Infection and Drug Resistance

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CASE REPORT

HIV Complicated with Talaromyces Marneffei Multisystem Infection: A Case Report and Literature Review

Guomin Zhang, Guangrong Wu, Yuanyuan Xu, Li Yang, Wei Yang

Department of Radiology, The Third Affiliated Hospital of Zunyi Medical University (The First People's Hospital of Zunyi), Zunyi, People's Republic of China

Correspondence: Wei Yang, Email coxsackie@163.com

Abstract: HIV-infected individuals typically present with diverse clinical manifestations and heightened susceptibility to various opportunistic infections. We present a case of a hospitalized HIV patient presenting with dizziness, headache, and lip numbness. Neuroimaging revealed disseminated lesions involving bilateral cerebral hemispheres, spinal cord, pulmonary parenchyma, and mesenteric lymph nodes, subsequently confirmed through cerebrospinal fluid analysis and genetic testing as systemic TM infection. Following a 10-day course of intravenous amphotericin B, the patient demonstrated symptomatic improvement and was discharged. Post-discharge management included combination antiretroviral therapy (Bictegravir/Emtricitabine/Tenofovir alafenamide) with oral itraconazole prophylaxis. One-year follow-up imaging demonstrated near-complete resolution of systemic lesions. This report highlights characteristic radiological patterns and emphasizes the importance of considering disseminated TM infection in HIV patients with neurological involvement, particularly in endemic regions.

Keywords: talaromyces marneffei, multisystem infection, HIV, CT, MRI, case report

Introduction

Talaromyces marneffei (TM), a thermally dimorphic fungus endemic to Southeast Asia, represents a significant opportunistic pathogen in HIV-positive populations.[1] Ranking as the third most prevalent opportunistic infection in this cohort after tuberculosis and cryptococcosis,[2] TM infection constitutes a leading cause of mortality among immunocompromised individuals in the region. However, multisystemic Talaromyces marneffei (TM) infections, though underreported, are relatively common in HIV patients in endemic regions such as Southeast Asia and southern China.[3] The disease progression mirrors other systemic mycoses, governed by intricate host-pathogen interactions. Hematogenous dissemination typically results in multi-organ involvement through reticuloendothelial system infiltration.[4]

This case of HIV and *Talaromyces marneffei* co-infection is notable for its extensive multi-organ involvement, distinct imaging characteristics, and dynamic changes in inflammatory and viral biomarkers throughout treatment. The comprehensive analysis of radiologic progression, combined with biochemical marker trends, highlights the diagnostic complexity of disseminated TM infection in advanced HIV and underscores the potential value of multimodality imaging and biomarker monitoring in guiding individualized therapy. Moreover, the favorable response to combined antiretroviral and antifungal treatment in this case provides valuable insight into optimizing therapeutic strategies for similar patients.

Case Presentation

A 40-year-old male diagnosed with HIV on April 14, 2023, presented to our hospital on June 24, 2023, with symptoms of upper lip numbness, dizziness, and headache. In addition to neurological complaints, the patient also reported intermittent low-grade fever, weight loss, generalized fatigue, and mild abdominal discomfort over the preceding weeks. Given the systemic symptoms and the concern for possible opportunistic infections with multi-organ involvement, a comprehensive

Received: 29 April 2025
Accepted: 2 July 2025
Published: 21 July 2025

imaging evaluation was performed, including contrast-enhanced and non-contrast brain MRI, non-contrast spinal MRI, and CT scans of the chest, abdomen, and pelvis.

Imaging Findings

Brain MRI

Multiple patchy, nodular, and clustered lesions were observed in the bilateral cerebral hemispheres, cerebellar hemispheres, and brainstem. These lesions exhibited mildly hypointense signals on T1-weighted imaging (T1WI), hyperintense signals on T2-weighted imaging (T2WI), and significant perilesional edema. Target-like morphology (Figure 1A and B) with nodular/annular enhancement was noted post-contrast (Figure 1C and D). Diffusion-weighted imaging (DWI) demonstrated ring-like and punctate hyperintensity with reduced apparent diffusion coefficient (ADC) values (Figure 1E and F).

