

Talaromyces marneffe infection in non-HIV-infected patients in mainland China

Liya He^{1,2}  | Xin Mei³ | Sha Lu² | Jianchi Ma² | Yongxuan Hu⁴ | Dongdong Mo¹ | Xinsheng Chen¹ | Ruiqiang Fan¹ | Liyan Xi^{2,5} | Ting Xie¹

¹Department of Dermatology, The Second Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou, China

²Department of Dermatology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China

³Department of Neurosurgery, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China

⁴Department of Dermatology and Venereology, The 3rd Affiliated Hospital of Southern Medical University, Guangzhou, China

⁵Dermatology Hospital of Southern Medical University, Guangzhou, China

Correspondence

Liyan Xi, Department of Dermatology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, 510120, Guangzhou, China.
Email: xiliyan@mail.sysu.edu.cn

Ting Xie, Department of Dermatology, The Second Affiliated Hospital of Guangzhou University of Chinese Medicine, 510120, Guangzhou, China.
Email: drxieting@126.com

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Abstract

Background: *Talaromyces marneffe*, formerly known as *Penicillium marneffe*, is a significant emerging pathogenic fungus in Southeast Asia which can generate life-threatening systemic infections. Human immunodeficiency virus (HIV) infection is considered as the most underlying disease among systemic infections. However, infections due to *T. marneffe* without HIV are increasing in recent years.

Objectives: Research the characteristics of *T. marneffe* infection in non-HIV individuals in mainland China.

Methods: In this study, we searched Pubmed, China National Knowledge Infrastructure (CNKI) and WanFang from inception to 31 December 2019 for studies reporting *T. marneffe* infection. Our research concentrates on non-HIV-infected cases and their epidemiology, clinical manifestations, laboratory findings, treatment methods and prognosis.

Results: *T. marneffe* infections in non-HIV individuals are increasing. Due to frequent present with atypical symptoms, these non-HIV-infected cases were usually misdiagnosed as other diseases, containing tuberculosis (80.7%), bacterial pneumonia (20.5%), lung cancer (5.1%) or other diseases (5.1%).

Conclusions: *T. marneffe* infection in non-HIV individuals should be taken seriously. Their symptoms and signs are not typical. Accurate diagnosis and timely antifungal agent treatment is the key to the treatment for the disease.

KEYWORDS

AIDS, epidemiology, *Penicillium marneffe*

1 | INTRODUCTION

Talaromyces, an infection caused by a thermally dimorphic fungus *Talaromyces marneffe*, is an emerging and endemic disease in areas of South East Asia,¹ particularly Thailand,² India, Vietnam and southern

China.^{3,4} At present, it is believed that bamboo rats and their living environment are significant sources of *T. marneffe*.⁵ Since the first case of *T. marneffe* infection was reported in 1973,⁶ the disease had been recognised by humans. From then on, a noticeable increase in the number of infection due to *T. marneffe* has been observed. Most infections occurred in individuals with HIV, and the primarily reason

Liya He and Xin Mei contributed equally to this work.

accounting for the increase in the number of cases is HIV pandemic.⁷ Infections caused by *T. marneffeii* have become one of the common AIDS-defining illnesses in endemic areas.

Previously, our group reviewed totally 668 cases of infection due to *T. marneffeii* in mainland China from January 1984 to December 2009.⁸ It could be found that approximately 99.4% of the cases were reported in the southern part of China. HIV infection was therefore regarded as the most underlying disease (87.72%). Common clinical manifestations of infection caused by *T. marneffeii* included fever, weight loss, anaemia, lymphadenopathy, hepatosplenomegaly, respiratory signs and skin lesions. Additionally, amphotericin B, itraconazole and voriconazole, which are used alone or in combination with other agents, were the most frequently administered first-line therapies.

However, in recent years, the number of *T. marneffeii* infections has increased dramatically in HIV-negative patients,^{9,10} immunocompromised or non-immunocompromised population. Their clinical symptoms and laboratory examination remained obscure, leading to misdiagnosis and delayed diagnosis. The emerging patients of non-HIV-infected who are infected by *T. marneffeii* should not be ignored. As a result, we reviewed the characteristics and clinical features of *T. marneffeii* infection in non-HIV-infected patients in mainland China, from 2001 to 2019.

