

Successful Rescue Therapy for Talaromycosis Complicated by Severe Acute Hepatorenal Failure with Hepatic Encephalopathy in an HIV/HCV-Coinfected Patient: A Case Report

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Background: Treatment of critically ill patients with *Talaromyces marneffe* (*T. marneffe*, TM) infection involving multiple organ dysfunction remains a major clinical challenge. As an important contributor to mortality among individuals with Acquired Immunodeficiency Syndrome (AIDS), talaromycosis remains associated with mortality rates of up to 30% even with appropriate antifungal therapy. Severe hepatic and renal impairment may restrict antifungal dosing and thus further compromise therapeutic efficacy. However, current clinical evidence regarding the management of *Talaromyces marneffe* infection complicated by hepatic encephalopathy and acute renal failure remains limited.

Case Presentation: A 39-year-old female with a newly identified hepatitis C virus (HCV) infection and newly diagnosed Human Immunodeficiency Virus (HIV) infection was admitted to our hospital because of recurrent fever and abdominal pain. Abdominal ultrasound revealed hepatosplenomegaly, while chest and abdominal computed tomography scan showed bilateral pulmonary nodular lesions, multiple enlarged intra-abdominal and retroperitoneal lymph nodes, and splenomegaly. On the second day after admission, quantitative real-time polymerase chain reaction analysis of blood detected a *T. marneffe* load of 1.7×10^6 copies/mL, and disseminated talaromycosis was subsequently confirmed by blood culture. The patient therefore started on antifungal treatment with liposomal amphotericin B (L-AmB) at 3 mg/kg per day. Shortly after treatment initiation, she developed hepatic encephalopathy and acute renal failure and was transferred to the intensive care unit for further management. With the artificial liver support therapy and continuous renal replacement therapy (CRRT), full-dose L-AmB was maintained, allowing the patient to successfully completed the induction therapy with L-AmB. Her liver and renal function ultimately normalized, and the patient remained clinically stable with no evidence of *T. marneffe* recurrence at the one-year follow-up.

Conclusion: Early recognition of hepatorenal failure and timely initiation of CRRT combined with artificial liver support within 24 hours are essential for maintaining the antifungal effect of full-dose L-AmB.

Keywords: HIV/HCV/TM, hepatic encephalopathy, acute liver failure, liposomal amphotericin B, continuous renal replacement therapy, artificial liver support

Background

Talaromycosis is an invasive fungal disease caused by *Talaromyces marneffe* (*T. marneffe*, TM), the only thermally dimorphic fungus within the genus *Penicillium*. It is endemic throughout Southeast and South Asia, including southern China, northern Thailand, Malaysia, and Vietnam.¹ The disease predominantly affects individuals with advanced Acquired



Immunodeficiency Syndrome (AIDS) or an immunocompromised status.^{2–5} Typical clinical manifestations include fever, respiratory and gastrointestinal symptoms, hepatosplenomegaly, superficial lymphadenopathy, and characteristic umbilicated papules. Laboratory evaluation shows cytopenias and radiological evidence of pulmonary lesions.^{6–9} Although effective antifungal therapy can significantly reduce the risk of mortality, liver and kidney impairment can complicate antifungal administration.¹⁰ Elevated transaminases and renal impairment (e.g., an elevated urea-to-albumin ratio) have been identified as independent predictors of mortality.^{11–13} Severe hepatic or renal impairment may restrict antifungal dosing and thereby compromise treatment efficacy.^{14,15} Liver function impairment is common in *T. marneffeii* infection; however, rapid deterioration leading to hepatic failure is rare.^{16,17} Currently, no clear guidelines exist regarding antifungal selection for patients with hepatic or renal failure, particularly those with hepatic encephalopathy.¹⁸ Herein, we reported the first case of successful treatment of disseminated *T. marneffeii* infection in a patient with HIV/HCV coinfection complicated by severe hepatic and renal dysfunction and hepatic encephalopathy.