Spinal MRI

T2WI revealed central canal dilation and patchy intramedullary hyperintensities (Figure 1G–H).

CT Imaging

New subcentimeter pulmonary nodules and enlarged retroperitoneal lymph nodes (short-axis diameter >1.5 cm) were identified compared to 2021 baseline imaging (Figure 2A–D).

Laboratory Results

Cerebrospinal fluid (CSF) analysis showed elevated protein levels (1.8 g/L) and lymphocytic pleocytosis (32 cells/μL). Peripheral blood tests indicated leukocytosis (12.5×10^9/L) with neutropenia (1.1×10^9/L). CSF metagenomic sequencing confirmed Talaromyces marneffei infection (Figure 3).

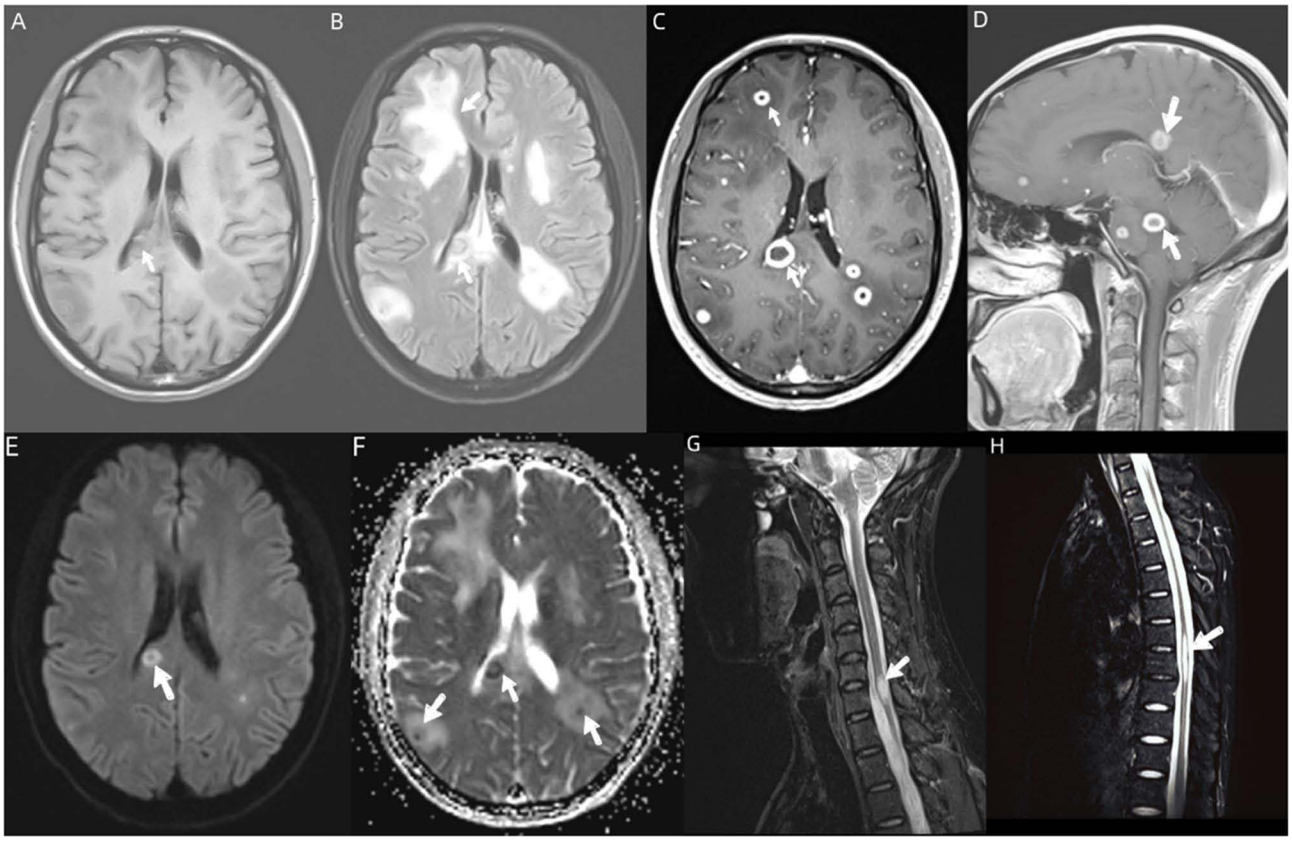

Figure 1 (**A** and **B**) Bilateral cerebral hemispheres, cerebellum, and brainstem with multiple patchy low-signal lesions on T1WI, high signal on T2-FLAIR, and different degrees of edema around the lesions with marked edema (white arrows); (**C** and **D**) Post-contrast Magnetic resonance imaging showed nodular and