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CASE REPORT

Talaromyces marneffei Infection Misdiagnosed as Lung Cancer and Retrospective Literature Analysis

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Background: *Talaromyces marneffei* (TM), an opportunistic fungal pathogen, causes severe infections in immunocompromised individuals. While endemic to tropical regions of Southeast Asia and South Asia, sporadic cases have been reported in non-endemic areas. Diagnosis is often delayed due to nonspecific clinical and laboratory features, contributing to high mortality.

Case Presentation: A HIV-positive patient subsequently developed TM pulmonary infection. Clinical symptoms and laboratory test results were non-specific. Imaging studies revealed pulmonary masses, and the patient was misdiagnosed with lung cancer outside the hospital, leading to an erroneous surgical resection. The patient did not improve postoperatively but instead developed high fever and persistent cough, with symptoms worsening. During treatment at our hospital, the patient was definitively diagnosed with TM lung infection, not lung cancer. Due to the rarity of TM infection and lack of experience, treatment was delayed, leading to worsening of the patient's condition. The patient exhibited gastrointestinal bleeding, progressive neurological dysfunction, hydrocephalus, and multi-organ dysfunction, which ultimately resulted in the death of the patient.

Conclusion: TM infections often present with insidious onset, prolonged course, and lack of specific clinical symptoms, imaging findings, or laboratory test characteristics, making diagnosis challenging and frequently leading to misdiagnosis or missed diagnosis, resulting in high mortality rates. Therefore, clinicians should enhance their diagnostic and treatment experience regarding TM infections in HIV-positive individuals or populations in non-endemic regions, initiate pathogen culture and histopathological diagnosis as early as possible, and integrate the results of mNGS and mass spectrometry analysis to improve the detection rate and early diagnosis rate of TM infections. This will ensure that patients can receive timely and accurate treatment, which is crucial for improving their prognosis.

Keywords: *Talaromyces marneffei*, HIV-positive patient, infection, diagnosis, treatment

Introduction

Talaromyces marneffei (TM) is a thermo-dimorphic fungus that causes lethal systemic mycoses and is endemic to tropical/subtropical Asia and southern China.[1] The prevalence of TM among human immunodeficiency virus (HIV)-positive populations is a major public health concern in areas with an Acquired Immune Deficiency Syndrome(AIDS) epidemic, with approximately 3.3% of patients developing life-threatening disseminated infections.[2,3] As demonstrated in studies, the common presentation of TM infection is characterised by fever, respiratory signs, lymphadenopathy, hepatomegaly and splenomegaly.[4] The presence of insidious, atypical and latent infections can complicate the process of TM diagnosis, resulting in diagnostic delays and an increased mortality rate of up to 81%.[5] The ability of TM to disseminate throughout the body via the monocyte-macrophage system is of particular concern, as it frequently results in life-threatening infections, with the lung tissue and lymphatic system being particularly vulnerable.[6] The lungs are the most common site of infection in TM, which may show diffuse punctate and nodular shadows, as well as enlarged hilar and mediastinal lymph nodes on CT.[7] It is imperative to consider TM disease as a differential diagnosis in patients with a history of pulmonary disseminated infection, particularly those with AIDS. In recent years, there has been an observed

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increase in the number of AIDS-combined TM infections. The complexity and variety of clinical manifestations, in addition to the absence of specificity, often lead clinicians to misdiagnose TM disease as tuberculosis, lung cancer, and other diseases. This misdiagnosis can have fatal consequences.

Although the clinical diagnosis and treatment of TM infection have been the subject of previous studies, based on our knowledge and a comprehensive search of relevant databases, fewer cases of misdiagnosis as lung tumour have been reported, and detailed descriptions are still lacking. The objective of this article is to present a case of disseminated TM infection that was initially misdiagnosed as a lung tumour. In addition, it will provide a concise overview of the clinical features and treatment of the disease. It is challenging to diagnose TM accurately in clinical practice due to its resemblance to lung cancer, which can lead to delays in diagnosis and treatment, potentially resulting in severe patient outcomes. Consequently, a review of analogous cases was conducted to enhance clinical awareness of TM infectious disease, thereby providing a highly valuable reference for differential diagnosis and treatment of TM. Adherence to comprehensive management, encompassing treatment planning and effective follow-up, is also imperative for improving prognosis.