Case Description

A 39-year-old female living in Guangxi, China, was admitted to the Fourth People's Hospital of Nanning on May 12, 2024, with recurrent fever and abdominal pain. The patient initially presented recurrent fever, followed by jaundice, progressive abdominal pain, and diarrhea. She had a history of intravenous drug use and had not received treatment for HCV infection. Abdominal computed tomography (CT) at the local hospital revealed multiple enlarged intraperitoneal and retroperitoneal lymph nodes and splenomegaly. She was diagnosed locally with AIDS, bacterial pneumonia and suspected of an invasive fungal infection. Meropenem and itraconazole were initiated, leading to the resolution of fever; however, abdominal symptoms persisted and oliguria developed. Given that she was HIV positive and suspected of having *T. marneffeii* infection, she was transferred to our tertiary infectious disease center for further management. Physical examination showed marked jaundice, absence of palmar erythema and spider nevi, and mild abdomen distension with periumbilical tenderness. Suboptimal patient cooperation precludes a detailed palpation of the liver and spleen.

Laboratory investigations at admission showed markedly elevated white blood cell (WBC) count and C-reactive protein (CRP) levels, mild anemia, thrombocytopenia, and elevated creatinine and transaminase levels. The CD4+ T-lymphocyte count was 64 cells/ μ L and the HCV RNA load was 2.03×10^7 IU/mL (Table 1). Abdominal ultrasound confirmed hepatosplenomegaly. Chest-abdominal CT showed bilateral pulmonary nodular and multiple enlarged abdominal and retroperitoneal lymph nodes. Blood qPCR detected *T. marneffeii* (1.7×10^6 copies/mL) on hospital day 2 (Figure 1B).

On admission, the patient was immediately empirically administered with liposomal amphotericin B (L-AmB, 3 mg/kg/day), meropenem (1 g q12h). The patient developed marked anuria (<30 mL/24h). By day 3, she developed worsening progressive disorientation, flapping tremor, and drowsiness, abdominal and back pain, severe fatigue, and nausea. Non-contrast cranial CT demonstrated no abnormal findings. These findings were consistent with acute-on-chronic liver failure-1 (ACLF-1), grade 2 hepatic encephalopathy. Repeated Laboratory tests showed worsening leukocytosis, progressive thrombocytopenia, elevated bilirubin, rising creatinine (559 μ mol/L), urea (23.5 mmol/L), and hyperammonemia (125 μ mol/L) (Table 1). NGS detected *T. marneffeii* on hospital day 3 and blood culture confirmed *T. marneffeii* infection on hospital day 6. The dynamics of laboratory indicators are shown in Figure 1C–E.

Therefore, the patient was diagnosed with disseminated talaromycosis complicated by stage 3 acute kidney injury and ACLF-1, grade 2 hepatic encephalopathy. High-flow noninvasive ventilation was initiated, antibacterial therapy was switched to imipenem–cilastatin sodium (500 mg q12h), with full-dose L-AmB (3 mg/kg/day) continued throughout the treatment course, and voriconazole (200 mg bid) was added after 2 weeks of the original L-AmB regimen. Continuous renal replacement therapy (CRRT) combined with artificial liver plasma exchange therapy was administered, along with supportive care (Figure 1A). The patient achieved clinical stability and was discharged with a prescription for oral itraconazole (200 mg twice daily) for 10 weeks and bictegavir/emtricitabine/tenofovir alafenamide. She remained clinically stable without recurrence of *T. marneffeii* infection during one year of follow up.

Discussion

According to the current guidelines, amphotericin B is the first-line treatment for systemic *T. marneffeii* infections.¹⁹ However, amphotericin B deoxycholate (C-AmB) is associated with a wide range of adverse effects, including dose-dependent