ring-like enhancement, and no enhancement in the center of the lesion (white arrows); (**E** and **F**) DWI shows ring and point high signal shadows with reduced ADC values (white arrows). (**G** and **H**) MRI showed localized dilatation of the central canal of the cervicothoracic and thoracolumbar spinal cord, with abnormal signal lesions in the spinal cord (white arrows).

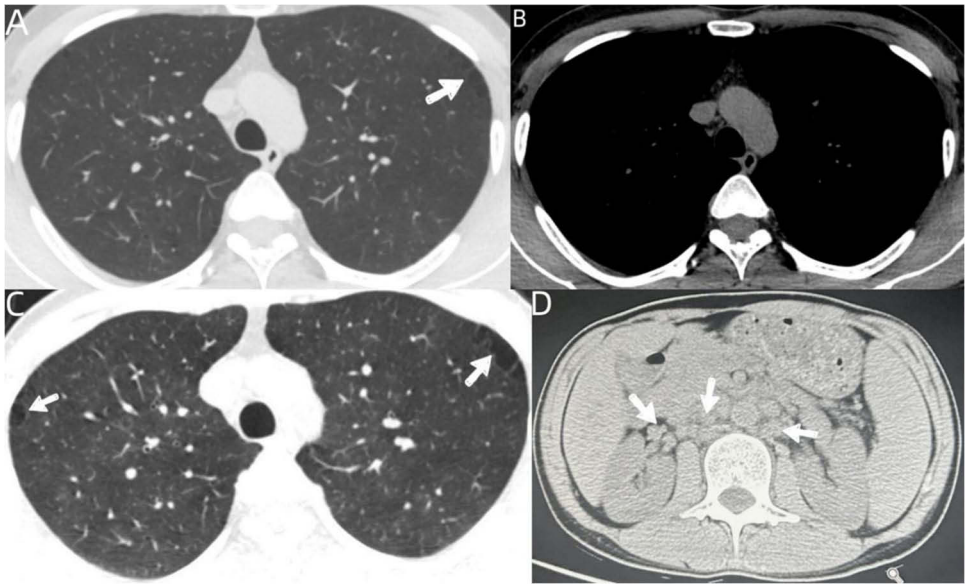

Figure 2 (**A** and **B**) Computed tomography scan showed multiple small nodular lesions in the upper lobe of the right lung and restrictive emphysema of both lungs in the lung and mediastinal windows on April 4, 2023 (white arrows); (**C**) Computed tomography scan showed new nodular lesions, and paraseptal emphysema in both upper lobes of both lungs in the lung windows on June 25, 2023, compared with the last chest CT examination (white arrows). (**D**) Abdominal CT scan showed multiple enlarged retroperitoneal lymph node lesions (white arrows).