Case Report

The patient is a 54-year-old male who has experienced a cough and expectoration of white sputum for approximately one month. He has received a diagnosis of lung cancer from a local hospital and is scheduled to undergo surgical intervention (the details of which are not specified). Following the operation, his cough persisted. Three days prior to admission, the patient exhibited recurrent fever (39.6 °C), impaired consciousness, and no hemoptysis or chest pain. The Department of Pathology at our hospital performed immunohistochemical staining and found no malignant tumor cells, ruling out neoplasia. The pathological diagnosis is TM infection with necrosis. In order to seek further diagnosis and treatment, the patient was admitted to the hospital. On the first day of admission, the patient was found to be conscious, with Neck resistance test (suspiciously positive), disorientation, cognitive impairment, decreased numeracy, scattered papules on the skin of the face and neck, partially accompanied by scabs, stable respiration, congestion and erosion of the oral mucosa, symmetry of the breath sounds of the lungs bilaterally, coarse breath sounds of the lungs, a slight tension of the abdominal muscles, accompanied by pressure pain, and rebound pain was not obvious. The patient's chest thin-layer high-resolution three-dimensional imaging plain Computed Tomography (CT) scan showed scattered patches, streaks, and nodular shadows in both lungs, some of which were distributed in clusters, with a prominent distribution in the upper lobe of the right lung and the lower lobes of both lungs, and the patient was considered to have infectious lesions involving the mesenchymal stroma. The patient exhibited an increase and enlargement of the mediastinal lymph nodes. A minor accumulation of fluid was observed within the right pleural cavity, partially encapsulated (Figure 1). The head CT scan revealed the presence of artifacts that interfere with the subcranial plate and posterior cranial fossa. These findings are indicative of mild cerebral atrophy and mild demyelinating changes in the cerebral white matter.

Scattered foci of ischemic infarction in the brain parenchyma were possible, and the midline structures of the brain were centered. Admission tests: hemoglobin Hemoglobin(HB) 69g/L, Platelet(PLT) 53×10^9/L, White Blood Cell(WBC) 3.65×10^9/L, Neutrophil(N)% 94.4%; Human immunodeficiency virus (HIV) (2.97×10^6 copies/mL), Interleukin-6 (IL-6) 68.1pg/mL, C-Reactive Protein(CRP) 107.00mg/L, Procalcitonin(PCT)0.28ng/mL, albumin 19.4g/L; Fungal (13)-b-D glucan 409.20pg/m, Aspergillus galactomannan antigen (GM) test 6.98 GMI; Absolute T-cell count:CD3 cell subpopulation 72.00% (98 cell/ul), CD4 cell subpopulation 0.70% (1 cell/ul), CD8 cell subpopulation 64.30% (87 cell/ul), CD4/CD8 ratio 0.01. The patient was treated with piperacillin sodium tazobactam sodium to combat the infection and voriconazole to address the underlying fungal element. On the 2th day of hospitalisation, the presence of fungal growth was detected in sputum, bronchoalveolar lavage fluid, and blood cultures. All cerebrospinal fluid microbiological examinations yielded negative results. Among them, the sputum smear revealed the presence of "one river, two banks" fungal spores, which were suspected to be TM (Figure 2A). The blood culture was positive, and red mycelium was seen under Gram stain (Figure 2B). The TM manifested as a mold at 28°C, exhibiting filamentous characteristics (Figure 2C). At 36°C, yeast-like colonies were observed, characterised by a yellow-brown pigmentation (Figure 2D). The lactophenol cotton blue staining revealed a dark blue colouration (Figure 2E and F). The agar exhibited a soluble red wine pigment, which was identified as TM by Bruker Matrix-assisted laser desorption ionization tandem time-of-flight mass spectrometer (MALDI-TOF MS) (Figure 3). On the 3th day of treatment, the clinician continued to administer piperacillin-tazobactam Intravenous injection (4.5g/8h, IV), voriconazole intravenous injection (200mg/12h, IV) and

