· Case Report ·

Analysis of two fatal cases of AIDS complicated with Talaromyces marneffei infection

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Abstract

Background Talaromyces marneffei infection combined with acquired immunodeficiency syndrome(AIDS) has a high mortality rate. This article presents two cases of sudden death from AIDS complicated by Talaromyces marneffei septicemia.

Case presentation Both patients were diagnosed with AIDS complicated by Talaromyces marneffei infection, with $CD4^+$ T-lymphocyte counts of 1 cell/μL (Case A) and 63.72 cells/μL (Case B), respectively. Both cases exhibited varying degrees of elevated liver enzymes, hypoalbuminemia, and increased procalcitonin (PCT) as well as hypersensitive C-reactive protein (hs-CRP) levels. Following admission, both received comprehensive treatment regimens including antiretroviral therapy, anti-bacterial agents, anti-fungal agents, and prophylaxis against Pneumocystis jirovecii pneumonia. The cause of death in Case A may be attributed to Talaromyces marneffei septicemia complicated by meningitis and cerebral hernia. In Case B, the cause of death may be multifactorial, involving adrenal insufficiency, T. marneffei septicemia, electrolyte imbalance, and pulmonary infection.

Conclusion HIV patients with $CD4^+$ counts < 100 cells/μL require close monitoring to enable the early identification of warning signs of Talaromyces marneffei infection and prompt intervention, thereby reducing the risk of sudden death. For HIV patients presenting with any combination of "fever + rash/elevated liver enzymes/electrolyte imbalance/altered consciousness" (especially those with $CD4^+$ < 100 cells/μL), immediate screening for T. marneffei, empirical antifungal therapy, and comprehensive organ function monitoring are essential. This approach is the key to mitigating the risk of sudden death.

Keywords: AIDS, talaromyces marneffei, septicemia, sudden death

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Introduction

Patients in the AIDS stage of human immunodeficiency virus (HIV) infection often develop various opportunistic infections due to their compromised immune function. Infection with Talaromyces marneffei is commonly seen in AIDS patients. A meta-analysis revealed that the prevalence of Talaromyces marneffei co-infection among HIV patients is 3.6%. Vietnam showed the highest prevalence (6.4%), followed by Thailand (3.9%), China (3.3%), India (3.2%), and Malaysia (2.1%). Among the HIV population in China, the infection is most prevalent in southern regions (15.0%), whereas the prevalence is relatively lower in the southwest (0.3%)[1]. In southern China, Talaromyces marneffei co-infection is common among hospitalized HIV/AIDS patients, and its case fatality rate is higher than that of patients with other HIV-related complications[2]. The onset is insidious, and if left undiagnosed and untreated, the mortality rate is high as the disease progresses[3]. Early symptoms (e.g., fever, rash, liver injury) often overlap with other opportunistic infections, delaying diagnosis. Complications like central nervous system involvement or adrenal insufficiency can lead to rapid progression to sudden death, necessitating urgent clarification of early warning indicators for such critical illnesses. Currently, reports on such fatal cases are scarce in the existing clinical literature. Both patients in this report succumbed to sudden death, complicated by specific comorbidities. Notably, both exhibited marked abnormalities in biochemical indicators prior to the fatal event. Through the analysis of these aberrant laboratory findings and parameters, this study offers valuable insights to assist clinicians in the cautious management of similar cases and in predicting therapeutic outcomes. Diagnosis in both cases was established in accordance with the "Guidelines for the Diagnosis and Treatment of AIDS in China (2024 Edition)"[4].

Case report A

Patient, male, 32 years old, admitted on April 14, 2025 due to "dizziness and fatigue for half a month, accompanied by fever for one week." The highest body temperature reached 39 °C, with no apparent temporal pattern to the fever.

Admission physical examination: T: 36.3 ℃, P: 77 beats/min, R: 20 breaths/min, BP: 122/73 mmHg. The patient appears moderately anemic, with scattered grayish-brown maculopapules and hyperpigmentation, with some papules exhibiting central umbilication on the skin throughout the body.