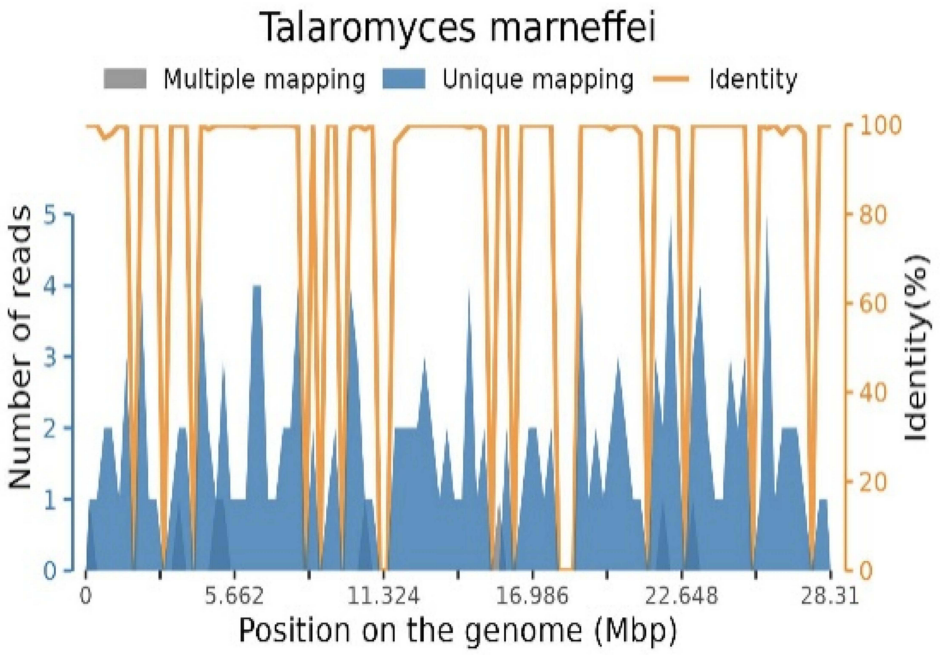

Figure 3 The total length covered to the genome was 8446 (bp), the coverage was 0.0298%, and the average depth was 1.01X. The total length covered to the genome was 8446 (bp), the coverage was 0.0298%,and the average depth was 1.01X.

Clinical Course

The patient received intravenous amphotericin B (0.7 mg/kg/day) for 10 days during hospitalization, resulting in symptomatic improvement. Post-discharge therapy included oral bictegravir-based antiretroviral therapy and itraconazole (200 mg twice daily). At the September 4, 2024 follow-up: Imaging demonstrated near-complete resolution of systemic