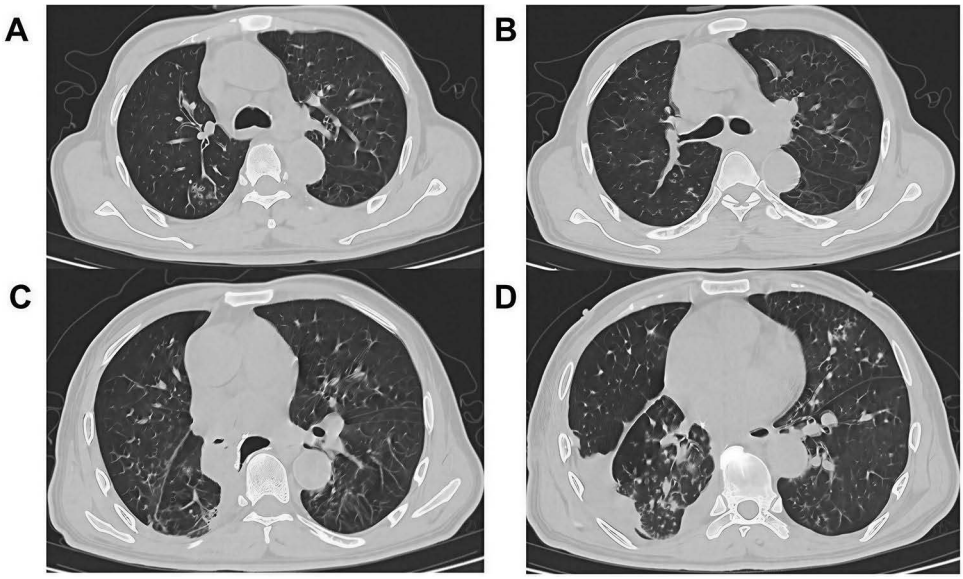

Figure 1 (**A**–**D**) The enhanced CT scan of the chest shows bilateral pulmonary nodular shadows, suggestive of infectious lesions involving the interstitium, with enlarged mediastinal lymph nodes.

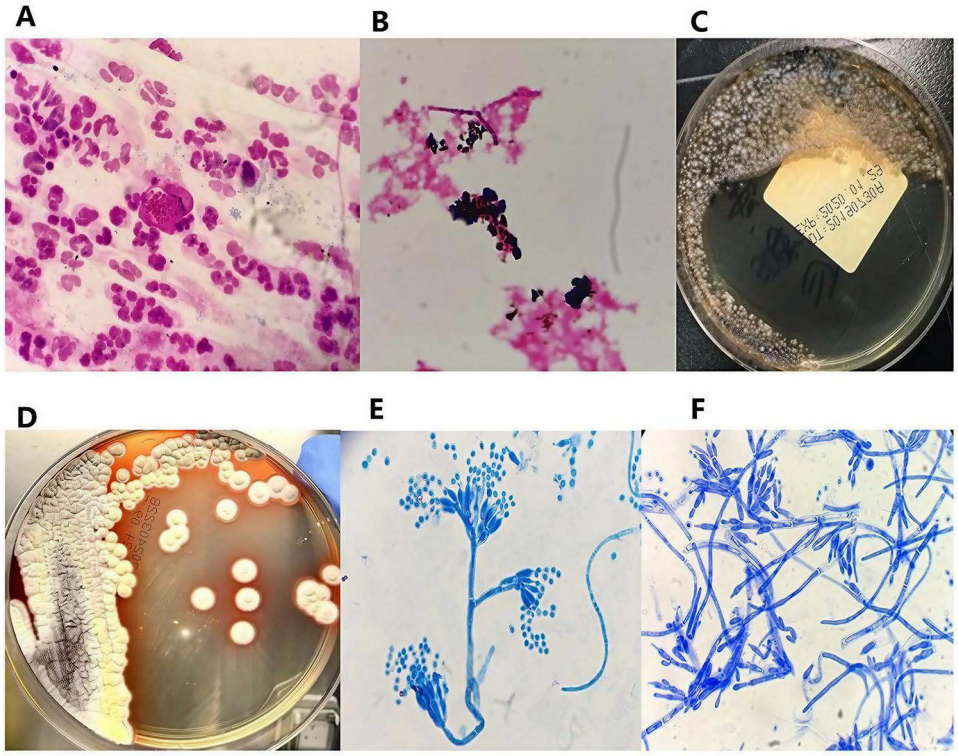

Figure 2 (**A**) Gram staining of a sputum smear revealed dachshund - like yeast - like cells with a central septum. (**B**) The results of blood culture was positive, and red mycelium was visible microscopically upon Gram-staining. (**C**) *Talaromyces marneffei* shows filamentous growth at 28°C. (**D**) At 36°C, T*alaromyces marneffei* exhibits yeast-like characteristics. (**E** and **F**) P*Talaromyces marneffei* stains dark blue in lactophenol cotton blue.

cotrimoxazole (Sulfamethoxazole 0.4g/8h+Trimethoprim 80mg/8h, Oral) in an attempt to combat the infection. On the 4th day, the patient was found to be co-infected with the influenza A virus (H3N2) and was administered oseltamivir (75mg/12h, Oral). On the 8th day of hospitalisation, the patient exhibited signs of bilateral lower limb oedema and scattered trunk rash, accompanied by pruritus, both of which were noted to be progressively worsening. A multidisciplinary consultation was