2 | MATERIALS AND METHODS

2.1 | Study design

To investigate the characteristics of infection due to *T. marneffeii* in non-HIV-infected patients in mainland China, we performed an evidence-based review of published literature. China National Knowledge Infrastructure (CNKI) (<http://cnki.net/>), Wanfang (<http://www.wanfangdata.com.cn/>) and PubMed data from inception to December 2019 were searched.

2.2 | Procedures

We systematically searched Pubmed, CNKI and WanFang from inception to 31 December 2019, for research articles published in both the English and Chinese languages. Search terms contained '*Talaromyces marneffeii*', '*Penicillium marneffeii*', '*marneffeii*', 'penicilliosis' or 'talaromycosis' cross-referenced with 'China'. Proven infection was considered based on the international consensus by Defining Opportunistic Invasive Fungal Infections in Immunocompromised Patients with Cancer and Hematopoietic Stem Cell Transplants¹¹: clinical signs and symptoms, as well as positive for *T. marneffeii* by direct smear, culture or histopathology. An article was included in our research if it could satisfy the following criteria: (1) *T. marneffeii* was identified by direct smear, culture or histopathology; (2) the clinical syndrome was in consistent with infection; (3) the patient was HIV-negative and (4) available data with clinical manifestations,

laboratory findings, treatment and outcomes. We excluded articles if (1) they were reviews or duplicate studies and (2) research objects were animals. We extracted the following information from each eligible case including age, sex, underlying disease, personal history, misdiagnosed diseases, clinical signs, laboratory findings, antifungal treatment, outcome, reported year and distribution.

2.3 | Statistical analysis

We employed the χ^2 test or Fisher's exact test for categorical variables to compare covariates between groups. *p* values of < .05 were considered statistically significant. All statistical calculations were performed based on Statistical Product and Service Solutions (SPSS, version 20).

3 | RESULTS

With the subject term, from inception to December 2019, by removing the undesirable literatures, 96 articles with a total of 162 cases were analysed (Figures 1 and 2). The infection showed a sex bias