Complete necessary examinations after admission: Blood routine test: absolute neutrophil count (NEU#) 2.19×10^9/L(3.5~9.5), absolute lymphocyte count (LY#) 0.15×10^9/L(1.1~3.2), hemoglobin (HGB) 6.7 g/dL (13.0~17.5), high-sensitivity C-reactive protein (HS-CRP) 79.25 mg/L(<5). Biochemical results: Serum albumin (ALB) 2.71 g/dL(4~5.5), aspartate aminotransferase (AST) 270.40 U/L(15~40), alanine aminotransferase（ALT） 112.20 U/L(9~50), Lactate dehydrogenase (LDH) 927.9 U/L(120~250), Blood urea nitrogen (BUN) 4.65 mmol/L(3.1~8.8), Serum creatinine (CREA) 49.9 umol/L(44~80), Serum potassium (K) 3.16 mmol/L (3.5~5.3), Serum calcium (Ca) 1.90 mmol/L(2.1~2.6); Procalcitonin (PCT) 1.09 ng/ml(<0.05). The electrocardiogram (ECG) shows normal results. Fungal D-glucan test: 334.500 Pg/mL(<60), HIV antibody positive, HIV-1 RNA quantitative (HIV1DL): 1.21×10^6 IU/mL(<100). $CD8^+$ T lymphocyte count 114 cells/μL (300~1250), $CD4^+$ T lymphocyte count 1 cell/μL(450~1600).

Administer Bictegravir/Emtricitabine/Tenofovir Alafenamide 1 tablet qd for antiretroviral therapy, Sulfamethoxazole 960mg tid for Pneumocystis jirovecii infection, Piperacillin/Tazobactam 4.5 g q12h IV for antibacterial treatment, Fluconazole 200 mg qd for antifungal therapy, and Glutathione 1.2 g qd IV for liver function improvement and electrolyte imbalance correction.

Blood culture positive for Talaromyces marneffei on April 22, 2025. Fluconazole was discontinued and replaced with intravenous Voriconazole 200 mg every 12 hours for antifungal treatment.

The patient exhibited transient spatial disorientation on the morning of April 22, 2025. MRI results of the brain showed: 1. Abnormal signals in the left basal ganglia and left frontal lobe, with a high likelihood of infection. (Figure 1).

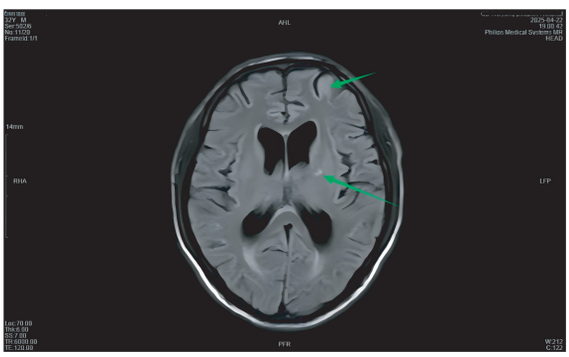

Figure 1. Brain MRI display left basal ganglia region, left frontal lobe infectious lesions)

At around 22:00 on April 22, 2025, during the night ward round, the patient could still walk independently in the ward without any significant discomfort. However, at 23:17 on April 22, 2025, the patient suddenly experienced cardiac and respiratory arrest. At 23:59 on April 22, 2025 ECG diagnosis: Accelerated idioventricular rhythm (Figure 2). Although active rescue measures were taken, unfortunately the patient was declared clinically dead at 1:13 a.m. on April 23, 2025.

Case report B

A middle-aged male was admitted to the hospital on May 28, 2025, due to "poor appetite and fatigue for half a month, and diarrhea for 3 days." Medical history: Has a history of HIV infection for 1 month, but has not received antiretroviral therapy. Physical examination: body temperature: 37.9 ℃ , Emaciated body type, coarse breath sounds in both lungs, moist rales heard at the bottom of both lungs, and bowel sounds at 8 times per minute.