https://doi.org/10.2147/IDR.S534364

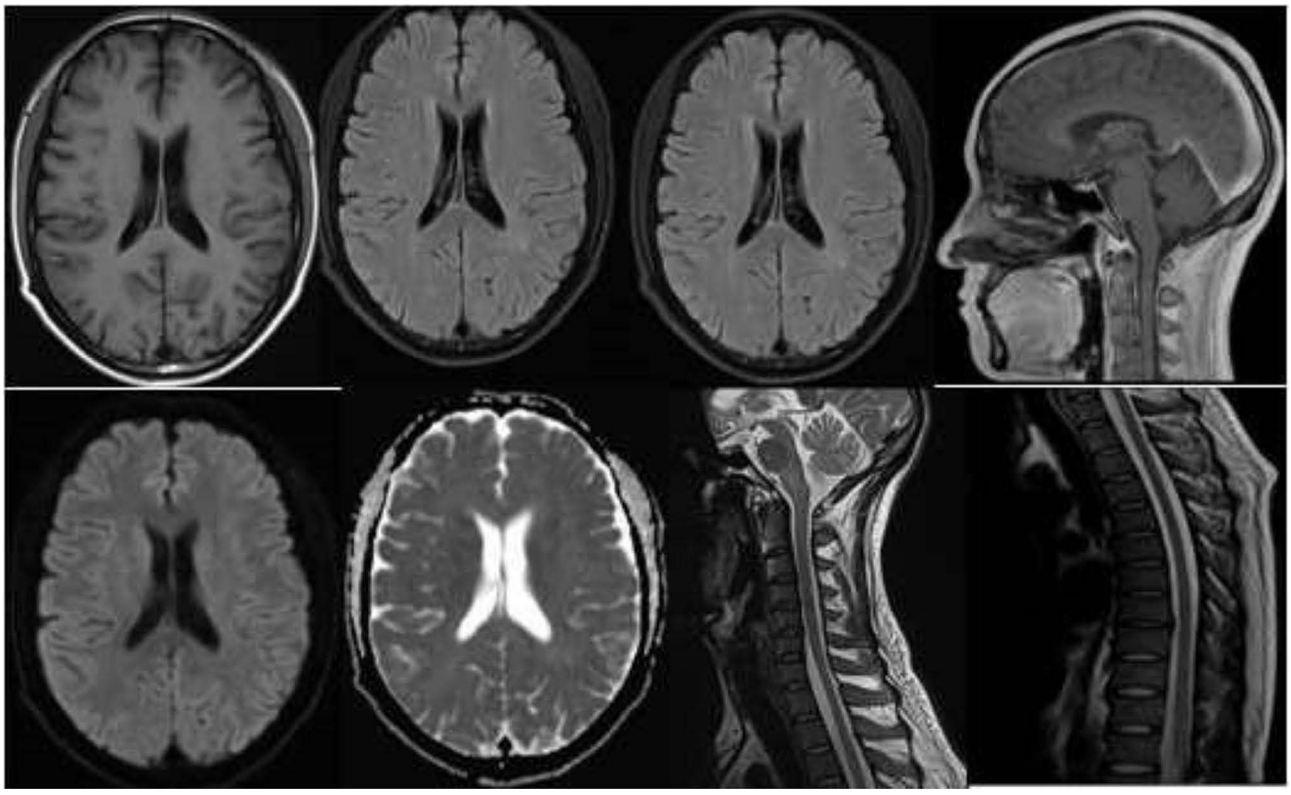

Figure 4 In 2024, MRI reexamination showed that multiple lesions in the brain and spinal cord were basically absorbed.

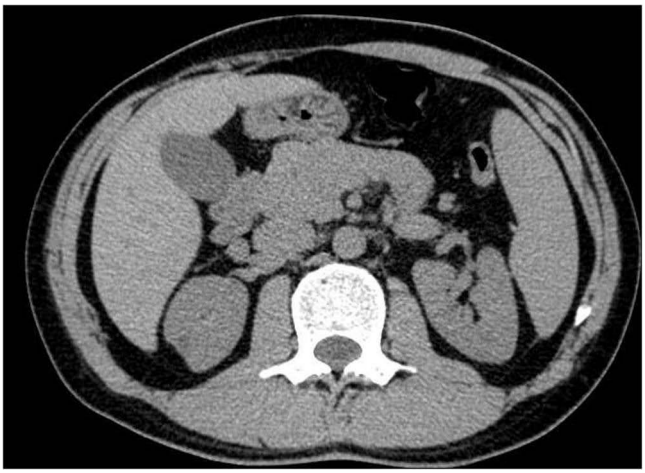

Figure 5 In 2024, abdominal CT reexamination showed that compared with before treatment, multiple abdominal lymph nodes disappeared.

lesions (Figures 4 and 5). $CD4^+$ T-cell count increased from 85 to 320 cells/μL. Body weight normalized (48 kg → 68 kg; BMI 16.2 → 22.7 kg/m²). The patient reported full resolution of neurological symptoms and improved functional status.

Discussion

This case involves a 40-year-old HIV-positive male patient whose imaging studies revealed multi-organ involvement consistent with disseminated Talaromyces marneffei (TM) infection. This diagnosis was subsequently confirmed by genetic sequencing. Therefore, early and comprehensive imaging evaluation played a critical role in timely diagnosis and intervention.

