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CASE REPORT

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# Disseminated talaromycosis in HIV-negative patients with lung cancer: a rare case report and literature review

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## Abstract

**Background** Talaromycosis has long been considered to be exclusively associated with human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS). In recent years, with effective control measures for HIV, the number of talaromycosis patients without HIV infection has been increasing annually. All of these patients have various immunosuppressive factors, including tumors. However, we find that talaromycosis among HIV-negative lung cancer patients remains a rarity and is without comprehensive reviews, contributing to significant gaps in clinical knowledge.

**Case presentation** We report a case of lung squamous cell carcinoma combined with *Talaromyces marneffei (T.marneffei)* infection in an HIV-negative patient. The patient, a male with a history of long-term smoking, presented with recurrent fever and cough. Chest computed tomography (CT) scans revealed pleural effusion and nodules. The patient was diagnosed with lung squamous cell carcinoma and talaromycosis through sputum cytology and blood/cerebrospinal fluid metagenomics next-generation sequencing (mNGS). The patient underwent only antifungal therapy and succumbed to respiratory failure, liver and kidney failure, and sepsis in January 2024, before receiving any anti-tumor therapy.

**Conclusion** The mortality rate of talaromycosis combined with lung cancer is extremely high. Therefore, regardless of whether patients have a history of travel to endemic areas of *T. marneffei* infection, it is crucial to test for HIV and anti-IFN-γ autoantibodies (AIGA) in patients suspected of having a pulmonary fungal infection, as well as conducting multiple cultures of specimens from different sites and utilizing mNGS to enhance diagnostic accuracy. Additionally, it is essential to perform biopsies in various methods from multiple sites to ascertain the presence of lung cancer. With effective control of *T. marneffei* infection and timely diagnosis and treatment of lung cancer, there can be a significant improvement in patient survival rates.

**Keywords** *Talaromyces marneffei*, Talaromycosis, Lung cancer, HIV-negative, Non-HIV-infected

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## Introduction

*Talaromyces marneffei (T. marneffei)*is an endemic fungus in Southeast Asian countries and southern China, that can cause life-threatening disseminated infections in humans, with mortality rates reaching as high as 33%. Over the past several decades, talaromycosis has been regarded as the third most common opportunistic infection among human immunodeficiency virus (HIV)-positive patients [1]. However, in recent years, owing to the reduction in the transmission of HIV and the widespread use of highly active antiretroviral therapy (HAART), a significant decrease in the prevalence of talaromycosis among HIV-positive patients has been observed. Simultaneously, an increase in the incidence of talaromycosis among HIV-negative patients has been noted, with mortality rates reaching up to 55% [2]. Currently, research on HIV-negative talaromycosis co-occurring with malignant tumors primarily focuses on the hematological system, with few reports on patients with concurrent lung cancer. Therefore, it is imperative to enhance awareness regarding these patients to reduce the incidence of missed and incorrect diagnoses, ultimately aiming to lower mortality rates and better the prognosis.

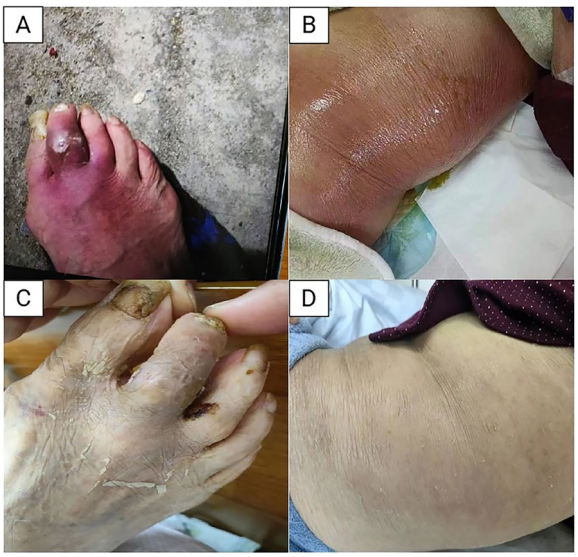


**Fig. 1** **a** The skin on the second toe of the right foot is swollen, erythematous, and ulcerated, with an increased local skin temperature. **b** The left lateral lumbar region and groin area exhibit swelling and erythema accompanied by persistent pain. **c** Following treatment, the swelling and erythema of the skin on the right foot subsided, the wound healed, and the skin temperature returned to normal. **d** Following treatment, the marked swelling and erythema of the skin in the left lateral lumbar region and groin area significantly subsided, and the pain dissipated