Medical test results: HS-CRP 96.01 mg/L(<5); Biochemistry: ALB 2.0 g/dL(4~5.5), AST 296.1 U/L(15~40), LDH 1196.8 U/L(120~250), Glucose (GLU) 4.12 mmol/L(3.9~6.2), blood urea nitrogen (BUN) 12.41 mmol/L(3.1~8.8), CREA 115.4 umol/L(44~80), Serum sodium (Na) 124.7 mmol/L(135~147), Serum chloride (Cl) 91.8 mmol/L(99~110), Ca 1.92 mmol/L (2.1~2.6); PCT: 0.64 ng/ml(<0.05). The ECG shows sinus tachycardia with T-wave Cl changes. Fungal D-glucan test (G-test): 131.385 Pg/mL(<60). HIV1DL: 5.12×10^5 IU/mL(<200). $CD8^+$ T lymphocyte count: 545.76 cells/μL(300~1250), $CD4^+$ T lymphocyte count: 63.72 cells/μL(450~1600).

Administer Bictegravir/Emtricitabine/Tenofovir Alaf-

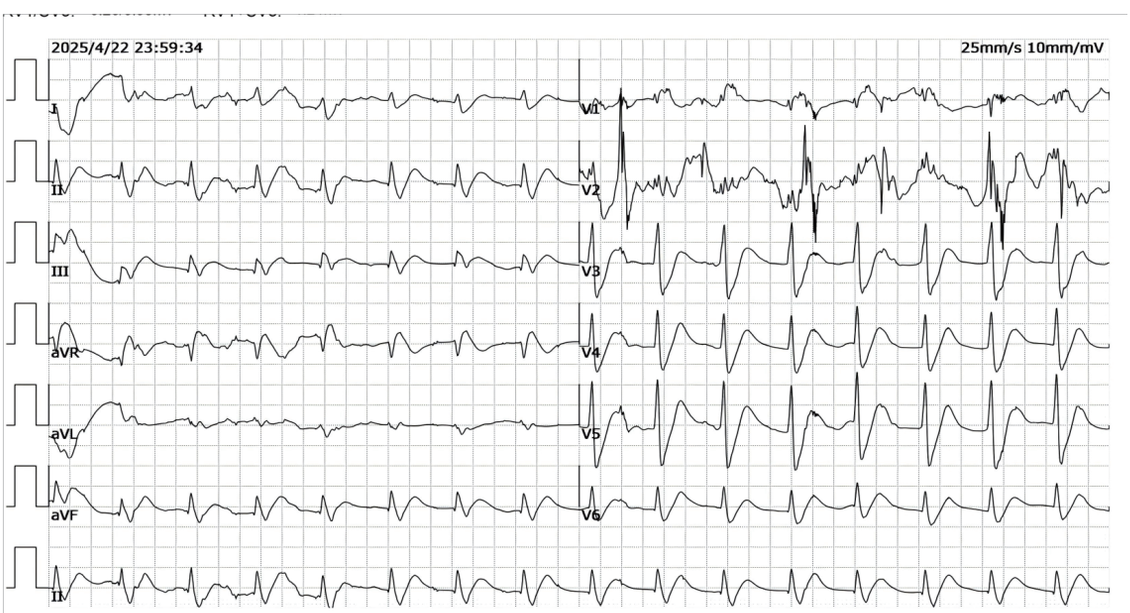

Figure 2. The ECG shows frequent unrelated P waves with abnormal QRS complexes, suggesting accelerated idioventricular rhythm.

enamide 1 tablet qd orally for antiretroviral therapy, Clindamycin 600 mg q12h IV for Pneumocystis jirovecii infection, and Glutathione 1.2 g qd IV to improve liver function and correct electrolyte imbalance.