TM, a thermally dimorphic mycosis endemic to Southeast Asia and subtropical China (including Yunnan-Guizhou Plateau), represents a leading AIDS-defining opportunistic infection. This case involves a long-term resident of Yunnan Province in southwestern China, a hyperendemic region for TM. The main clinical manifestations of TM infection in HIV-infected individuals include fever (93%–97%), malaise (91%), skin lesions (28%–81%), lymphadenopathy (33%–62%), cough (40%–49%), anemia (78%–79%), and abnormal chest X-ray findings (45%).[5] Talaromyces marneffei infection manifests as either localized or disseminated disease. Hematogenous dissemination typically results in systemic invasion, predominantly affecting the lungs (76%), integumentary system (63%), gastrointestinal tract (41%), and reticuloendothelial organs (spleen/liver/lymph nodes in 89%).[6] Despite the gastrointestinal tract's abundant mucosa-associated lymphoid tissue (MALT) - a prime target for fungal dissemination - Despite the gastrointestinal tract's abundant mucosa-associated lymphoid tissue (MALT) -a prime target for fungal dissemination-gastrointestinal involvement, including life-threatening gastrointestinal bleeding, has been increasingly recognized as a critical manifestation in TM infection. This observation highlights gaps in understanding fungal tropism mechanisms.Gastrointestinal involvement in Talaromyces marneffei infection has historically been underrecognized. However, emerging evidence indicates that gastrointestinal manifestations, including abdominal pain, diarrhea, and most importantly, gastrointestinal bleeding, are not only more common than previously thought but may also represent life-threatening complications. Pan et al (2020) reported cases where TM infection involved ulcerative lesions throughout the gastrointestinal tract, leading to severe bleeding requiring emergency intervention. These findings underscore the need for clinicians to remain vigilant for gastrointestinal symptoms in TM-infected patients, particularly those with advanced HIV/AIDS, and to consider gastrointestinal endoscopy and biopsy in suspicious cases [6]. Delayed recognition of gastrointestinal involvement may result in catastrophic hemorrhagic events, and thus, early diagnostic work-up is crucial for improving patient outcomes.[7] Current understanding of Talaromyces marneffei pathogenesis remains incomplete, though three key mechanisms emerge: (1) Transmission: Primary infection typically occurs through inhalation of airborne conidia, with alveolar macrophages serving as initial defense. (2) Immune Dynamics: Competent hosts: Granulomatous inflammation mediated by Th1/Th17 responses (IFN-γ/IL-17 dominance) Immunocompromised hosts: Uncontrolled hyphal proliferation → hemorrhagic necrosis (TNF-α/IL-10 dysregulation). (3) Dissemination: Reticuloendothelial system invasion correlates with $CD4^+$ depletion severity ($r=-0.72$, $p<0.01$ in AIDS-TM cohorts).[8]

TM, while classically recognized as a pulmonary mycosis via macrophage-mediated proliferation (J Clin Microbiol 2023), demonstrates paradoxical neurotropic dissemination in this case. Beyond the newly developed pulmonary nodules, multisystem involvement manifested as: (1) Neuroaxial lesions: Cerebritis (bilateral frontoparietal), cervical/thoracic myelitis; (2) Reticuloendothelial infiltration: Mesenteric lymphadenopathy (SUVmax 8.2 on PET/CT); This dimorphic fungus causes invasive disease in 92% of untreated HIV patients in Southeast Asia (Clin Infect Dis 2022). Diagnostic challenges arise from: (1) Clinical mimicry: 78% of cases present with non-specific constitutional symptoms; (2) Microbiological latency: CSF culture sensitivity <40% in early stages. When neuroinvasive TM is suspected, immediate actions should include: (1) Neurological workup: Contrast-enhanced MRI brain/spine; (2) Molecular confirmation: CSF metagenomic next-generation sequencing (mNGS); (3) Empirical therapy: Liposomal amphotericin B (5mg/kg/day) + early ART initiation.

Lymphadenopathy secondary to TM infection represents an atypical presentation, with CT imaging lacking pathognomonic features. Key radiological patterns observed in TM-associated lymphadenopathy include: (1) Morphological changes: Bulky lymphadenopathy (short-axis diameter >15mm, per RECIST 1.1 criteria) with irregular margins, as evidenced by retroperitoneal involvement in this case; (2) Density alterations: Homogeneous enhancement (attenuation >40 HU),[9] reflecting granulomatous inflammation or fibrotic replacement. (3) Perinodal reactions: Fat stranding (CT attenuation: −30 to −10 HU) and fascial thickening (>3mm), indicative of cellulitis-like changes. Although mesenteric lymph node enlargement may suggest TM-related reticuloendothelial dissemination, CT features lack specificity and overlap with other opportunistic infections such as tuberculosis or lymphoma. Therefore, histopathological or microbiological confirmation remains essential, and the exact etiology in this case remains uncertain. While clinical manifestations remain non-specific, the presence of multifocal lesions on imaging (particularly involving ≥3 anatomical compartments) should raise suspicion for TM infection in HIV-positive individuals from endemic regions.