## Case report

A 59-year-old male farmer, with a history of hypertension and long-term smoking yet without diabetes or familial lung cancer history, presented with redness and pain in the second toe of his right foot following a field injury, persisting for two weeks (Fig. 1a). This condition was neither attended to nor treated. One week later, the patient developed redness and persistent pain in the left lumbar and groin areas (Fig. 1b), which was accompanied by coughing, expectoration, and a fever peaking at 38 °C. He was admitted to a local hospital. Initial blood tests and a chest CT scan suggested the possibility of a bacterial infection (Table 1). Despite a week of empirical anti-infective treatment with piperacillin-tazobactam (4.5 g q8 h), the patient showed no improvement. Upon transfer to our hospital, a physical examination revealed the following vital signs: body temperature 39.1 °C, heart rate 136 beats per minute, respiratory rate 36 breaths/minute, blood pressure 140/75 mmHg, and oxygen saturation 85%. The patient was stuporous, responsive to vocal stimuli yet unable to answer questions, with bilateral pupils which were equal, round, and reactive to light. An irregular heartbeat and coarse breath sounds were observed in both lungs, with no rales detected. Further blood tests, cerebrospinal fluid (CSF) analysis, and chest/brain CT scans (Table 1 and Fig. 2(a, d)) were performed, yielding negative results for HIV, AIGA, blood G test, GM test, and blood cultures. Serial sputum cultures were conducted over three consecutive days. The initial specimen was excluded due to inadequacy (WBC < 10/LPF, epithelial cells 201/LPF), as it failed to meet ATS/IDSA validity criteria (WBC > 25/LPF, epithelial cells < 10/LPF). *Candida albicans* isolated from this specimen was discarded as a contaminant. Subsequent valid specimens exhibited cellular profiles consistent with lower respiratory origin (WBC 35–50/LPF, epithelial cells 5–8/LPF), with persistent isolation of *Burkholderia cepacia* (2/2 cultures). Antimicrobial susceptibility testing indicated sensitivity to meropenem (MIC 4 μg/mL). Electrocardiogram indicated atrial fibrillation. *T.marneffei* was identified in both blood and CSF via metagenomics next-generation sequencing (mNGS) testing three days later. The patient was administered immediate treatment with meropenem (1 g q8 h) and intravenous amphotericin B lipid complex (5 mg/kg/day) for the infection. Imaging findings after one week of treatment are depicted in Table 2 and Fig. 2(b, e, f).

The patient declined biopsy and bronchoscopic examination; however, sputum cytology unexpectedly revealed squamous carcinoma cells (Fig. 3). Considering all examination results, the patient was ultimately diagnosed with disseminated talaromycosis coexisting with squamous carcinoma. Notably, *T.marneffei* was not detected in subsequent, repeated blood and sputum cultures. Two weeks

**Table 1** Clinical timeline of disseminated talaromycosis in an HIV-negative lung cancer patient

| Phase | Timeframe | Symptoms/Signs | Investigations | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Laboratory Examination | | | | | |
| | | | White blood cell count ($\times 10^9$/L) | Neutrophil count ($\times 10^9$/L) | Neutrophil percentage creatinine(%) | Albumin (g/L) | C-reactive protein (μmol/L) | Procalcitonin (ng/mL) |
| Initial Symptoms | Week 1-2 | Skin: right second toe erythema/pain | / | | | | | |
| Systemic Progression | Week 3 | Skin: left lumbar/groin erythema/pain<br>Respiratory: cough,expectorate<br>Systemic: fever | 15.41 | 6.3 | 92.6 | 29 | 90.8 | 3.05 |
| Critical Deterioration | Week 4 | Neurological: stupor<br>Cardiac: atrial fibrillation<br>Respiratory: hypoxia ($SpO_2$ 85%) | 10.01 | 10.08 | 92.8 | 22.8 | 176.8 | 30.58 |
| Transient Improvement | Week 5-6 | Skin: fading erythema/pain<br>Neurological: clear consciousness | 6.91 | 6.22 | 89.7 | 35 | 12.9 | 0.24 |
| Terminal Decline | Week 7 | Systemic: chills, recurrent fever<br>Organ Failure: oliguria, dyspnea,stupor<br>Hemodynamics: refractory shock | 21.41 | 20.64 | 96.4 | 28.4 | 180.8 | 7.44 |