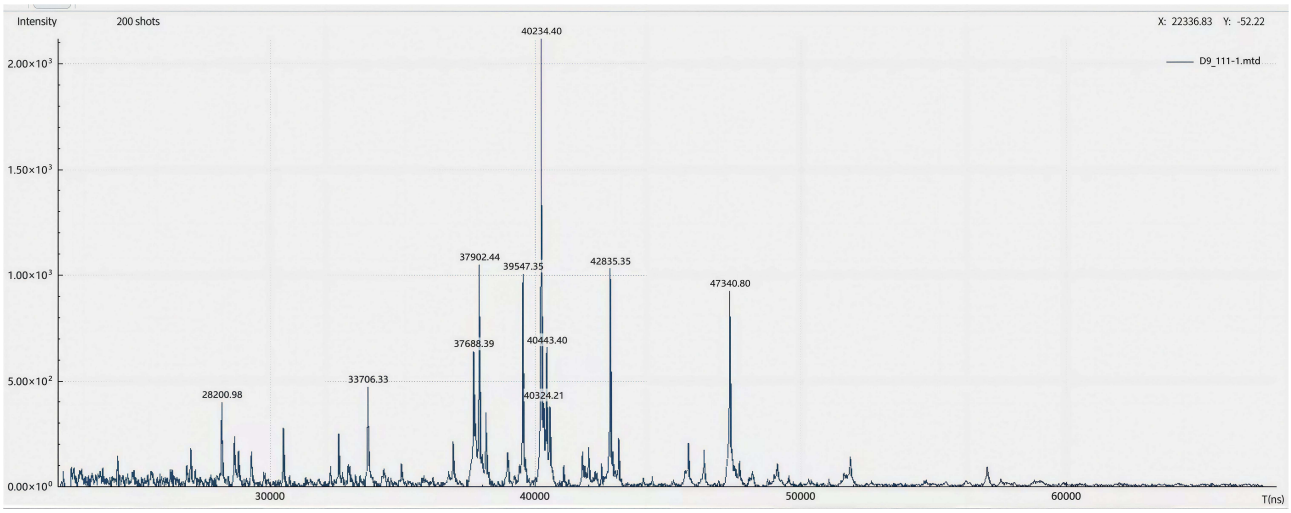

Figure 3 The Bruker MALDI-TOF MS analysis yielded a score of 2.3, identifying the organism as *Talaromyces marneffei*.

convened, and it was posited that the symptoms in question were attributable to the adverse effects of voriconazole and compound sulfamethoxazole. Furthermore, the presence of fungal cultures from blood, bronchoalveolar lavage fluid (BALF), and sputum was confirmed TM. The medication was discontinued, and the antifungal therapy was adjusted to intravenous meropenem (1 g /8h, IV) and intravenous amphotericin B (1.0 mg/kg/d, IV). On the 10th day of admission, during the treatment period, the patient vomited 100 mL of a coffee-like substance and exhibited positive fecal occult blood, which was indicative of gastrointestinal haemorrhage. The patient was administered gastric protection, arrest the haemorrhage, and intravenous rehydration. On the 11th day following admission, magnetic resonance imaging (MRI) was performed. The following results were obtained from the head examination: The patient exhibited the following pathologies: mild cerebral atrophy, enlarged ventricles, combined hydrocephalus requiring drainage, sclerosis of the wall of the C6 segment of the right internal carotid artery, and mild narrowing of the lumen. On the 13th day following admission, it was demonstrated that the blood, BALF, and sputum specimens of the patient continued to yield cultures of TM. The patient exhibited a significantly diminished level of consciousness, being in a somnolent state and unresponsive to verbal prompts. A thorough examination revealed that both pupils exhibited a diameter of 4 mm, accompanied by the presence of bilateral light reflexes. Notably, the examination did not reveal any signs of Babinski's sign. The patient is experiencing paroxysmal choking cough and is unable to ingest food. Furthermore, the family refused to insert a gastric tube, and the patient continued to receive anti-infective, antifungal, and intravenous nutritional supplementation, as well as other therapeutic interventions. On the 14th day of hospitalization, the condition of the patient deteriorated, presenting with symptoms including drowsiness, unresponsiveness, and delayed pupillary light reflexes. The condition deteriorated rapidly, and the family refused further testing. The complete blood count (CBC) of the patient was reviewed, revealing the following results: WBC 1.77×10^9/L, PLT 66×10^9/L, HB 56g/L, N% 84.2%; Absolute T-cell count: CD3 59.90% (112 cell/μL), CD4 0.00% (0 cell/μL), CD8 53.80% (101 cell/μL), CD4/CD8 0.00; PCT 0.21 ng/mL, IL6 36.80 pg/mL, CRP 78.50 mg/L (Table 1). The heart rate was recorded at 106 beats/min, the respiration rate at 22 beats/min, and the blood pressure at 123/83 mmHg. It was during the course of treatment that the patient began to manifest signs of a fever and chills, as well as leukopenia, anaemia, abnormal liver and kidney function, and an electrolyte imbalance. The decision to initiate leukocyte-enhancing therapy and supportive treatment to protect liver and kidney function was made in response to a strong suspicion of amphotericin B-related adverse reactions. As the condition of the patient was deemed critical, with the potential for immediate deterioration and even fatality, the family opted to pursue discharge after meticulous deliberation. Subsequent follow-up results indicated that the patient passed away one week after being discharged from the hospital. The timeline illustrating the entire treatment process of the patient is presented in Figure 4.