The patient experienced systemic chills, fever, and altered consciousness at 03:47 on May 31, 2025. Vital signs were as follows: body temperature 38.1 °C, heart rate 125 beats/min, respiratory rate 29 breaths/min, blood pressure 148/103 mmHg, oxygen saturation 92%. Random blood glucose was 2.2 mmol/L, which increased to 6.4 mmol/L after intravenous glucose injection. CT findings showed no significant abnormalities in the head imaging, with moderate peritoneal and pelvic fluid accumulation. Differential diagnosis should be made between special pulmonary infection and pulmonary edema (Figure 3, Figure 4). The patient was in a deep coma at 04:45 on May 31, 2025, and despite active resuscitation efforts, passed away at 05:46 on the same day. The laboratory reported Talaromyces marneffei in peripheral blood culture one day after the patient's death.

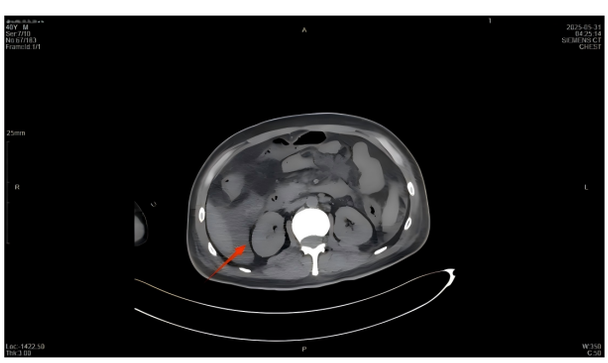

Figure 3. Abdominal CT display moderate peritoneal effusion

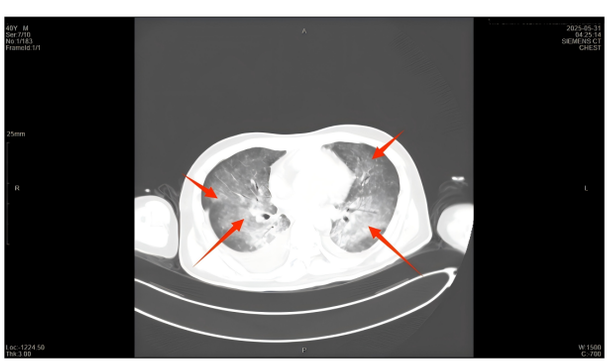

Figure 4. Chest CT display bilateral pulmonary exudative changes with local nodules and patchy opacities

Discussion

Two patients showed acute onset and rapid disease progression. There are both similarities and differences in their clinical courses worthy of our discussion.

Common points: By analyzing the relevant clinical manifestations and laboratory findings, we can draw some valuable lessons. Both patients had $CD4^+$ T lymphocyte counts below 100 cells/μl. When the $CD4^+$ T lymphocyte count falls below 100 cells/μl, patients are more susceptible to various fungal infections, and the associated mortality rate may also rise due to fungal infections.[5, 6]. Individuals with HIV and $CD4^+$ T lymphocyte counts <50 cells/μL may be at particularly high risk for Talaromyces marneffei infection[7]. Both patients showed varying degrees of elevated ALT and AST levels, along with decreased Alb levels. Some studies suggest that Talaromyces marneffei induces hepatocyte destruction by activating the Absent in Melanoma 2–caspase-1/4–Gasdermin D (AIM2–caspase-1/-4–GSDMD) axis. The activation of these pathways induces pyroptosis of hepatocytes and extensive inflammatory responses, leading to elevated transaminases and hypoalbuminemia. This subsequently weakens anti-infective capacity, creating a vicious cycle of "infection-inflammation-organ damage"[8, 9]. Both patients in this study exhibited elevated levels of ALT, AST, PCT, and the blood urea nitrogen/albumin ratio. Correspondingly, their risk of mortality may have increased significantly compared to other HIV-infected individuals[10, 11]. And conditions are accompanied by varying degrees of electrolyte imbalance, which may be a significant factor contributing to sudden cardiac death in patients. Studies have shown the C-reactive protein to prealbumin ratio (CPAR) and procalcitonin to albumin ratio (PAR) are independent risk factors for mortality in patients with HIV and Talaromyces marneffei infection[12], the PAR(Case A: 0.40, Case B: 0.32, Normal values <0.001) values of both patients were significantly higher than those of the normal population.