**Table 1** (continued)

| Phase | Investigations | | | | | | | Interventions |
|---|---|---|---|---|---|---|---|---|
| | Laboratory Examination | | | | | Imaging Findings | | |
| | N-terminal pro b-type natriuretic peptide (pg/mL) | Alanine aminotransferase (U/L) | Aspartate aminotransferase (U/L) | Creatinine (μmol/L) | Others | Chest CT | Brain CT/MRI | |
| Initial Symptoms | | | | | | | | / |
| Systemic Progression | 10675 | 11 | 16 | 295.5 | / | A mass in the posterior segment of the upper left lung and multiple small nodules in both lungs. | / | Piperacillin-tazobactam(4.5 g q8h) ×7 days |
| Critical Deterioration | 12845 | 55 | 58 | 469 | Blood/CSF mNGS: *T. marneffei*<br>CSF: Appearance clear and colorless, Pandy's test positive (+), white blood cell count 0.011×10^9/L, mononuclear cells 7.4%, polymorphonuclear cells 92.6%, red blood cells 0.00×10^12/L; aspartate aminotransferase 20 U/L, creatine kinase 3.9 U/L, glucose 3.9 mmol/L, chloride 122.2 mmol/L, adenosine deaminase 2 U/L, CSF protein 0.39 g/L; cytology: no abnormalities detected.<br>Sputum culture: *Burkholderia cepacia* and *Candida albicans*. | A mass in the upper left lung and multiple nodules in both lungs. Bilateral pleural effusion and inflammation in both lower lungs (Fig. 2a). | CT: Multiple intracranial masses (Fig. 2d) | Amphotericin B lipid complex (5 mg/kg/day) ×20 days+ Meropenem (1 g q8h)×10 days |
| Transient Improvement | 5641 | 21 | 15 | 165.9 | Sputum cytology: squamous carcinoma cells | (Week 5) A mass in the upper left lung and multiple nodules in both lungs, with bilateral pleural effusion slightly reduced from before, with no other significant changes (Fig. 2b).<br>(Week 6) The mass in the upper left lung and multiple nodules in both lungs were similar to previous findings, with a small amount of pleural effusion in the left side slightly reduced from before, with the rest remaining unchanged (Fig. 2c). | CT: Similar to previous findings (Fig. 2e).<br>MRI: Multiple plaques and nodular lesions in the bilateral centrum semiovale, basal ganglia, and left temporal (Fig. 2f). | |
| Terminal Decline | 81081 | 1391 | 7010 | 422 | Blood cultures: *Escherichia coli* | / | | tienam(1 g q8h) + Vancomycin (20 mg/kg q12h)×4 days |

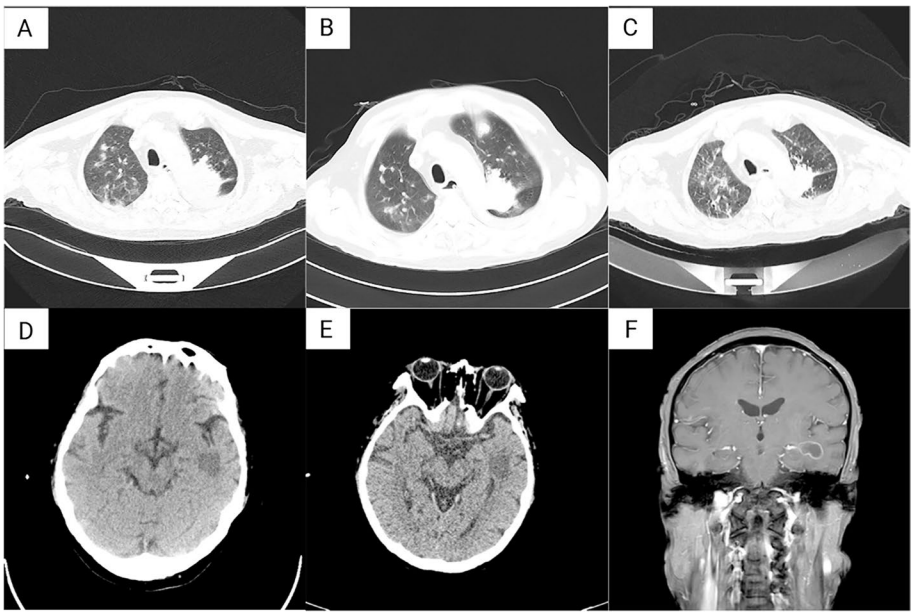


**Fig. 2** **a** Chest CT (Week 4): A mass in the upper left lung and multiple nodules in both lungs. Bilateral pleural effusion and inflammation in both lower lungs. **b** Chest CT (Week 5): Bilateral pleural effusion slightly reduced from before, with no other significant changes. **c** Chest CT (Week 6): A small amount of pleural effusion in the left side slightly reduced from before, with the rest remaining unchanged. **d** Brain CT (Week 4): Multiple low-density nodules were seen in the brain parenchyma, and the largest size was about 1.9 cm × 2.0 cm, which was located in the left temporal lobe. **e** Brain CT (Week 5): Similar to the previous, no significant changes. **f** MRI of the brain with contrast (Week 5): Multiple plaques and nodular lesions in the bilateral centrum semiovale, basal ganglia, and left temporal lobe