Table 1 Results of Laboratory Test Indicators at Different Time Points During the Treatment Period of the Patients

Indicators/Time	Day1	Day3	Day7	Day10	Day14
PCT (ng/mL)	0.28	0.18	0.37	0.57	0.21
IL-6 (pg/mL)	68.1	17.6	563.0	9.0	36.8
CRP (mg/L)	107	69.3	98.6	79.9	78.5
RBC ($\times 10^{12}$/L)	2.59	2.33	2.38	2.37	2.04
HB (g/L)	69	62	65	63	56
WBC ($\times 10^{9}$/L)	3.65	3.8	4.55	5.74	1.77
N(%)	94.4	95.1	96.0	94.3	84.2
TP (g/L)	58.9	66.5	59.9	63.4	69.1
Alb (g/L)	19.4	30.1	22.6	30.8	38.0
CD3 (cell/ul)	NA	98	NA	NA	112
CD4 (cell/ul)	NA	1	NA	NA	0
CD8 (cell/ul)	NA	87	NA	NA	101

Abbreviations: NA, Data not available; PCT, Procalcitonin; IL-6, Interleukin-6; CRP, C-Reactive Protein; HB, Hemoglobin; PLT, Platelet; WBC, White Blood Cell; N, Neutrophil; TP, Total Protein; Alb, Albumin.

Discussion

It has been established that AIDS is a chronic infectious disease caused by the HIV, which primarily affects CD4+T lymphocytes, mediates impaired cellular immunity and significantly reduces the ability of the body to clear TM pathogens.[8] Research has demonstrated that lethal disseminated TM infections are most prevalent among patients with HIV/AIDS and those with impaired cellular immunity, particularly those with defective CD4+ T-cell activity, with a 100% prevalence.[2] The patient in our study was an HIV-positive infected patient with a dramatic decrease in CD4+ T lymphocyte counts and CD4/CD8 ratio, indicating that the immune cell function of the patient was severely impaired, which served as

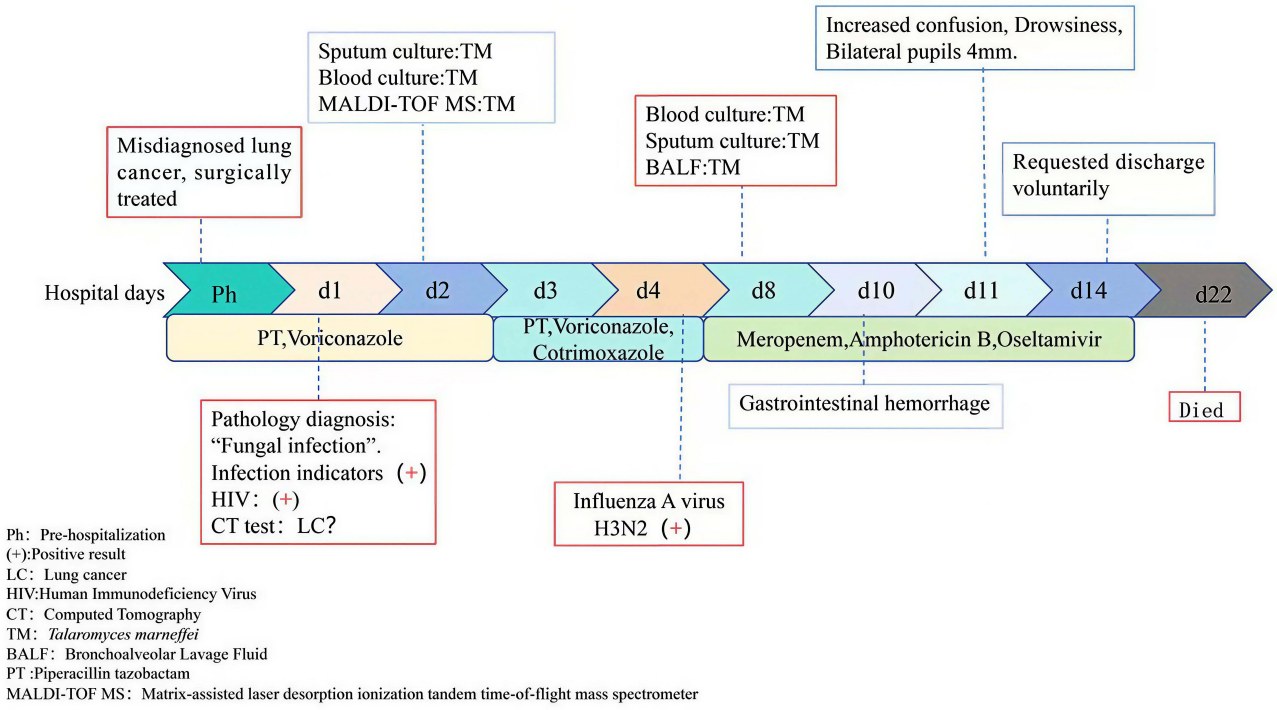

Figure 4 The key points in the treatment of the patient is shown as a time line.

