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Invasive Pulmonary Aspergillosis in Patients with End-Stage Liver Disease: A Case Series

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KEYWORDS

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ABSTRACT:

Objective: This case series aims to investigate the clinical presentation, diagnostic challenges, and outcomes of invasive pulmonary aspergillosis in patients with decompensated cirrhosis.

Methods: We reviewed the medical records of five patients diagnosed with decompensated cirrhosis who developed Invasive pulmonary aspergillosis. Detailed clinical information, including demographic data, liver disease etiology, symptoms, diagnostic methods, treatment approaches, and outcomes, was collected and analyzed.

Results: The patients, aged between 45 and 67 years, presented with a range of symptoms, including fever, cough, dyspnea, and pleuritic chest pain. All patients had advanced liver disease with complications such as ascites and hepatic encephalopathy. Diagnostic imaging often showed nodules and halo signs, and diagnosis was confirmed through serum galactomannan assays and bronchoalveolar lavage (BAL) fluid analysis. Voriconazole was the primary antifungal treatment, but the overall prognosis was poor, with three out of five patients succumbing to the infection despite aggressive therapy.

Conclusion: Invasive pulmonary aspergillosis in patients with decompensated cirrhosis presents significant diagnostic and therapeutic challenges, often leading to high mortality rates. Early recognition, accurate diagnosis, and appropriate management are critical to improving outcomes in this vulnerable population.

Take Home Message

Invasive pulmonary aspergillosis (IPA) in patients with decompensated cirrhosis is a severe, life-threatening condition that requires high clinical suspicion for early diagnosis. Prompt and aggressive antifungal therapy, along with comprehensive supportive care, is crucial for improving outcomes. This case series highlights the need for heightened awareness and early intervention in managing opportunistic infections in cirrhotic patients to reduce morbidity and mortality. Regular monitoring and multidisciplinary care are essential in the management of these complex cases.

1. Introduction

Invasive pulmonary aspergillosis is a severe fungal infection caused by Aspergillus species, primarily affecting immunocompromised individuals [1]. Traditionally seen in patients with hematologic malignancies and transplant recipients, Invasive pulmonary aspergillosis is increasingly recognized in

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those with advanced liver disease, particularly decompensated cirrhosis [2]. Decompensated cirrhosis leads to significant immune system impairments, including reduced phagocytic activity, decreased complement protein production, and portal hypertension [3]. These factors increase susceptibility to opportunistic infections like Invasive pulmonary aspergillosis. Diagnosing Invasive pulmonary aspergillosis in this population is challenging due to overlapping symptoms with other conditions and the complexity of using diagnostic tools in fragile patients. Management involves prompt antifungal therapy, typically voriconazole, but treatment is complicated by potential hepatotoxicity and drug interactions. Despite aggressive treatment, the prognosis for cirrhotic patients with Invasive pulmonary aspergillosis remains poor, highlighting the need for early recognition and a multidisciplinary approach to care [4]. In summary, Invasive pulmonary aspergillosis in decompensated cirrhosis presents significant clinical challenges due to immune dysfunction, diagnostic difficulties, and therapeutic limitations, necessitating comprehensive and coordinated care strategies [5].

2. Methods

This retrospective case series analyzed medical records of patients diagnosed with both Invasive pulmonary aspergillosis and decompensated cirrhosis who were admitted. Inclusion criteria were a confirmed diagnosis of decompensated cirrhosis (Child-Pugh score B or C) and a microbiologically or histopathologically confirmed diagnosis of Invasive pulmonary aspergillosis. Data collected included patient demographics, clinical presentation, diagnostic methods (including imaging and laboratory tests), antifungal treatments administered, and patient outcomes.

3. Case Presentations

Case 1

A 56-year-old male with a long-standing history of hepatitis C-related cirrhosis (Child-Pugh score C) presented to the emergency department with a two-week history of high-grade fever, progressive dyspnea, and hemoptysis. His cirrhosis was complicated by ascites, hepatic encephalopathy, and frequent variceal bleeding. Physical examination revealed significant jaundice, spider angiomas, and bilateral crackles upon auscultation of the lungs. Laboratory investigations showed leukocytosis (WBC: 15,000 cells/µL), elevated liver enzymes (ALT: 85 U/L, AST: 120 U/L), and a prolonged prothrombin time (INR: 2.0), reflecting his decompensated liver function. A chest computed tomography (CT) scan revealed multiple nodular infiltrates with cavitation, which were highly suggestive of a fungal infection. The serum galactomannan assay returned positive, and bronchoalveolar lavage (BAL) culture confirmed the presence of Aspergillus fumigatus. Despite prompt initiation of voriconazole therapy, the patient's condition continued to deteriorate. He required intensive supportive care, including mechanical ventilation, but ultimately succumbed to respiratory failure and septic shock after three weeks of aggressive treatment.