post-treatment, the patient's fever resolved, consciousness cleared, and significant improvement in the redness, swelling, and pain in the right toe and left lumbar region was observed, (Fig. 1c, d) enabling him to get out of bed and perform simple activities. The chest CT scan remained largely unchanged (Fig. 2c). However, 1 week later, the patient's condition worsened, marked by the onset of chills and high fever, with temperatures reaching up to 39 °C. Blood cultures yielded growth of *Escherichia coli*. Despite the addition of tienam (1 g q8 h) and vancomycin (20 mg/kg q12 h) to the treatment regimen, the patient developed oliguria, hypotension, worsening hypoxemia, clouded consciousness, and progressive hepatic/renal failure. The family declined further treatment, and the patient succumbed shortly after discharge.

## Discussion

*Talaromyces marneffei* (*T. marneffei*) is a pathogenic thermally dimorphic fungus originating from Southeast Asia. In its natural environment, the fungus grows as a saprophytic mold, but transforms into a pathogenic yeast form at mammalian physiological temperatures (37 °C). Previous studies have indicated that human infection may occur through the inhalation of conidia of *T. marneffei*conidia from soil, with cutaneous and gastrointestinal routes also considered potential pathways for infection [3]. In this case, the patient's occupation (farmer), foot trauma history, and symptom resolution post-antifungal therapy strongly suggest a cutaneous route of entry. While *T. marneffei*infection has been historically associated with HIV/AIDS, its prevalence among HIV-positive populations has declined owing to improved treatments. In contrast, reports of non-HIV-associated talaromycosis in immunocompromised individuals, including those with various types of immunodeficiencies, malignancies, autoimmune diseases, and following organ transplants, are on the rise [4]. Notably, both lung cancer and *T. marneffei* infection exhibit overlapping pulmonary symptoms, such as fever, cough, expectoration, and lymphadenopathy, which complicates differential diagnosis. Despite this clinical challenge, research into the co-infection is limited to case reports, with a paucity of large-scale studies. To address this gap, we conducted searches using terms "*Penicillium/Penicillium Marneffei/Marneffei*/Talaromycosis/*Talaromyces Marneffei/T.marneffei*" and "lung cancer/carcinoma/malignant tumor/tumors" in Chinese databases (Wanfang Med Online and CNKI) and PubMed from January 1970 to November 2024. Seven relevant case reports were identified, with cases having incomplete data being excluded. We included a total of eight cases of concurrent lung cancer and

**Table 2** Clinical features of patients with talaromycosis complicated with lung cancer between 1970 and 2024

| | | | |
|---|---|---|---|
| General Information | Age | Age Range | 50–76 years |
| | | median Age | 59 years |
| | Gender | male | 6 (75%) |
| | | female | 2(25%) |
| | Location of patients | traditional epidemic area (southern China) | 7(87.5%) |
| | | non-traditional epidemic area (the State of California, USA) | 1(12.5%) |
| | long-term smoking history | yes | 6 (75%) |
| | | not mentioned | 2 (25%) |
| Symptoms | | cough | 8 (100%) |
| | | fever | 4(50%) |
| | | chest pain | 2 (25%) |
| | | shortness of breath after activity | 2(25%) |
| | | weight loss | 2(25%) |
| | | dyspnea | 2(25%) |
| | | swollen lymph nodes | 1(12.5%) |
| | | skin manifestations (redness, swelling and heat pain) | 1(12.5%) |
| | | cataphora | 1(12.5%) |
| human immunodeficiency virus (HIV) | | negative | 8 (100%) |
| | | positive | 0 |
| Anti-IFN-γ autoantibodies (AIGA) | | negative | 1(12.5%) |
| | | positive | 2 (25%) |
| | | not mentioned | 5(62.5%) |
| Serum (1, 3)-beta-D-glucan (G) test | | negative | 5(62.5%) |
| | | positive | 1(12.5%) |
| | | not mentioned | 2 (25%) |
| Serum galactomannan (GM) test | | negative | 4(50%) |
| | | positive | 2 (25%) |
| | | not mentioned | 2 (25%) |
| Bronchoalveolar lavage fluid (BALF) Galactomannan (GM) test | | positive | 2 (25%) |
| | | not mentioned | 6 (75%) |
| CT | | mass | 4(50%) |
| | | nodule | 5(62.5%) |
| | | pleural effusion | 4(50%) |
| | | shadows | 3(37.5%) |
| | | pulmonary cavity | 2 (25%) |
| | | pleural thickening | 1(12.5%) |
| | | hilar lymph node enlargement | 1(12.5%) |
| | | mediastinal lymph node enlargement | 2 (25%) |
| Diagnostic Methods | Talaromycosis | sputum culture | 2 (25%) |
| | | blood culture | 0 |
| | | lung biopsy<br>tissue culture | 2 (25%) |
| | | bronchoalveolar lavage fluid (BALF) cultures | 1(12.5%) |
| | | BALF metagenomics next-generation sequencing (mNGS) | 1(12.5%) |
| | | blood mNGS | 1(12.5%) |
| | | cerebrospinal fluid mNGS | 1(12.5%) |
| | | Several yeast-like organisms with red cell wall and clear PAS-negative cell content were identified in the biopsy tissue | 1(12.5%) |
| | Lung cancer | transbronchial lung biopsy (TBLB) | 5(62.5%) |
| | | lung puncture biopsy | 2 (25%) |
| | | Sputum cytology found squamous cell carcinoma cells | 1(12.5%) |

