirrhotics with hepatorenal syndrome: a phase II study. *Gut* 2000; 47(2): 288–295.
6. Arvaniti V, D'Amico G, Fede G, et al. Infections in patients with cirrhosis increase mortality four-fold and should be used in determining prognosis. *Gastroenterology* 2010; 139(4): 1246–561256.
7. Yang Y-Y and Lin H-C. Bacterial infections in patients with cirrhosis. *J Chin Med Assoc* 2005; 68(10): 447–451.
8. Borzio M, Salerno F, Piantoni L, et al. Bacterial infection in patients with advanced cirrhosis: a multicentre prospective study. *Dig Liver Dis* 2001; 33(1): 41–48.
9. Caly WR and Strauss E. A prospective study of bacterial infections in patients with cirrhosis. *J Hepatol* 1993; 18(3): 353–358.
10. Merli M, Lucidi C, Giannelli V, et al. Cirrhotic patients are at risk for health care-associated bacterial infections. *Clin Gastroenterol Hepatol* 2010; 8(11): 979–985.
11. Khan R, Abid S, Jafri W, et al. Model for end-stage liver disease (MELD) score as a useful prognostic marker in cirrhotic patients with infection. *J Coll Physicians Surg Pak* 2009; 19: 694–698.
12. Obstein KL, Campbell MS and Reddy KR. Association between model for end-stage liver disease and spontaneous bacterial peritonitis. *Am J Gastroenterol* 2007; 102: 2732–2736.
13. Juntermanns B, Manka P, Hoyer DP, et al. Infectious complications in the era of MELD. *Ann Transplant* 2015; 20: 297–302.
14. Lin K-H, Wang F-L, Wu M-S, et al. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection in patients with liver cirrhosis: a systematic review and meta-analysis. *Diagn Microbiol Infect Dis* 2014; 80(1): 72–78.
15. Guo J, Shi J, Wang H, et al. Emerging Gram-positive bacteria and drug resistance in cirrhosis patients with spontaneous bacterial peritonitis: a retrospective study. *Exp Ther Med* 2019; 17(6): 4568–4576.
16. Garg R, Mohammed A, Singh A, et al. Trends and outcomes of acute diverticulitis in inflammatory bowel disease: a propensity-matched national study. *Inflamm Bowel Dis*. Epub ahead of print 2 February 2021. DOI: 10.1093/ibd/izab017.
17. Pérez De, Isla L, Zamorano JL, Almería C, et al. [Infective endocarditis in patients with chronic liver disease: clinical and prognostic assessment]. *Rev Esp Cardiol* 2003; 56(8): 794–800.
18. Fernández Guerrero ML, González López J and Górgolas M. Infectious endocarditis in patients with cirrhosis of the liver: a model of infection in the frail patient. *Eur J Clin Microbiol Infect Dis* 2010; 29(10): 1271–1275.
19. Bajaj JS, O'Leary JG, Reddy KR, et al. Second infections independently increase mortality in hospitalized patients with cirrhosis: the North American consortium for the study of end-stage liver disease (NACSELD) experience. *Hepatology* 2012; 56(6): 2328–2335.
20. Levesque E, Hoti E, Azoulay D, et al. Prospective evaluation of the prognostic scores for cirrhotic patients admitted to an intensive care unit. *J Hepatol* 2012; 56(1): 95–102.
21. Lehner S, Stemmler HJ, Mück A, et al. Prognostic parameters and risk stratification in intensive care patients with severe liver diseases. *J Gastrointestin Liver Dis* 2010; 19: 399–404.
22. Ekpanyapong S and Reddy KR. Infections in cirrhosis. *Curr Treat Options Gastroenterol* 2019; 17(2): 254–270.
23. Bonnel AR, Bunchorntavakul C and Reddy KR. Immune dysfunction and infections in patients with cirrhosis. *Clin Gastroenterol Hepatol* 2011; 9(9): 727–738.
24. Sort P, Navasa M, Arroyo V, et al. Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis. *N Engl J Med* 1999; 341(6): 403–409.
25. Navasa M, Follo A, Filella X, et al. Tumor necrosis factor and interleukin-6 in spontaneous bacterial peritonitis in cirrhosis: relationship with the development of renal impairment and mortality. *Hepatology* 1998; 27(5): 1227–1232.
26. Kimmann M, Tergast TL, Schultalbers M, et al. Sustained impact of nosocomial-acquired spontaneous bacterial peritonitis in different stages of decompensated liver cirrhosis. *PLoS ONE* 2019; 14(8): e0220666.
27. Merli M, Lucidi C, Di Gregorio V, et al. An empirical broad spectrum antibiotic therapy in health-care-associated infections improves survival in patients with cirrhosis: a randomized trial. *Hepatology* 2016; 63(5): 1632–1639.
28. Ferrer R, Martin-Loeches I, Phillips G, et al. Empiric antibiotic treatment reduces mortality in severe sepsis and septic shock from the first hour: results from a guideline-based performance improvement program. *Crit Care Med* 2014; 42(8): 1749–1755.