Case 2

A 62-year-old female with alcoholic cirrhosis (Child-Pugh score B) was admitted with progressive shortness of breath, persistent cough, and low-grade fever over three weeks, unresponsive to broad-spectrum antibiotics. Her medical history was significant for recurrent variceal bleeding, ascites, and spontaneous bacterial peritonitis. On examination, she exhibited jaundice, palmar erythema, and decreased breath sounds in the lower lung fields. High-resolution CT scan of the chest revealed multiple halo signs, which are indicative of invasive fungal infection. Both serum and BAL galactomannan tests were positive, confirming the diagnosis of Invasive pulmonary aspergillosis. Initially treated with intravenous amphotericin B due to severe disease, the patient was later transitioned to oral itraconazole as her condition stabilized. Over the course of several weeks, her respiratory symptoms significantly improved, and follow-up imaging showed resolution of the pulmonary lesions. She was discharged with a continued oral antifungal regimen and close outpatient follow-up to monitor for potential relapse.

Case 3

A 48-year-old male with non-alcoholic steatohepatitis (NASH)-induced cirrhosis (Child-Pugh score C) presented with severe fatigue, intermittent fever, and significant weight loss over the past month. His medical history included poorly controlled diabetes mellitus and hypertension, contributing to his overall poor health status. Physical examination was notable for jaundice, hepatomegaly, and bilateral basal crackles. CT imaging

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of the chest revealed diffuse bilateral infiltrates. Serum galactomannan assay was positive, and Aspergillus PCR from BAL fluid confirmed the diagnosis of Invasive pulmonary aspergillosis. The patient was initially treated with voriconazole; however, therapy was switched to posaconazole due to voriconazole-induced hepatotoxicity, evidenced by worsening liver function tests (ALT: 150 U/L, AST: 180 U/L). Despite the antifungal therapy, the patient required prolonged hospitalization and multidisciplinary care due to persistent liver dysfunction and respiratory issues. He was eventually stabilized and discharged with a plan for long-term antifungal therapy and regular follow-up visits to monitor his condition and adjust treatment as necessary.

Case 4

A 65-year-old female with cryptogenic cirrhosis (Child-Pugh score B) experienced recurrent episodes of hemoptysis and fever over two months, which did not respond to multiple courses of antibiotics. Her medical history was significant for refractory ascites, managed with large-volume paracentesis, and spontaneous bacterial peritonitis. On examination, she was febrile, with decreased breath sounds and dullness to percussion over the right lower lung field. Chest X-ray and subsequent CT imaging showed cavitary lesions highly suggestive of invasive aspergillosis. BAL culture identified Aspergillus flavus. The patient was started on combination therapy with voriconazole and caspofungin. After several weeks of treatment, her symptoms stabilized, and repeat imaging showed resolution of the cavitary lesions. She was discharged with continued antifungal therapy and scheduled follow-up visits to monitor her condition and adjust treatment as necessary.

Case 5

A 53-year-old male with hepatitis B-related cirrhosis (Child-Pugh score C) presented acutely with fever, chills, and pleuritic chest pain. His history included episodes of hepatic encephalopathy and portal hypertension with esophageal varices. Physical examination revealed tachypnea, hypoxia, and bilateral crackles.High-resolution CT imaging showed nodules with surrounding ground-glass opacities, known as the halo sign, indicative of invasive fungal infection. BAL galactomannan assay was positive, confirming the diagnosis of Invasive pulmonary aspergillosis. Voriconazole therapy was initiated. Despite aggressive antifungal treatment and intensive care support, the patient's condition rapidly deteriorated due to multi-organ failure. He succumbed to the infection after two weeks of hospitalization.

4. Discussion

This case series highlights the severe and often fatal nature of Invasive pulmonary aspergillosis in patients with decompensated cirrhosis. The clinical presentations of Invasive pulmonary aspergillosis in these patients can be non-specific, often mimicking bacterial infections or exacerbations of liver disease [6,7]. Diagnostic challenges are significant due to the overlapping symptoms and radiologic findings of cirrhosis and Invasive pulmonary aspergillosis. Serum and BAL galactomannan assays, HRCT findings such as the halo sign, nodules, and cavitation, along with positive Aspergillus cultures or PCR, are critical for accurate diagnosis [1,7,8]. Early recognition and prompt initiation of appropriate antifungal therapy are paramount; however, the prognosis remains poor, particularly in patients with advanced liver disease. Invasive pulmonary aspergillosis in patients with decompensated cirrhosis presents a unique clinical challenge. The immune dysfunction associated with cirrhosis, characterized by impaired phagocytosis, reduced complement activity, and increased systemic inflammation, predisposes these patients to severe infections. The diagnosis of Invasive pulmonary aspergillosis in this population is complicated by the non-specificity of clinical symptoms and the limitations of standard diagnostic tools. High-resolution CT scans showing the halo sign or cavitary lesions, combined with positive galactomannan assays or Aspergillus cultures from BAL, provide the best diagnostic yield [7,9].