**Table 2** (continued)

| | | |
|---|---|---|
| Comorbidities | diabetes | 3(37.5%) |
| | hypertension | 2 (25%) |
| | atrial fibrillation | 2 (25%) |
| | chronic obstructive pulmonary disease | 1(12.5%) |
| | latent tuberculosis | 1(12.5%) |
| Side effects of Amphotericin B (A total of 6 patients were treated with Amphotericin) | renal impairment | 2(33.3%) |
| | infusion reaction | 1(16.7%) |
| | hypokalemia | 1(16.7%) |
| | not mentioned | 2(33.3%) |
| Clinical Outcomes | Improved | 4(50%) |
| | Deceased | 4(50%) |

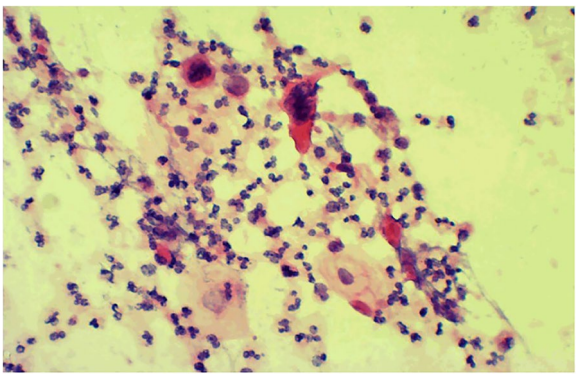

**Fig. 3** Sputum cytology revealed squamous carcinoma cells

talaromycosis, one of which was reported by our team (Fig. 4). Our analysis aims to synthesize epidemiological, diagnostic, and therapeutic patterns in order to enhance the clinical management of this complex comorbidity (Table 2).

### Epidemiology

Our study highlights distinct epidemiological patterns in the co-occurrence of lung cancer and talaromycosis. The male predominance, likely linked to agricultural occupations and higher smoking rates [5], and advanced median age suggest occupational exposure and cumulative risk factors as key drivers. Notably, most cases were clustered in Southern China, a historical endemic zone for *T. marneffei* [6]. However, one patient who had been residing in California long-term, with neither a history of active animal exposure nor travel to Asia, (Fig. 5) aligns with recent reports of talaromycosis in non-endemic regions, such as Northern China, Australia, France, and Germany [7]. This expansion, likely driven by global mobility, underscores that a lack of travel history alone cannot exclude infection—clinicians must consider local exposure risks and host immunosuppression even in non-traditional settings.

### Clinical manifestations

We found that cough (100%) and fever (50%) are the most common symptoms in patients, with other symptoms including chest pain, shortness of breath after activity, weight loss, dyspnea, swollen lymph nodes, cataphora, and skin manifestations such as redness, swelling, and heat pain. Chest CTs in patients most commonly show nodules, masses, pleural effusion, and can also reveal pulmonary cavities, pleural thickening, hilar lymph node enlargement, and mediastinal lymph node enlargement. This demonstrates that *T. marneffei* infection and lung cancer exhibit highly similar clinical manifestations and chest imaging findings. Differentiating between the infection and tumor presence based on these aspects is extremely challenging and contributes significantly to both misdiagnosis and delayed diagnosis.