Differences: Case A cranial MR shows multiple infec-

tious lesions, and the infectious lesions in the brain may be the direct cause of the patient's death, direct neuronal damage mediated by Tau protein and GSDMD-dependent pyroptosis, as well as indirect inflammatory injury mediated by M1-polarized microglia [13]. Lesions in the basal ganglia and frontal lobe align with common Talaromyces marneffei central nervous system infection sites; Tau protein-mediated neuronal damage and microglial activation may exacerbate perilesional edema and brainstem compression. It cannot be ruled out that meningitis lesions affecting the medullary center led to cardiorespiratory arrest. Patient B developed chills and fever prior to death, which was suspected to be caused by sepsis. Case A's hypokalemia (3.16 mmol/L) and hypocalcemia (1.90 mmol/L) impaired myocardial electrical stability, combined with central infection-induced brainstem suppression, causing cardiac/respiratory arrest. Case B's severe hyponatremia (124.7 mmol/L) and hypochloremia (91.8 mmol/L) were related to adrenal crisis, and hypoglycemia may stem from adrenal insufficiency-induced gluconeogenesis impairment [14]. The chest CT showed diffuse ground-glass opacities in both lungs with multiple nodules, predominantly located in the lower lungs [15, 16], suggesting a possible Pneumocystis jirovecii infection. The cause of death may be related to multiple factors including adrenal crisis, Talaromyces marneffei septicemia, electrolyte imbalance, and Pneumocystis jirovecii infection. The two patients differed in their $CD8^+$ T lymphocyte counts. A reduction in $CD8^+$ T lymphocytes may also be a significant risk factor for mortality in patients with Talaromyces marneffei bloodstream infections; Case A's extremely low $CD4^+$ count (1 cell/μL) and reduced $CD8^+$ count (114 cells/μL, <200) increased the risk of intracranial infection [17]. Case B's adrenal crisis may have resulted from adrenal damage caused by long-term untreated HIV. Central nervous system infections are more prevalent in patients with $CD4^+$ counts below 50 cells/μL (often accompanied by elevated G-test results), whereas adrenal crises are associated with chronic adrenal inflammation due to uncontrolled HIV and recurrent infections.

Limitations

This is a single-center, small-sample (2 cases) study with potential selection bias – larger cohort studies are needed for validation. Adrenal function indicators (e. g., serum cortisol, Adrenocorticotropic Hormone (ACTH)) were not tested, precluding laboratory confirmation of adrenal crisis. Autopsy was refused by family members, preventing histopathological confirmation of lesion distribution and direct cause of death.

Conclusion

Based on the analysis of two fatal cases of AIDS complicated with Talaromyces marneffei septicemia, clinicians should be vigilant about the risk of sudden death in HIV patients with this infection if they exhibit elevated levels of ALT, AST, BUN, CPAR, and PAR, abnormally decreased $CD4^+$ and $CD8^+$ T lymphocytes, or are complicated by central nervous system infection and adrenal crisis.

Based on relevant clinical studies and guideline consensus opinions, for HIV patients with $CD4^+ < 100$ cells/μL presenting with fever (especially persistent high fever), rash, elevated liver enzymes, or electrolyte disorders, highly suspect T. marneffei infection. Initiate empirical Voriconazole (loading + maintenance dose) promptly without waiting for blood culture results (5–7 days). Actively correct electrolyte imbalances, supplement albumin, and monitor blood glucose/adrenal function.

Acknowledgments

None.

Ethical approval

No approval is required. All authors have complied with the journal's ethical and policy requirements.

Author contributions

ZWL responsible for case report writing and submission, YCL responsible for case data collection,BBH responsible medical record organization, archiving, and verification of data integrity and accuracy, ZWC in charge of case report writing instruction.

Conflict of interest

All authors declare no conflicts of interest.

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