The pathogenesis of spinal cord involvement in Talaromyces marneffei (TM) infection remains incompletely elucidated. Current evidence does not support direct neurotropic invasion, as TM predominantly exhibits tropism for

superficial anatomical compartments (epidermis, dermal appendages) with limited penetrative capacity into deeper tissues. Consequently, primary spinal cord involvement represents an exceptional clinical entity (<2% of disseminated TM cases, per J Neurol 2022). While TM typically spares the central nervous system (CNS), immunocompromised hosts may develop systemic dissemination ($CD4^+$ <50 cells/μL in 89% cases) with potential secondary neural axis compromise. Notably, literature documenting TM-associated myelitis remains sparse, with fewer than 15 MRI-documented cases worldwide (Clin Radiol 2023). This case demonstrates unique neuroimaging correlates: (1) Structural changes: Fusiform spinal cord enlargement (cervical C3-C5, thoracic T4-T7); (2) Signal abnormalities: T2 hyperintensity spanning cervicothoracic (C7-T2) and thoracolumbar (T10-L1) junctions,STIR sequence confirmation of edema patterns (Figure 3). (3) Contrast enhancement: Leptomeningeal enhancement along dorsal columns. These findings underscore TM's capacity for hematogenous CNS seeding in advanced immunosuppression, challenging conventional understanding of its tissue tropism.

TM induces cutaneous/mucocutaneous manifestations in humans; its neuroinvasive form (TM encephalitis) occurs in up to 12% of disseminated cases, particularly in immunocompromised hosts,Crucially, MRI findings lack pathognomonic specificity, mandating integration with clinical biomarkers (eg, CSF analysis, $CD4^+$ counts) and molecular diagnostics (PCR/metagenomics) to achieve diagnostic certainty.[10] Encephalitis caused by TM infection usually needs to be differentiated from tuberculous encephalitis and toxoplasmic encephalitis.[11] The MRI hallmarks of tuberculous meningitis encompass: (1) Basal cistern engagement: Leptomeningeal enhancement predominantly involving interpeduncular and suprasellar cisterns; (2) Meningeal pathology: Sulcal effacement with pachymeningeal thickening (3–5mm),T1-isointense/T2-hypointense signals relative to CSF (T1WI: 450–600ms; T2WI: 80–120ms); (3) Post-contrast patterns: Linear dural-arachnoid enhancement along Sylvian fissures; (4) Parenchymal changes: Non-enhancing vasogenic edema (prolonged T1/T2 relaxation times). In this TM encephalitis case, neuroimaging revealed: (1) Lesion distribution: Multifocal clustered nodules in supratentorial (frontal/parietal lobes) and infratentorial (brainstem/cerebellar peduncles) regions; (2) Signal characteristics: T1 hypointensity (SI ratio 0.6–0.8 vs white matter), T2 hyperintensity with marked perilesional edema (FLAIR+); (3) Enhancement patterns: Targetoid (central necrosis) and annular (peripheral fibrotic rim) configurations; (4) Diffusion metrics: Restricted diffusion (ADC=650×10^{-6} mm²/s) correlating with fungal microabscesses. While tuberculous and TM encephalitis share overlapping MRI features (eg, basal predilection), key discriminators include: (1) CSF biomarkers: TM shows elevated β-D-glucan (>500pg/mL) vs adenosine deaminase increase in TB; (2) Enhancement architecture: TM's dual enhancement patterns vs TB's linear dural emphasis. Toxoplasmic encephalitis typically demonstrates: (1) Core imaging triad: T1-isointense/T2-hyperintense necrotic cores, Eccentric target enhancement ("owl's eye" sign), Mass effect with midline shift (>5mm in 70% cases); (2) Distinct from TM: Absence of concomitant spinal lesions and meningeal involvement.This imaging paradigm underscores MRI's pivotal role in differentiating TM encephalitis from other HIV-associated neuropathologies through pattern recognition of enhancement characteristics and lesion topography.[12]