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strong evidence of a high risk factor for opportunistic TM infections. Furthermore, the decline in CD4+ T lymphocytes resulted in impaired cellular immune defence against TM, thereby increasing the transmission of TM infection.[8]

Clinicians encounter considerable challenges in the early diagnosis of TM infection due to the absence of specific clinical manifestations associated with the condition. The clinical manifestations of TM infection in HIV-positive patients primarily encompass fever, weight loss, weakness, anaemia, and specific skin lesions.[9] In our study, the patient exhibited symptoms including prolonged coughing and sputum, recurrent high fever for 3 days, severe anaemia, and scattered papules with crusting on the skin of the face and neck. These symptoms are typically indicative of TM infection. The precise pathogenic mechanism of TM infection remains to be elucidated. However, it is recognised that the respiratory system is frequently and early affected, with subsequent potential dissemination to the skin, reticuloendothelial system, bone marrow, and intestinal tract via the bloodstream, resulting in systemic infection.[10] In our article, the patient presented with a diffuse multisystemic infection with neurologic deficits in the brain, congested vesicles in the oral mucosa, and a slightly tense abdominal muscle with tenderness in addition to a pulmonary infection. It is important to note that the imaging manifestations of lung involvement in TM infections are highly variable. This variability can make it difficult to distinguish between TM infections and lung cancer. In the present study, the patient presented with nodular lung occupancy, which was erroneously diagnosed as "lung cancer" at the local hospital and subsequently underwent surgical resection. A subsequent postoperative chest CT review of both lungs revealed the presence of diffuse nodules, ground-glass shadows, pleural effusion, and multiple enlarged mediastinal lymph nodes, among other findings. Following a comprehensive evaluation that incorporated the results of the pathology consultation and culture, the patient was diagnosed with a TM lung infection. The patient exhibited an aggressive postoperative anti-infection that proved refractory to effective control. Despite this, she continued to experience recurrent coughs and fevers, the development of brain abscesses, and the manifestation of neurological symptoms that were more severe than pulmonary signs. Consequently, early diagnosis and effective antifungal therapy are pivotal in improving prognosis.

At present, the gold standard for the diagnosis of TM infection remains the use of pathogenic cultures of blood, bone marrow, sputum, faeces, alveolar lavage fluid, and tissue biopsy specimens.[11] The sensitivity of bone marrow, skin biopsy, and blood for detecting TM was found to be 100%, 90%, and 76%, respectively. Imaging tests (CT, MRI, and PET-CT) may provide additional information for the diagnosis and treatment of TM infection.[12] Furthermore, the fungal (13)-b-D glucan test(G) has potential for travellers to non-endemic areas, whereas Galactomannan Test(GM) may cross-react with other fungi, which may affect its specificity.[13] Despite its diagnostic sensitivity of 91% and specificity of 89% in mixed infections, metagenomic Next-generation sequencing (mNGS) is encumbered by a high cost and a high degree of specialisation in the interpretation of the report. It can be used as a complementary method to traditional diagnostic methods.[14] The immunoassays of the newly developed TM diagnostic kits, Mp1p and 4D1, exhibited high specificity and sensitivity, and it is anticipated that further validation will be forthcoming for application in clinical TM diagnosis.[3,13] It is imperative to emphasise that histopathologic examination is pivotal in mitigating the risk of misdiagnosis, particularly in HIV-positive patients, where the presence of Malnifauna nematodes in macrophages or histiocytes can be detected using hematoxylin-eosin staining, peroxynitrite-Schiff staining, or Grocott urotropin silver staining.[15] In this study, the patient was diagnosed with a sporulating fungal infection by postoperative lung histopathological examination. Concurrently, the serum PCT and IL-6 inflammatory indexes were significantly elevated, and the results of the fungal G test and GM were strongly positive, which suggested an invasive fungal infection. This indicated the necessity of a high degree of vigilance for the possibility of TM infection. Following admission, the blood cultures and BALF of the patient were repeatedly cultured for TM, which was ultimately diagnosed as a TM infection. This case demonstrates the significance of early BALF samples and sputum specimens for pathogen culture and mNGS testing in the diagnosis of clinically mild patients with respiratory symptoms and unclear pathogens. This approach has the potential to facilitate therapeutic decision-making, alleviate economic stress, and reduce patient suffering.[6,8] Consequently, the timely diagnosis and initiation of antifungal treatment are pivotal in reducing the duration of the disease and enhancing the prognosis.