Table 1 Laboratory Findings

Variable	Reference Range	On Admission	On Day 3	Induction Therapy for 2 Weeks	Before Discharge
White blood cell count (10 ⁹ /L)	3.5–9.5	16.8	23.8	1.2	3.0
Hemoglobin (g/L)	115–150	106	94	60	67
Platelets (× 10 ⁹ /L)	125–350	61	36	59	54
Neutrophils rate (%)	40–75	89.7	88.4	71.5	41
C-reactive protein (mg/L)	0–10	200.0	157.5	19.6	<5
Total bilirubin concentration (μmol/L)	0–21	165.0	226.7	61.2	25.2
Direct bilirubin concentration (μmol/L)	0–8	142.0	174.2	51.1	22.3
Aspartate aminotransferase (U/L)	13–35	210	98	58	19
Alanine aminotransferase (U/L)	7–40	34	17	8	10
Albumin concentration (g/L)	40–55	20.3	19.5	23.9	31
Creatinine (μmol/L)	41–73	191	559	265	69
Urea level (mmol/L)	2.6–7.5	9.48	23.5	8.33	4.16
Ammonia (μmol/L)	18–72	–	125	–	–
Prothrombin time (sec)	11.0–14.5	15.3	14.9	13.7	–
Activated partial thromboplastin time (sec)	28.0–43.0	50.5	52.8	43.1	–
Fibrin degradation products (g/L)	2.0–4.00	3.64	3.90	3.67	–
International Normalized Ratio	0.70–1.30	1.18	1.14	1.28	1.02
Candida mannan content (pg/mL)	0–100	500.0	–	<25.0	–
Aspergillus galactomannan (μg/L)	<0.5	5.89	–	5.71	–
CD4+ T lymphocytes (cells/μL)	387–1350	64	–	–	–
HCV RNA load (IU/mL)	<100	2.03 × 10 ⁷	–	–	–
HIV RNA load (copies/mL)	<20	3.87 × 10 ⁵	–	–	–

nephrotoxicity, acute infusion-related reactions, and electrolyte disturbances *e.g.*, hypokalemia). These limitations have restricted its clinical application.¹⁴ We reported a case of HIV/HCV/TM complicated by stage 3 acute kidney injury, ACLF-1 and grade 2 hepatic encephalopathy and acute renal failure that was successfully managed with L-AmB combined with adjuvant therapy of artificial liver support system and CRRT. In the treatment of hepatorenal failure induced by severe infection, artificial liver support and CRRT serve as key measures to protect vital organs,^{20,21} however, the overall survival rate remains unsatisfactorily low. For instance, patients with liver failure complicated by hepatorenal syndrome present a considerably high mortality rate.²² In 2023, Liang Xu et al reported a renal transplant patient complicated with *T. marneffeii* infection. Despite severe hepatorenal injury occurring during treatment, the patient recovered and was discharged after antifungal therapy with voriconazole and amphotericin B.²³ In 2024, Shanshan Yang et al reported an HIV-negative patient infected with *T. marneffeii* after renal transplantation. The patient still developed multiple organ dysfunction syndrome and hepatic encephalopathy despite amphotericin B deoxycholate antifungal treatment and died after treatment withdrawal.²⁴ Although there is some experience with the use of L-AmB in patients undergoing CRRT treatment,^{25–27} its use in a patient with HIV/HCV/TM coinfection complicated by hepatic encephalopathy and acute renal failure has rarely been documented. L-AmB exhibits lower hepatic and renal toxicity, which ensures the efficacy and timeliness of antifungal therapy and ultimately contributes to a successful clinical outcome.

T. marneffeii infection mainly involves the skin, lungs, liver, spleen, lymph nodes, and circulatory system.⁶ Central nervous system (CNS) involvement is rare but may cause meningitis or parenchymal lesions, leading to altered consciousness.²⁸ When the CNS is involved, the disease progresses rapidly with an extremely high case fatality rate: most patients succumb within 10 days, and the overall case fatality rate stands at 81%.²⁹ Even with appropriate antifungal therapy, the mortality rate in this population remains about 30%.³⁰ Delayed antifungal therapy further compromises clinical outcomes.³¹ Furthermore, coinfection with viral hepatitis is associated with severe liver injury in people living with HIV.³² Both HIV and HCV can directly damage brain tissue through neurotoxicity and inflammation, which increases the risk of neurocognitive impairment or hepatic encephalopathy.³³ Although the lumbar puncture was rejected,