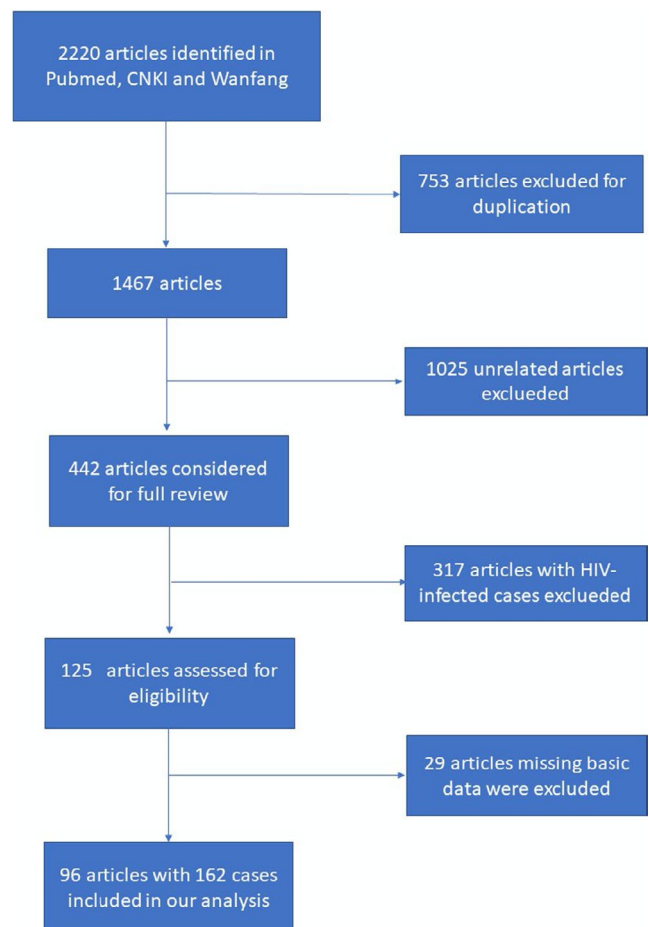


FIGURE 1 Flow diagram of literature search and article selection in this study

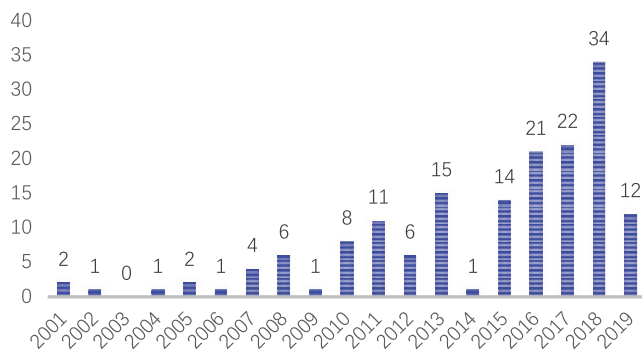


FIGURE 2 Cases of *Talaromyces marneffeii* infection in non-HIV patients reported from inception to 31 December 2019 in mainland China

with a ratio of 2.84:1, when comparing male with female (114–48) and child with adult (38–124), with the mean age of 37.0 years (ranging from 3 months to 80 years). There were 51 cases (31.48%) with underlying disease and 111 cases (68.52%) without any documented underlying disease (Table 1).

3.1 | Epidemiological features

The infection has been reported from 16 provinces of Mainland China with higher prevalence in Guangxi Province (47 cases, 29.0%) and Guangdong Province (41 cases, 25.3%) (Figure 3).

3.2 | Clinical manifestations and laboratory findings

After analysing the cases without HIV infection, from 2001 to 2019, we concluded that common manifestations of non-HIV-infected patients included respiratory signs (85.19%), fever (82.71%), lymphadenopathy (66.04%), skin lesions (53.08%), anaemia (44.44%), hepatosplenomegaly (37.65%), weight loss (29.01%) and osteolysis (24.69%) (Table 2). Laboratory examination of the *T. marneffeii* infections without HIV-infected could be found in Table 3. Surprisingly, among the recorded 78 misdiagnosed cases of without HIV infection, 63 cases (80.77%) were misdiagnosed as tuberculosis, 16 cases (20.51%) were misdiagnosed as bacterial pneumonia, 4 cases (5.13%) were misdiagnosed as lung cancer, and 4 cases (5.13%) were misdiagnosed as other diseases.

3.3 | Treatment and prognosis

Once diagnosed with *T. marneffeii* infection, amphotericin B, itraconazole, fluconazole and voriconazole were regarded as most frequently administered first-line therapies. There was existed no significant difference in the rates of favourable outcome between patients treated with these four medicines. Among all the

TABLE 1 Underlying diseases in cases of *Talaromyces marneffeii* infection without HIV-infected

| Underlying diseases | Number of patients (%) (n = 51) |
|--------------------------------|---------------------------------|
| Diabetes | 8 (15.69%) |
| Tumour | 7 (13.73%) |
| Kidney transplantation | 7 (13.73%) |
| Tuberculosis | 7 (13.73%) |
| SLE | 4 (7.84%) |
| HBV infection | 2 (3.92%) |
| Schistosomiasis | 2 (3.92%) |
| HCV infection | 2 (3.92%) |
| COPD | 2 (3.92%) |
| Scleroderma | 1 (1.96%) |
| Asthma | 1 (1.96%) |
| Neuromyelitis | 1 (1.96%) |
| Dermatomyositis | 1 (1.96%) |
| Cerebral haemorrhage | 1 (1.96%) |
| Cushing's syndrome | 1 (1.96%) |
| Interstitial pneumonia | 1 (1.96%) |
| Thyroiditis | 1 (1.96%) |
| Hyperimmunoglobulin E syndrome | 1 (1.96%) |
| Hyperimmunoglobulin M syndrome | 1 (1.96%) |
| Cirrhosis | 1 (1.96%) |

Abbreviations: COPD, chronic obstructive pulmonary disease; SLE, systemic lupus erythematosus.

non-HIV-infected individuals, 106 (65.43%) were cured or recovered, 53 (32.72%) of them died and 3 (1.85%) patients had no follow-up. The most popular treatment method referred to amphotericin B combined with itraconazole. Table 4 presented different combinations of antifungal agents and their curative effect of non-HIV-infected cases.