A comprehensive search was conducted using the keywords "TM" and "misdiagnosis of lung cancer" across the major bibliographic databases, PubMed, Embase, and Web of Science (as of April 2025). Following extensive screened, only two case reports that were very similar to this study were found. The first case[16] details a 59-year-old male patient who presented to the hospital with a three-month history of progressive coughing up of blood. Imaging and

bronchoscopy revealed a tumour in the basal segment of the left lung. The patient was initially misdiagnosed with lung cancer and received anti-early oncological therapy for a period of one month. Following this, he underwent a lobectomy. The final pathological diagnosis was determined to be TM, as determined by immunohistochemical staining. The patient received antifungal therapy of the precision variety, with the drug voriconazole, at a dosage of 200 milligrams, administered twice per day for a period of 12 weeks. At the 1-year follow-up, no significant respiratory symptoms were observed, and the patient's daily physical activities were not limited. The second case[17] describes a 52-year-old male patient who had visited a local hospital several times and had been misdiagnosed with lung cancer. The chest CT scan revealed left lung atelectasis, enlarged mediastinal lymph nodes, and pleural effusion on the left side. The PET-CT scan showed a maximum standardized uptake value of 11.4 in the left lung, multiple nodules in both lungs, increased glucose metabolism in the cervical, mediastinal, abdominal, and retroperitoneal lymph nodes, and multiple osteolytic lesions in the sternum and ribs. Bronchoscopy revealed chronic inflammatory changes in the bronchi, and the patient was treated with antibiotics. However, the fever persisted. The patient consumed bamboo rat meat one year ago. The patient exhibited multiple submucosal nodules in the left main bronchus, and a subsequent pathological examination revealed submucosal congestion and oedema with significant lymphocytic infiltration and granulomatous lesions. The pleural effusion sample culture demonstrated TM, which was ultimately diagnosed as TM. Following the administration of a standardised treatment plan, the patient has demonstrated a complete recovery.

Current treatment guidelines advocate the administration of liposomal amphotericin B for a duration of two weeks, followed by the prescription of oral itraconazole for a period of ten weeks, and subsequently, the implementation of secondary prophylaxis.[12] Amphotericin B therapy has been demonstrated to significantly accelerate fungal clearance and reduce recurrence rates. However, amphotericin B is associated with a relatively high incidence of adverse effects, including fever and chills, leukopenia, and abnormal liver and kidney function.[18] Itraconazole and voriconazole are both widely utilised as alternatives to amphotericin B. However, it is imperative to meticulously monitor their blood levels.[19] The investigation revealed that delayed diagnosis of TM resulted in an increase in mortality from 24% to 50%, which was significantly reduced if patients received timely antifungal therapy.[20] In this study, patients received voriconazole followed by amphotericin B therapy. Despite the partial resolution of symptoms, patients also exhibited adverse effects of varying severity. These included lower limb oedema, pruritus, fever and chills, leukopenia, anaemia, and abnormal liver and kidney function. Research has found that invasive TM infections are typically associated with severe cellular immune dysfunction and are more likely to be transmitted through blood and involve the central nervous system (CNS) compared to HIV-negative patients.[21] The patient exhibited severe CNS symptoms, which included somnolence, unresponsiveness, hydrocephalus, and delayed pupillary light reflexes. It is hypothesised that the TM infection may have originated in the lungs and spread via haematogenous dissemination to affect the CNS.[12] In light of the severity of the condition of the patient and the refusal of the family to consent to cerebrospinal fluid sampling for further examination, the aetiology of the illness could not be ascertained. As indicated by literature reports, cases of TM infections of the CNS are extremely rare (<1%), and primarily observed in immunocompromised populations, such as those with HIV in Southeast Asia. The clinical presentations of these conditions are typically non-specific, encompassing symptoms such as meningitis, meningoencephalitis, or the presence of intracranial lesions.[21] Patients may exhibit symptoms such as altered consciousness, sensory disturbances, decreased muscle strength in both lower limbs, urinary and fecal incontinence, and a positive Babinski sign.[22] However, in this case, the patient demonstrated a negative Babinski sign and did not present with urinary or fecal incontinence or muscle weakness. The present study is not equipped to make a definitive conclusion on the aetiology of the severe CNS symptoms exhibited by the patient, specifically whether these symptoms were caused by TM infection.