### Risk factors

Our analysis revealed a critical shift in understanding *T. marneffei* infection risk: all patients diagnosed with concurrent lung cancer were HIV-negative, challenging the historical link between talaromycosis and AIDS. This finding strongly suggests that lung cancer itself may act as an independent risk factor, potentially through tumor-induced immunosuppression rather than traditional HIV-associated pathways. Notably, the first reported case of this co-infection only emerged in 2016 (Fig. 6), likely due to previous diagnostic limitations that led to under-recognition and fatal treatment delays. Importantly, two fatal cases in our cohort tested positive for anti-IFN-γ autoantibodies (AIGA), a marker of adult-onset

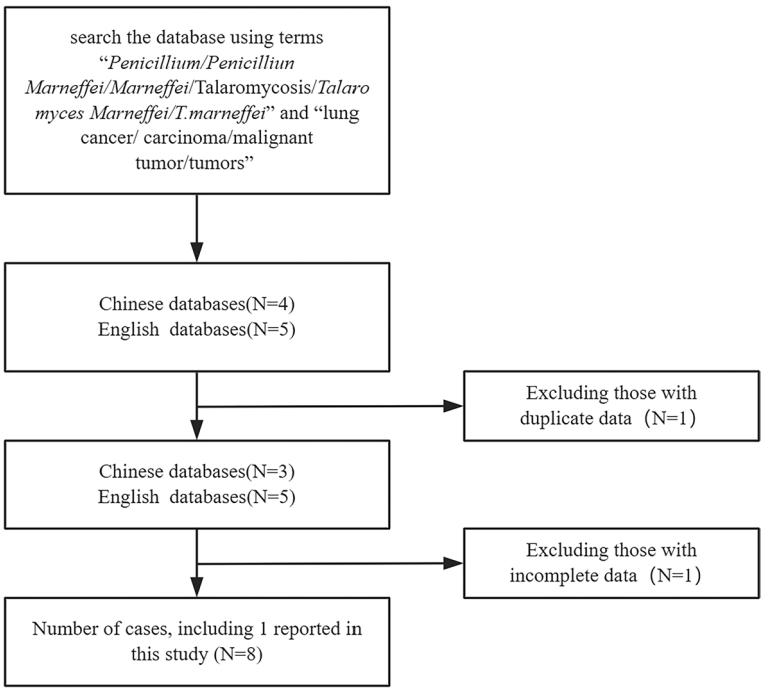


**Fig. 4** Flowchart of literature screening and selection process of patients with talaromycosis complicated with lung cancer between 1970 and 2024


**Fig. 5** Geographic distribution and countries of reported cases of patients with talaromycosis complicated with lung cancer

immunodeficiency associated with severe fungal infections [8, 9]. Recent studies demonstrate 94.8% AIGA positivity in HIV-negative talaromycosis patients, with 46.7% exhibiting concurrent opportunistic infections [10, 11]. underscoring the necessity of routine AIGA screening to assess immune status. Therefore, it is necessary to screen for the presence of AIGA in patients with talaromycosis complicated with lung cancer to comprehensively evaluate the immune status of patients. Intriguingly, the proteasome inhibitor bortezomib shows dual therapeutic promise: it not only reduces AIGA levels to improve fungal infection outcomes but also enhances the efficacy of chemotherapy in lung cancer treatment, offering a potential combined therapeutic strategy [12, 13]. Among comorbidities, diabetes (37.5% prevalence) emerged as a key predisposing factor, likely due to hyperglycemia-induced impairment of neutrophil function and enhanced fungal proliferation [14], while other

conditions (hypertension, atrial fibrillation, etc.) showed less clear associations. Crucially, talaromycosis diagnosis preceded or coincided with lung cancer detection in all cases, in stark contrast to hematologic malignancies, where 73% of fungal infections occur post-chemotherapy [4]. This temporal pattern further supports lung cancer's unique role in predisposing to *T. marneffei* infection, independent of iatrogenic immunosuppression, and highlights the need for heightened clinical vigilance in this patient population.

### Diagnosis

Previous studies have indicated that β-D-glucan (BDG), a cell wall polysaccharide found in most fungi, is a significant non-culture-based method for diagnosing invasive fungal disease [15]. Galactomannan (GM) is a heteropolysaccharide found in the cell walls of most *Aspergillus* and *Talaromyces*, which consists of a non-immunogenic mannose backbone and an immunogenic galactose side chain [16]. Both BDG and GM are reliable clinical indicators that can effectively identify fungal infections, especially *T.marneffei*. However, these two non-culture diagnostic methods showed limited utility in our cohort. While BDG positivity reaches 50% in HIV-negative pediatric talaromycosis [17], only 12.5% of our patients tested positive—a discrepancy that may stem from cancer-induced fungal growth suppression or sampling bias. Similarly, serum GM sensitivity (25%) was lower than previous reported values (57% in HIV-negative talaromycosis patients without fungemia) [18]. However, combining BALF GM testing improved detection, as seen in one patient with negative serum but positive BALF results. These findings collectively suggest that multisite sampling is critical to enhance diagnostic yield.