4 | DISCUSSION

T. marneffeii is thermally dimorphic fungus and an intracellular pathogen that causes disseminated, progressive and life-threatening systemic mycosis, which is becoming an emerging infection in mainland China. Our research demonstrated that *T. marneffeii* infection without HIV is prevalent in southern China, and most cases were reported from Guangxi, Guangdong, Jiangxi, Zhejiang and Fujian Province. Bamboo rats and their living environment are known to be significant sources of *T. marneffeii*.¹² There are 5 patients in our research with personal history of contacting or eating bamboo mice. However, there are other patients who had not touched the bamboo rats or had not travelled to the endemic area. It can be assumed that there might be other routes of transmission of *T. marneffeii* infection.¹³

FIGURE 3 Cases distribution of *Talaromyces marneffe* infection without HIV-infected in mainland China (2001–2019)

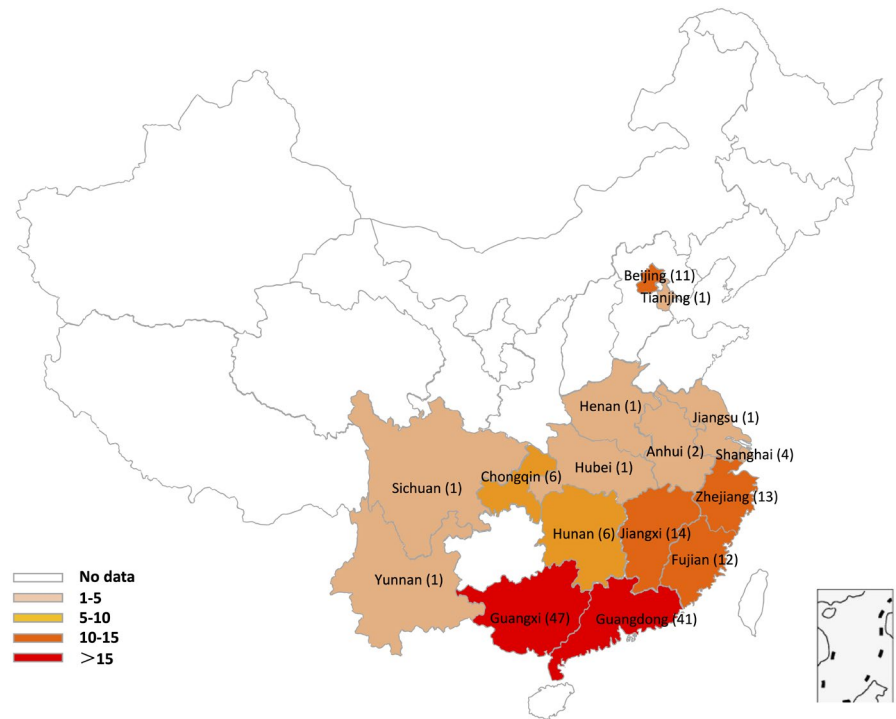


TABLE 2 Clinical manifestations of the *Talaromyces marneffe* infections without HIV-infected

| Clinical manifestations | Positive | Abnormality (%) (n = 162) |
|-------------------------|----------|------------------------------|
| Respiratory signs | 138 | 85.19 |
| Fever | 134 | 82.72 |
| Lymphadenopathy | 107 | 66.05 |
| Skin lesions | 86 | 53.09 |
| Anaemia | 72 | 44.44 |
| Hepatosplenomegaly | 61 | 37.65 |
| Weight loss | 47 | 29.01 |
| Osteolysis | 40 | 24.69 |

The first case of infection due to *T. marneffe* in China was reported in 1984.¹⁴ Before 2001, few people knew talaromycosis and reported cases usually did not undergo HIV antibody test. As an increasing number of cases were reported, researchers found its close connection with AIDS. In the meanwhile, as shown in Figure 2, infections due to *T. marneffe* without HIV are also increasing in recent years. Our research object involved reported cases, and there were numerous unpublished cases with missing data. Moreover, we believe that certainly a large quantity of cases might be diagnosed. One of the reasons might be that *T. marneffe* infection had not been highly recognised by physician and other health officials. A large number of physicians consider that only AIDS patients could be infected with *T. marneffe*, which might lead to the ignorance of some non-HIV-infected cases. Another reason is the symptoms and signs of non-HIV-infected patients were not typical, which were confused with other diseases.