This case represents a distinct clinical entity among HIV-TM coinfections, demonstrating unprecedented multiorgan dissemination (CNS-pulmonary-reticuloendothelial axis involvement). Notably, while disseminated talaromycosis carries grave prognosis, our patient achieved sustained remission through optimized cART/antifungal synergy. While standard amphotericin B-based regimens remain the therapeutic mainstay, clinical outcomes frequently prove suboptimal. Remarkably, our case demonstrated near-complete radiologic resolution following 12-month combined antiretroviral therapy (cART) and itraconazole maintenance, an exceptionally rare therapeutic response. This observation prompts crucial consideration of cART's potential synergistic role in TM clearance.Clinical features in HIV-positive and HIV-negative patients are relatively independent, with multiorgan involvement and disease progression being more common in HIV-negative patients.[13] Our patient, an individual who was HIV - positive, developed a rare TM infection. Notably, just two months after being diagnosed with HIV, this patient experienced multisystem involvement. However, following one - year of treatment that included intravenous amphotericin B, regular oral Bictegravir Sodium, Emtricitabine, and Tenofovir Alafenamide Fumarate for antiretroviral therapy, along with oral itraconazole for antifungal treatment, the patient's overall condition improved. Imaging results indicated that lesions from multiple systemic diseases had been largely absorbed.

Conclusion

In conclusion, as this case demonstrates, although rare, TM can cause multisystem infections. Unlike previously reported cases which predominantly involved the respiratory or cutaneous systems, this patient exhibited an exceptionally disseminated pattern of infection, including neuroaxial lesions, pulmonary nodules, gastrointestinal symptoms, and mesenteric lymphadenopathy, confirmed by metagenomic sequencing.We hope that clinicians and imaging specialists will take TM infection into account when HIV-positive or negative patients in AIDS-prevalent regions show signs of systemic multisystem infections. In this case, the patient presented with neurological symptoms (such as upper lip numbness, dizziness, and headache) as well as systemic features like low-grade fever, weight loss, and mild abdominal discomfort—symptoms that did not respond to empirical anti-inflammatory therapy—raising clinical suspicion of an opportunistic disseminated fungal infection. This case not only broadens the diagnostic perspective for imaging specialists encountering such findings but also provides new treatment insights for clinicians, given the significant improvement the patient achieved under the prescribed treatment regimen.We anticipate that this case will offer new hope to patients with rare multisystem infections caused by TM, leading to timely diagnosis and effective treatment. Generally, when AIDS patients present with clinical symptoms such as fever, lymphadenopathy, abdominal pain, altered consciousness, neuropsychiatric symptoms, and headache, TM infection should be suspected. Especially when anti-inflammatory treatments prove ineffective and MRI findings are similar to those of tuberculous meningitis or toxoplasmic encephalitis, prompt cerebrospinal fluid pathogen detection should be carried out to identify the pathogen and intervene in the disease progression as early as possible. Additionally, if abnormal blood flow patterns or coagulation disorders are detected, clinicians should be vigilant about the possibility of bleeding disorders and take measures to prevent life-threatening situations. Early diagnosis through laboratory and imaging examinations is essential for reducing mortality, prolonging survival, and enhancing the quality of life for patients.

Abbreviations

TM, Talaromyces marneffei; CT, computed tomography; MRI, magnetic resonance imaging.

Ethics Approval and Informed Consent

This study was approved by the ethics committee of The First People's Hospital of Zunyi (The Third Affiliated Hospital of Zunyi Medical University). Institutional approval was not required for the publication of this case report as it does not involve sensitive patient information. All procedures performed in studies involving human participants were per the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The patient has provided written informed consent to have the case details and accompanying images published.

Consent to Publish

The authors affirm that human research participants provided informed consent for publication of all images in this article. The patient has provided written informed consent to have the case details and accompanying images published.

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.

Funding

This research was supported by Zunyi Science and Technology Plan Project (No. Zun Shi Ke He HZ [2023] 491.

Disclosure

The authors report no conflicts of interest in this work.

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