However, due to the prolonged residence of the patient in a non-endemic region, the TM infection did not manifest with overt clinical symptoms, resulting in an initial misdiagnosis of lung cancer. This diagnostic error resulted in a delay in the diagnosis and treatment of the TM infection. Despite adjustments to subsequent treatment regimens to voriconazole and amphotericin B, the delayed diagnosis had already enabled the TM infection to disseminate and deteriorate. Furthermore, the patient exhibited a concurrent mixed infection involving influenza A virus (H3N2), which posed significant challenges to the treatment regimen. Subsequent follow-up revealed that the patient did not undergo any further examinations or receive additional treatment after being discharged from hospital, and ultimately passed

away. The hypothesis that the cause of death may have been twofold is as follows: firstly, the misdiagnosis and delayed treatment likely exacerbated the condition; secondly, the severe side effects of the antifungal medication may have progressively deteriorated the physical condition of the patient, ultimately contributing to their demise. Similarly, it is not clear whether the death of the patient was directly related to other conditions affecting the CNS that may have arisen after discharge, including intracranial haemorrhage or thrombosis. Consequently, when patients present with unexplained fever, lymphadenopathy, pulmonary lesions, and other multisystem involvement, accompanied by markedly elevated inflammatory markers such as PCT and IL-6, strongly positive fungal G-test and GM results, and persistent clinical deterioration despite empirical therapy, it is imperative to consider the possibility of rare invasive fungal infections like TM. Furthermore, there is a necessity to enhance our experience in differentiating infections caused by rare pathogens and mixed infections with other diseases, enabling earlier diagnosis and timely treatment to improve cure rates and reduce mortality. It is evident that the present case is subject to certain limitations. Firstly, while it provides a comprehensive evaluation of the patient's immune function, it does not encompass a thorough investigation of the environmental and historical factors present in the early stages of the disease. Consequently, the relationship between the environment of patient and TM remains uncertain. Secondly, the nature of the case report precludes the possibility of a comprehensive evaluation of TM infection among HIV-positive patients in non-endemic regions and the formulation of treatment recommendations. This necessitates the execution of a large-scale retrospective or prospective case study.

Conclusion

Consequently, for patients exhibiting recurrent fever, cough with sputum production, and pulmonary infiltrates or masses who demonstrate an inadequate response to empirical treatment, the consideration of TM infection and other rare pathogen infections is recommended, in conjunction with inflammatory markers and fungal G-test and GM results. Based on HIV-positive status, the respiratory system is the primary site of TM invasion, making it highly prone to misdiagnosis as lung cancer. The most essential and commonly used methods for differential diagnosis include bronchoscopic pathological biopsy, mNGS, MALDI-TOF MS, and cultures of tissue, BALF, and sputum. This case report aims to enhance clinical awareness of TM infection among healthcare professionals in non-endemic regions outside subtropical areas and among HIV-positive patients, while improving clinical knowledge and management skills for rare diseases. Once TM infection is confirmed, the recommended treatment regimen is as follows: While administering other antimicrobial agents and implementing treatment plans for underlying conditions, conduct safe antimicrobial susceptibility testing on TM according to the CLSI M38 or M27 guidelines. This provides clinicians with precise and personalized treatment strategies, ensuring patients receive the safest and most effective care.

Abbreviations

HIV, Human immunodeficiency virus; TM, *Talaromyces marneffei*; AIDS, Acquired immunodeficiency syndrome; CT, Computed Tomograph; mNGS, Metagenomic Next-generation sequencing; BALF, Bronchoalveolar lavage fluid; MRI, Magnetic resonance imaging; PCT, Procalcitonin; IL-6, Interleukin-6; CRP, C-Reactive Protein; HB, Hemoglobin; PLT, Platelet; WBC, White Blood Cell; N, Neutrophil; TP, Total Protein; Alb, Albumin; MALDI-TOF MS Matrix-assisted laser desorption ionization tandem time-of-flight mass spectrometer; IV, Intravenous; G, (1,3)-β-D-Glucan Test.

Data Sharing Statement

All data supporting the findings of this study are available within the article.

Ethical Approval and Informed Consent

The documentation and publication of the case were approved by the Ethics Review Committee of West China Hospital, Sichuan University (Approval Number: 20231974). It conforms to the Declaration of Helsinki in 1995. No conflicts of interests are declared. Written informed consent for the publication of their details was obtained from the patients. The rights of subjects were adequately protected, and there was no potential risk to the subjects.

Consent for Publication

The present study has confirmed that the participant/patient has provided written informed consent for the publication of their personal or clinical details and any identifiable images in this study. All authors thank the patient and his family members for allowing us to understand her condition and write this case report. All authors agreed on the journal in which the article was to be submitted and unanimously agreed to publish it.

Acknowledgments

The present study has confirmed that the participant/patient has provided written consent for the publication of their personal or clinical details and any identifiable images in this study.

Author Contributions

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

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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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