TABLE 3 Laboratory examination of the *Talaromyces marneffe* infections without HIV-infected

| Laboratory examination | Positive | Total | Abnormality (%) |
|------------------------------|----------|-------|-----------------|
| Haemoglobin decreased | 59 | 162 | 36.42 |
| Thrombocytopenia | 21 | 162 | 12.96 |
| Leukocytosis | 83 | 162 | 51.23 |
| Leukopenia | 12 | 162 | 7.41 |
| AST increased | 54 | 156 | 34.62 |
| ALT increased | 51 | 156 | 32.69 |
| Albumin decreased | 75 | 156 | 48.08 |
| CD4 ⁺ T decreased | 21 | 28 | 75.00 |
| Culture | | | |
| Blood | 28 | 94 | 29.79 |
| Marrow | 18 | 67 | 26.87 |
| Purulence or tissue | 54 | 63 | 85.71 |
| Bronchoalveolar lavage fluid | 48 | 62 | 77.42 |

There were totally 51 non-HIV-infected cases in our study which were recorded with other underlying disease. Clinicians found that immunodeficiency is closely associated with *T. marneffe* infection.^{15,16} Their immunodeficiency may due to other autoimmune diseases,¹⁷ organ or hematopoietic stem cell transplantations,¹⁸ immunosuppressive drugs and novel anti-cancer targeted therapies.¹⁹ Qiu et al. suggested that HIV-negative individuals with underlying disease had a worse prognosis and higher mortality rate than those without underlying disease.²⁰ In the current study, there were 32 patients presenting immunocompromised conditions. Without

| Antifungal agent | Outcome | | | Rates of good outcome (%) |
|------------------|--------------------|------|-------------------|---------------------------|
| | Cured or recovered | Dead | Lost to follow-up | |
| AMB | 10 | 11 | 0 | 47.62 |
| ITC | 14 | 2 | 0 | 87.50 |
| FLU | 1 | 3 | 0 | 25.00 |
| VOR | 24 | 5 | 1 | 80.00 |
| AMB + ITC | 33 | 4 | 0 | 89.19 |
| AMB + FLU | 1 | 0 | 0 | 100 |
| AMB + VOR | 4 | 0 | 1 | 80.00 |
| AMB + ITC + FLU | 6 | 4 | 0 | 60.00 |
| ITC + FLU | 6 | 0 | 0 | 100 |
| ITC + VOR | 2 | 0 | 1 | 66.67 |
| Others | 5 | 7 | 0 | 41.67 |
| No | 0 | 17 | 0 | 0 |
| Total | 106 | 53 | 3 | 65.43 |

TABLE 4 Treatment and outcome of the *Talaromyces marneffe* infections without HIV-infected

Abbreviations: AMB, amphotericin B; FLU, fluconazole; ITC, itraconazole; VOR, voriconazole.

relevant genetic testing data, we cannot distinguish whether these are primary or secondary immune deficiencies. Moreover, 111 non-HIV-infected cases in our study were recorded without other underlying disease, lacking information on their immunological status. At the same time, we could not ensure that their immune function was normal. Pamela et al. explored the clinical features and immunological evaluations of 5 HIV-negative children with *T. marneffe* infection.²¹ All of them had abnormal immune functions at the time of infection. After performing in-depth research, they found that one patient was diagnosed with Hyperimmunoglobulin E syndrome, while another had functional defect in interleukin-12/interferon- γ axis, and three patients underwent lymphopenia with low natural killer cell counts. Consequently, immunological investigations should be performed in those HIV-negative patients with *T. marneffe* infection. Recent studies demonstrated that autoantibody against gamma interferon was linked to infections caused by intracellular organisms, including *T. marneffe*.^{3,22} Although little is known concerning the underlying mechanisms of this syndrome, it is currently believed that this antibody inhibits the activity of the downstream signalling pathway of interferon gamma.²³ In our study, three cases were recorded with autoantibody against gamma interferon status.^{24–26}