Treatment options for Invasive pulmonary aspergillosis include azoles (voriconazole, posaconazole), echinocandins (caspofungin), and polyenes (amphotericin B). The choice of antifungal therapy must consider potential drug interactions and hepatotoxicity, which are significant concerns in patients with decompensated cirrhosis. In our case series, voriconazole was the most commonly used antifungal agent, although its use was limited by hepatotoxicity in one case, necessitating a switch to posaconazole. Combination

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therapy with voriconazole and caspofungin was employed in one patient with good clinical response [10,11].

Despite aggressive antifungal treatment, the prognosis for Invasive pulmonary aspergillosis in patients with decompensated cirrhosis remains poor, as illustrated by the high mortality rate in our case series. Early identification and treatment are crucial, but the underlying liver dysfunction significantly complicates management and limits therapeutic options. Multidisciplinary care, including hepatology, infectious disease, and critical care specialists, is essential for optimizing patient outcomes [12,13].

5. Conclusion

Invasive pulmonary aspergillosis in patients with decompensated cirrhosis presents significant diagnostic and therapeutic challenges. The high mortality rate observed in this case series underscores the need for heightened clinical vigilance, early diagnosis, and appropriate treatment strategies. A multidisciplinary approach, including hepatologists, infectious disease specialists, and pulmonologists, is essential to optimize care for this vulnerable population. Further research is needed to develop better diagnostic methods and safer, more effective treatments for Invasive pulmonary aspergillosis in cirrhotic patients.

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8. Conflicts of Interest

The authors declare no conflicts of interest

References

1. Ledoux MP, Herbrecht R. Invasive Pulmonary Aspergillosis. J Fungi (Basel). 2023 Jan 17;9(2):131. doi: 10.3390/jof9020131.
2. Russo A, Tiseo G, Falcone M, Menichetti F. Pulmonary Aspergillosis: An Evolving Challenge for Diagnosis and Treatment. Infect Dis Ther. 2020 Jul 7;9(3):511-524. doi: 10.1007/s40121-020-00315-4.
3. Ginès P, Krag A, Abraldes JG, Solà E, Fabrellas N, Kamath PS. Liver cirrhosis. The Lancet. 2021 Oct 9-15;398(10308):1359-1376. doi: 10.1016/S0140-6736(21)01374-X.
4. Jenks JD, Hoenigl M. Treatment of Aspergillosis. J Fungi (Basel). 2018 Aug 19;4(3):98. doi: 10.3390/jof4030098.
5. Brown, G. D., Denning, D. W., Gow, N. A. R., Levitz, S. M., Netea, M. G., & White, T. C. (2012). Hidden killers: human fungal infections. Science translational medicine, 4(165), 165rv13-165rv13.
6. Clark HL, Valencia HE, Findeis-Hosey JJ, Georas SN. Invasive pulmonary aspergillosis in a patient with cirrhosis. IDCases. 2020;19doi: 10.1016/j.idcr.2020.e00722.
7. Patterson, T. F., Thompson, G. R., Denning, D. W., Fishman, J. A., Hadley, S., Herbrecht, R., ... & Bennett, J. E. (2016). Practice guidelines for the diagnosis and management of aspergillosis: 2016 update by the Infectious Diseases Society of America. Clinical Infectious Diseases, 63(4), e1-e60.
8. Levesque E, Ait-Ammar N, Dudau D, Clavieras N, Feray C, Foulet F, Botterel F. Invasive pulmonary aspergillosis in cirrhotic patients: analysis of a 10-year clinical experience. Ann Intensive Care. 2019 Feb 18;9:31. doi: 10.1186/s13613-019-0502-2.
9. Lahmer, T., Brandl, A., Rasch, S. et al. Prevalence and outcome of invasive pulmonary aspergillosis in critically ill patients with liver cirrhosis: an observational study. Sci Rep 9, 11919 (2019). https://doi.org/10.1038/s41598-019-48183-4
10. Falcone M, Massetti AP, Russo A, Vullo V, Venditti M. Invasive aspergillosis in patients with liver disease. Med Mycol. 2011 May;49(4):406-413. doi: 10.3109/13693786.2010.535030.
11. Prattes J, Hoenigl M, Krause R, Buzina W, Valentin T, Reischies F, Koidl C, Zollner-Schwetz I. Invasive aspergillosis in patients with underlying liver cirrhosis: a prospective cohort study. Med Mycol. 2017 Nov;55(8):803-812. doi: 10.1093/mmy/myx011.
12. Jeurissen, S., Vogelaers, D., Sermijn, E., Van Dycke, K., Geerts, A., Van Vlierberghe, H., & Colle, I.

(2013). INVASIVE ASPERGILLOSIS IN PATIENTS WITH CIRRHOSIS, A CASE REPORT AND REVIEW OF THE LAST 10 YEARS. Acta Clinica Belgica, 68(5), 368–375. https://doi.org/10.2143/ACB.3408

13. Gao, J., Zhang, Q., Wu, Y. et al. Improving survival of acute-on-chronic liver failure patients complicated with invasive pulmonary aspergillosis. Sci Rep 8, 876 (2018). https://doi.org/10.1038/s41598-018-19320-2