Given the limitations of biomarker assays, definitive diagnosis primarily depended on culture (sputum, BALF, biopsy) and metagenomic next-generation sequencing (mNGS). Notably, mNGS demonstrated superior accuracy (100% sensitivity, 98.7% specificity), particularly for cases with initial false-negative biopsies, underscoring its value in detecting rare or slow-growing pathogens [19, 20]. We found that many patients had negative blood and sputum cultures, but switching to other specimens (such as BALF) for culture or using mNGS yielded positive results. Therefore, performing multiple cultures from different sites alongside mNGS has great value in the early and rapid diagnosis of these patients, contributing to timely treatment and ultimately improving prognosis. As previously mentioned, almost all patients were diagnosed with lung cancer later than *T. marneffei* infection. Some patients were diagnosed with lung cancer after being readmitted due to recurring fever and chest pain symptoms despite improvement from antifungal treatment. This may be due to smaller initial lesions leading to false negatives in pathology, while larger lesions at a later stage increase the rate of positive pathology findings. Crucially, earlier dual diagnosis of talaromycosis and lung cancer correlated with better survival outcomes. Therefore, after diagnosing talaromycosis, we should not easily dismiss the possibility of lung cancer based on a single biopsy result. Instead, multiple biopsies from various sites should be conducted to ascertain whether lesions have different characteristics, especially when the patient responds poorly to antifungal treatment (Table 3).

### Treatment

Current therapeutic approaches for talaromycosis complicated by lung cancer are still extrapolated from HIV-associated cases, with a lack of specific guidelines. The standard regimen involving amphotericin B carries significant risks, with 67% of patients requiring alternative therapies due to complications including renal impairment, infusion-related reactions, and hypokalemia. Notably, research reports that Voriconazole and Itraconazole are safe in treating talaromycosis patients, and their efficacy matches that of Amphotericin B [4]. We found that

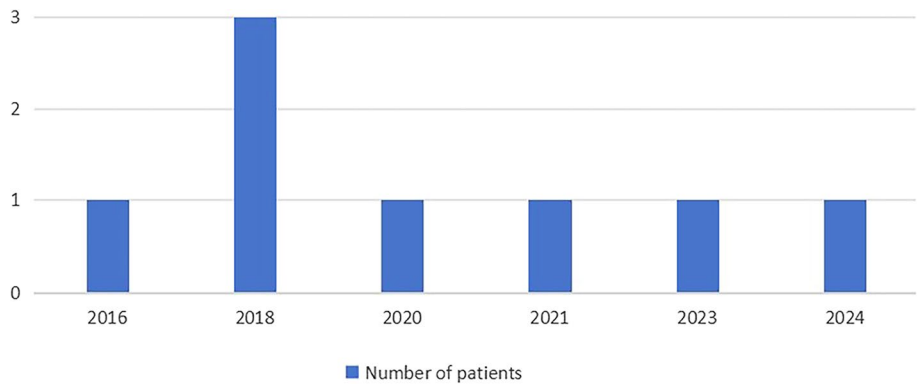


**Fig. 6** Annual reports and case numbers of patients with talaromycosis complicated with lung cancer

**Table 3** The diagnostic methods, timing, treatment and prognosis in eight patients with talaromycosis complicated with lung cancer