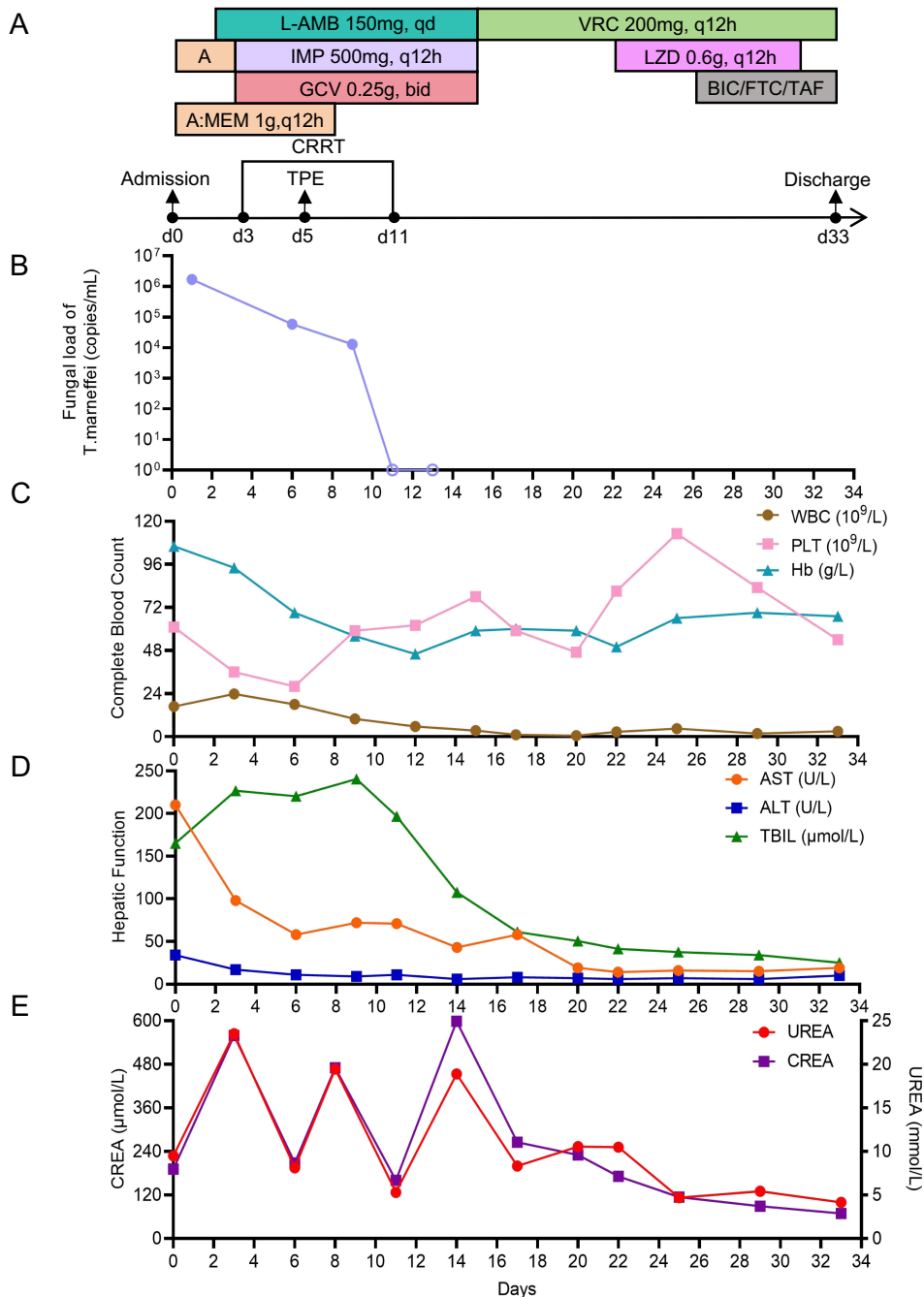


Figure 1 (A) Timeline of therapeutic interventions administered during hospitalization. Longitudinal dynamic of (B) *T. marneffeii* fungal load, (C) complete blood counts, (D) liver function biomarkers, and (E) renal function indicators (creatinine and urea).