The symptoms and signs of talaromycosis without HIV infection were not typical. The three most frequent symptoms included respiratory signs, fever and lymphadenopathy. In comparison with the HIV-infected cases,⁸ we found that non-HIV-infected individuals with less incidence of fever, weight loss, anaemia and hepatosplenomegaly and higher incidence of lymphadenopathy and osteolysis ($p < .05$), which is similar to the characteristics of non-HIV-infected cases in Thailand.²⁷ During the period of disease, there were 86 patients in our research with skin lesions. The skin lesions contain subcutaneous abscess (39.53%), nodule (25.58%), papule (17.44%), ulcerate (15.12%) and erythema (13.95%). The skin lesions of talaromycosis with HIV infection were always described as papule and

ulcerate,^{4,5,7} while non-HIV-infected patients have higher incidence of subcutaneous abscess and nodule. Researchers indicated that skin lesions of talaromycosis could be broadly classified into reactive and infective skin lesions.²⁵ Sweet's syndrome, a kind of reactive skin lesion, was supposed to be associated with *T. marneffe* infection among patients with autoantibody against interferon gamma.²⁶

Based on the data of laboratory examination, we indicated that routine laboratory test results were not specific, which is considered as a significant reason for the difficulty in diagnosis. Through recording 80 misdiagnosed cases of without HIV infection, we calculated that the average time of delay diagnosis was 5.39 months (ranging from 2 weeks to 24 months). Moreover, accurate and timely inspection methods should also be exploited. General laboratory diagnosis is time consuming, despite the exploitation of several tests for early diagnosis.^{28,29} There is a definite need for more accurate, rapid and convenient diagnostic methods in order to help physicians to make correct and fast diagnosis.

Amphotericin B, itraconazole, voriconazole and fluconazole were the most frequently used medicine which can be used to treat *T. marneffe* infection. However, fluconazole has not been recommended as antifungal agent in *T. marneffe* infection therapy in recent decade. Researchers discovered that voriconazole and itraconazole were active against *T. marneffe* isolates in vitro, and fluconazole might have unrealised usefulness in the treatment of infections caused by this yeast form.^{30,31} In the present study, the survival rate of fluconazole alone group was significantly lower than that of other antifungal treatment groups ($p < .01$). The survival rate of the patients treated with antifungal agent was significantly higher than the individuals who were not treated with antifungal agent ($p < .01$), indicating that timely and accurate diagnosis plays a critical role in the treatment of the disease.

Additionally, there were 38 non-HIV children in our research. Compared with the non-HIV adults infected *T. marneffe*, it could be

TABLE 5 Clinical manifestations of the *Talaromyces marneffe* infections without HIV-infected in children and adults

| Clinical manifestations | Children (n = 124) | | Adults (n = 124) | | p values |
|-------------------------|-----------------------|-----------------|---------------------|-----------------|----------|
| | Positive | Abnormality (%) | Positive | Abnormality (%) | |
| Respiratory signs | 34 | 89.50% | 104 | 83.90% | .395 |
| Fever | 34 | 89.50% | 100 | 80.60% | .208 |
| Lymphadenopathy | 20 | 52.60% | 87 | 70.20% | .046 |
| Skin lesions | 8 | 21.10% | 78 | 62.90% | .002 |
| Anaemia | 14 | 36.80% | 58 | 46.80% | .904 |
| Hepatosplenomegaly | 28 | 73.70% | 33 | 26.60% | <.01 |
| Weight loss | 3 | 7.90% | 44 | 35.50% | .012 |
| Osteolysis | 0 | 0 | 40 | 32.30% | — |

found that non-HIV-infected children have less incidence of lymphadenopathy ($p < .05$), skin lesions ($p < .01$) and weight loss ($p < .05$), with higher incidence of hepatosplenomegaly ($p < .01$). The mortality rate of non-HIV-infected children infected *T. marneffe* was higher than that of non-HIV adults ($p < .01$). Moreover, in the present study, mortality rate of non-HIV-infected patients is 32.7%. In our previous study in 2013, the mortality rate of HIV-infected patients is 24.5%. Herein, we believed that the mortality rate of non-HIV-infected patients was higher than that of HIV-infected patients in China ($p < .05$), which is similar to another research.³² (Table 5).

5 | CONCLUSION

To conclude, *T. marneffe* is an intracellular pathogen, which can thus threaten human health. HIV infection is the most frequent underlying disease while the cases without HIV infection should be taken seriously. Their symptoms and signs are not typical. Accurate diagnosis and timely antifungal agent treatment is the key to the treatment for the disease. When patients develop unexplained fever, fatigue, subcutaneous abscesses or other symptoms, and anti-TB treatment is ineffective, we should consider patients with or without *T. marneffe* infection.

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CONFLICT OF INTEREST

All the authors report no potential conflicts of interest. The authors alone are responsible for the content and writing of the paper.