| Case | Method of diagnosis (Talaromycosis) | Method of diagnosis (Lung cancer) | Diagnosis time of Talaromycosis (after admission, days) | Diagnosis time of lung cancer (after the diagnosis of Talaromycosis, days) | Primary Tumor Types | Treatment(Talaromycosis) | Treatment (Lung cancer) | Clinical Outcomes | Reference |
|---|---|---|---|---|---|---|---|---|---|
| 1 | culture (blood culture negative,lung biopsy tissue culture positive) | transbronchial lung biopsy (TBLB) | 77 | 225 | adenocarcinoma | Amphotericin B 13 days + Voriconazole 0.2 g q12 h | / | death | [8] |
| 2 | culture (transbronchial lung biopsy) | lung puncture biopsy | 13 | 281 | adenocarcinoma | Voriconazole 0.2 g q12 h + Amphotericin B 30 mg/day × 9 days +Itraconazole 0.1 g q12 h | icotinib | death | [21] |
| 3 | Several yeast-like organisms with red cell wall and clear PAS-negative cell content were identified in the biopsy tissue (whereas blood and sputum cultures negative) | transbronchial lung biopsy (TBLB) | / | almost simultaneously | Pulmonary lymphoepithelioma-like carcinoma (LELC) | Voriconazole 0.2 g q12 h + Itraconazole | Five cycles of docetaxel (120 mg) and carboplatin (600 mg) were followed by oral administration of apatinib | improved | [22] |
| 4 | culture (bronchoalveolar lavage fluid,BALF) | transbronchial lung biopsy (TBLB) | / | / | Squamous cell carcinoma | Amphotericin B + Posaconazole | / | death | [23] |
| 5 | culture (sputum) | transbronchial lung biopsy (TBLB) | < 12 | almost simultaneously | adenocarcinoma | Amphotericin B increased by 5 to 40 mg/day +Itraconazole | icotinib | improved | [24] |
| 6 | culture (sputum) | lung puncture biopsy | 9 | almost simultaneously | adenocarcinoma | individual use of Amphotericin B | / | improved | [25] |
| 7 | bronchoalveolar lavage fluid (BALF) metagenomics next-generation sequencing (mNGS) (whereas sputum cultures negative) | transbronchial lung biopsy (TBLB) | 5 | 90 | adenocarcinoma | Voriconazole 0.2 g q12 h × 3 months | radical operation of lung cancer | improved | [26] |
| 8 | blood and cerebrospinal fluid mNGS (whereas blood and sputum cultures negative) | Sputum cytology found squamous cell carcinoma cells | 3 | 15 | Squamous cell carcinoma | individual use of Amphotericin B 5 mg/kg/day× 20 days | / | death | this paper |

voriconazole monotherapy or itraconazole combination regimens achieved clinical improvement in 25% of cases without reported adverse events, demonstrating the reliability of this treatment plan.

Regarding oncologic management, 49% of patients died before initiating cancer-directed therapy, highlighting the critical importance of early malignancy detection. This mortality pattern underscores the necessity for coordinated diagnostic protocols addressing both infectious and neoplastic processes simultaneously.

## Conclusions

Through reports and retrospective analyses of patients with talaromycosis complicated with lung cancer, we have reexamined many previous notions [8, 21–26]. We recommend that for patients suspected of having a fungal lung infection, even if they are not in traditional endemic areas of *T. marneffei* infection, testing for HIV and AIGA should be conducted, along with multiple cultures from different sites, combined with mNGS to enhance diagnostic accuracy. Given the highly similar clinical presentations of patients with talaromycosis and lung cancer, which can lead to missed or incorrect diagnoses and contribute to the high mortality rate among these patients. Therefore, after a diagnosis of *T. marneffei* infection, lung cancer should not be prematurely ruled out based on a single biopsy result. Instead, multiple biopsies from various sites should be conducted, especially when a patient's response to antifungal treatment is poor. In treatment, due to the potential side effects of Amphotericin B, a treatment regimen of either Voriconazole alone or in combination with Itraconazole should be considered. We believe that through these measures, with effective control of the infection and timely diagnosis and treatment of lung cancer, the prognosis for patients can be significantly improved.

### Abbreviations

| | |
|---|---|
| HIV | Human immunodeficiency virus |
| AIDS | Acquired immune deficiency syndrome |
| *T.marneffei* | *Talaromyces marneffei* |
| CT | Computed tomograph |
| mNGS | Metagenomics next-generation sequencing |
| AIGA | Anti-IFN-γ autoantibodies |
| HAART | Highly active antiretroviral therapy |
| MRI | Magnetic resonance imaging |
| CSF | Cerebrospinal fluid |
| BDG | β-D-glucan |
| GM | Galactomannan |
| BALF | Bronchoalveolar lavage fluid |
| TBLB | Transbronchial lung biopsy |

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### Clinical trial

Not applicable.

### Authors' contributions

HH, LC and XX conceived the review and wrote the first draft. KZ, QH and AQ generated the tables. HF and YL generated the figures. BX and WP reviewed and revised the updated version of the manuscript and improved the corresponding descriptions. All authors read and approved the final manuscript.

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### Data availability

All relevant data to this case are included within the article.

## Declarations

### Ethics approval and consent to participate

Not applicable.

### Consent for publication

The authors affirm that human research participants provided informed consent for publication of the article and images.

### Competing interests

The authors declare no competing interests.

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