CNS invasion by *T. marneffeii* could not be excluded. Many risk factors for death have been reported in patients with talaromycosis. Multiple studies have shown that elevated bilirubin, increased AST/ALT levels, decreased endogenous creatinine clearance rate, and low hemoglobin levels are associated with higher mortality in patients with HIV/TM coinfection. Factors related to renal impairment and liver dysfunction serve as independent prognostic risk factors.^{34,35} Generally, in cases of severe hepatic and renal impairment, consideration should be given to dose reduction, treatment interruption, or discontinuation in clinical practice.¹⁴ Given the benefit of rapidly controlling invasive fungi infection outweighed the risk of drug-induced liver injury, full-dose L-AmB was administered. The patient achieved rapid clinical

remission, and hepatic and renal functions ultimately returned to normal. Therefore, aggressive antifungal treatment remains essential, even in the setting of hepatic and renal impairment. Antifungal therapy interruption or dose reduction due to concerns about potential drug toxicity should be avoided, as this may compromise therapeutic efficacy and result in poor prognosis.

Furthermore, active use of an artificial liver support system plays a vital role in the management of patients with liver failure, particularly in those with hepatic encephalopathy. Severe infection and liver failure can cause renal vasoconstriction and reduced renal perfusion, leading to acute kidney injury.^{36–38} After the patient developed oliguria and subsequent severe infection, rapid hepatic and renal failure occurred. With the support of artificial liver support system and CRRT, the patient was able to receive adequate and continuous L-AmB therapy for antifungal treatment, which successfully controlled the fungal infection and restored hepatic and renal function. For patients with sepsis-associated acute kidney injury, CRRT intervention within 12–24 hours can improve survival rate, shorten hospital stay and increase the recovery rate of renal function.^{20,39} Meanwhile, artificial liver therapy (plasma exchange) can eliminate infection-related inflammatory mediators and alleviate persistent multi-organ damage caused by systemic inflammatory response.^{21,40} This outcome highlights the indispensable role of supportive therapies such as artificial liver support system and CRRT in managing organ failure. Meanwhile, it also underscores the paramount importance of early identification and intervention for hepatic encephalopathy.

To our knowledge, this is the first reported case of advanced HIV-associated *T. marneffei* disease complicated by HCV coinfection, in which the patient developed hepatic encephalopathy and acute renal failure but was successfully treated with L-AmB. This case provides valuable reference experience for the clinical management of HIV/HCV/TM patients presenting with severe complications such as hepatorenal failure and hepatic encephalopathy. Timely initiation of CRRT within 12–24 hours after the onset of oliguria/anuria can protect vital organs and create a therapeutic window for antifungal treatment. This strategy is critical for the safe administration of full-dose L-AmB and the ultimate successful control of fungal infection.

This case demonstrates that L-AmB has excellent pharmacological properties and serves as a viable therapeutic option for critically ill patients with HIV/TM co-infection complicated by hepatorenal failure. Early recognition of life-threatening complications and immediate initiation of CRRT combined with artificial liver support therapy within 24 hours is an effective measure to protect vital organs. Furthermore, dosage adjustment of L-AmB is unnecessary during CRRT, and its full-dose fungicidal effect is pivotal to rapid clinical recovery. Therefore, for patients with multiple risk factors presenting HIV/TM/HCV co-infection and concurrent hepatorenal failure, timely intervention with CRRT combined with artificial liver support should be administered, alongside antifungal therapy with L-AmB.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article.

Ethics Statements and Informed Consent

This work was already approved by the Institutional Ethics Review Board of the Fourth People's Hospital of Nanning ([2026]04). Written informed consent was obtained from the patient for the publication of this case report. Institutional approval from Institutional Ethics Review Board of the Fourth People's Hospital of Nanning was required to publish the case details and was obtained.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

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