AUTHOR CONTRIBUTION

Liya He: Formal analysis (equal); Resources (equal); Writing-original draft (equal). **Xin Mei:** Data curation (equal); Methodology (equal);

Software (equal). **Sha Lu:** Software (equal); Writing-review & editing (equal). **Jianchi Ma:** Data curation (equal); Software (equal). **Yongxuan Hu:** Investigation (equal); Resources (equal). **Dongdong Mo:** Investigation (equal). **Xinsheng Chen:** Writing-review & editing (equal). **Ruiqiang Fan:** Supervision (equal); Writing-review & editing (equal). **Liyan Xi:** Funding acquisition (equal); Resources (equal); Supervision (equal). **Ting Xie:** Conceptualization (equal); Formal analysis (equal); Investigation (equal); Supervision (equal).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Liya He  <https://orcid.org/0000-0002-7477-5189>

REFERENCES

- Supparatpinyo K, Khamwan C, Baosoung V, Nelson KE, Sirisanthana T. Disseminated *Penicillium marneffe* infection in southeast Asia. *Lancet*. 1994;344(8915):110-113.
- Chariyalertsak S, Supparatpinyo K, Sirisanthana T, Nelson KE. A controlled trial of itraconazole as primary prophylaxis for systemic fungal infections in patients with advanced human immunodeficiency virus infection in Thailand. *Clin Infect Dis*. 2002;34(2):277-284.
- Browne SK, Burbelo PD, Chetchotisakd P, et al. Adult-onset immunodeficiency in Thailand and Taiwan. *N Engl J Med*. 2012;367(8):725-734.
- Duong TA. Infection due to *Penicillium marneffe*, an emerging pathogen: review of 155 reported cases. *Clin Infect Dis*. 1996;23(1):125-130.
- Vanittanakom N, Cooper CR Jr, Fisher MC, Sirisanthana T. *Penicillium marneffe* infection and recent advances in the epidemiology and molecular biology aspects. *Clin Microbiol Rev*. 2006;19(1):95-110.
- DiSalvo AF, Fickling AM, Ajello L. Infection caused by *Penicillium marneffe*: description of first natural infection in man. *Am J Clin Pathol*. 1973;60(2):259-263.
- Ampel NM. Emerging disease issues and fungal pathogens associated with HIV infection. *Emerg Infect Dis*. 1996;2(2):109-116.
- Hu Y, Zhang J, Li X, et al. *Penicillium marneffe* infection: an emerging disease in mainland China. *Mycopathologia*. 2013;175(1-2):57-67.
- Chen M, Houbraken J, Pan W, et al. Pulmonary fungus ball caused by *Penicillium capsulatum* in a patient with type 2 diabetes: a case report. *BMC Infect Dis*. 2013;13:496.

10. Ye F, Luo Q, Zhou Y, et al. Disseminated penicilliosis marneffei in immunocompetent patients: a report of two cases. *Indian J Med Microbiol.* 2015;33(1):161-165.
11. Ascioğlu S, Rex JH, de Pauw B, et al. Defining opportunistic invasive fungal infections in immunocompromised patients with cancer and hematopoietic stem cell transplants: an international consensus. *Clin Infect Dis.* 2002;34(1):7-14.
12. Huang X, He G, Lu S, Liang Y, Xi L. Role of *Rhizomys pruinosus* as a natural animal host of *Penicillium marneffei* in Guangdong, China. *Microb Biotechnol.* 2015;8(4):659-664.
13. Martín-Dávila P, Fortún J, López-Vélez R, et al. Transmission of tropical and geographically restricted infections during solid-organ transplantation. *Clin Microbiol Rev.* 2008;21(1):60-96.
14. Deng ZL, Connor DH. Progressive disseminated penicilliosis caused by *Penicillium marneffei*. Report of eight cases and differentiation of the causative organism from *Histoplasma capsulatum*. *Am J Clin Pathol.* 1985;84(3):323-327.
15. Lee PP, Mao H, Yang W, et al. *Penicillium marneffei* infection and impaired IFN-gamma immunity in humans with autosomal-dominant gain-of-phosphorylation STAT1 mutations. *J Allergy Clin Immunol.* 2014;133(3):894-896.e5.
16. Kudeken N, Kawakami K, Kusano N, Saito A. Cell-mediated immunity in host resistance against infection caused by *Penicillium marneffei*. *J Med Vet Mycol.* 1996;34(6):371-378.
17. Wong SS, Woo PC, Yuen KY. *Candida tropicalis* and *Penicillium marneffei* mixed fungaemia in a patient with Waldenstrom's macroglobulinaemia. *Eur J Clin Microbiol Infect Dis.* 2001;20(2):132-135.
18. Wang JL, Hung CC, Chang SC, Chueh SC, La MK. Disseminated *Penicillium marneffei* infection in a renal-transplant recipient successfully treated with liposomal amphotericin B. *Transplantation.* 2003;76(7):1136-1137.
19. Chan JF, Chan TS, Gill H, et al. Disseminated infections with *Talaromyces marneffei* in non-AIDS patients given monoclonal antibodies against CD20 and kinase inhibitors. *Emerg Infect Dis.* 2015;21(7):1101-1106.
20. Qiu Y, Liao H, Zhang J, Zhong X, Tan C, Lu D. Differences in clinical characteristics and prognosis of Penicilliosis among HIV-negative patients with or without underlying disease in Southern China: a retrospective study. *BMC Infect Dis.* 2015;15:525.
21. Lee PP, Chan KW, Lee TL, et al. Penicilliosis in children without HIV infection—are they immunodeficient? *Clin Infect Dis.* 2012;54(2):e8-e19.
22. Pruetpongpan N, Khawcharoenporn T, Damronglerd P, et al. Disseminated *Talaromyces marneffei* and *Mycobacterium abscessus* in a patient with anti-interferon-gamma autoantibodies. *Open Forum Infect Dis.* 2016;3(2):ofw093.
23. Wipasa J, Chaiwarith R, Chawansuntati K, Preparattanapan J, Rattanathammethee K, Supparatpinyo K. Characterization of anti-interferon-gamma antibodies in HIV-negative immunodeficient patients infected with unusual intracellular microorganisms. *Exp Biol Med.* 2018;243(7):621-626.
24. Su SS, Zhang SN, Ye JR, et al. Disseminated *Talaromyces marneffei* and *Mycobacterium avium* infection accompanied Sweet's syndrome in a patient with anti-interferon- γ autoantibodies: a case report. *Infect Drug Resist.* 2019;12:3189-3195.
25. Chan JW, Trendell-Smith NJ, Chan JY, et al. Reactive and infective dermatoses associated with adult-onset immunodeficiency due to anti-interferon-gamma autoantibody: Sweet's syndrome and beyond. *Dermatology.* 2013;226(2):157-166.
26. Xu H, Liu D, He X, Zheng D, Deng Y. Sweet's syndrome associated with *Talaromyces marneffei* and *Mycobacterium abscessus* infection due to anti-interferon-gamma autoantibodies. *Indian J Dermatol.* 2018;63(5):428-430.
27. Wong SS, Wong KH, Hui WT, et al. Differences in clinical and laboratory diagnostic characteristics of penicilliosis marneffei in human immunodeficiency virus (HIV)- and non-HIV-infected patients. *J Clin Microbiol.* 2001;39(12):4535-4540.
28. Zeng H, Li X, Chen X, et al. Identification of *Penicillium marneffei* in paraffin-embedded tissue using nested PCR. *Mycopathologia.* 2009;168(1):31-35.
29. Lu S, Li XQ, Calderone R, et al. Whole blood nested PCR and real-time PCR amplification of *Talaromyces marneffei* specific DNA for diagnosis. *Med Mycol.* 2016;54(2):162-168.
30. Liu D, Liang L, Chen J. In vitro antifungal drug susceptibilities of *Penicillium marneffei* from China. *J Infect Chemother.* 2013;19(4):776-778.
31. Lei HL, Li LH, Chen WS, et al. Susceptibility profile of echinocandins, azoles and amphotericin B against yeast phase of *Talaromyces marneffei* isolated from HIV-infected patients in Guangdong, China. *Eur J Clin Microbiol Infect Dis.* 2018;37(6):1099-1102.
32. Li HR, Cai SX, Chen YS, et al. Comparison of *Talaromyces marneffei* infection in human immunodeficiency virus-positive and human immunodeficiency virus-negative patients from Fujian, China. *Chin Med J.* 2016;129(9):1059-1065.

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