

CASE REPORT

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# A mass in the upper abdomen derived from *Talaromyces marneffe*i infected lymphadenopathy: a case report

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## Abstract

**Background:** An upper abdominal mass without tenderness often indicates a benign or malignant tumor once liver or spleen hyperplasia has been excluded. A lymphadenopathic mass from *Talaromyces marneffe*i infection is rare.

**Case presentation:** We report the case of a 29-year-old human immunodeficiency virus (HIV) infected man who presented with an upper abdominal mass and without any symptoms related with infection. Histopathology and next-generation sequencing (NGS) following biopsy of the mass confirmed *T. marneffe*i-infected lymphadenopathy, and the patient was successfully treated with amphotericin B and itraconazole.

**Conclusions:** This case report suggests that potential fungal infection should be considered during the diagnostic workup of a mass in clinical practice.

**Keywords:** *Talaromyces marneffe*i, HIV, AIDS, Upper abdominal mass, Next-generation sequencing

## Background

Upper abdominal distension, along with a non-tender mass, often suggests a benign or malignant tumor once liver or spleen hyperplasia has been excluded. A series of imaging and pathologic examinations are often required to diagnose the mass. However, an upper abdominal mass due to fungal lymphadenopathy is rare. Talaromycosis caused by *Talaromyces marneffe*i is a regional fungal disease that is endemic to Southeast Asia, India, and southern China [1, 2]. Talaromycosis is a life-threatening mycosis that primarily affects immunocompromised individuals and it is common in people living with HIV and is more likely to spread through the blood and affect the whole body [1]. As one of the acquired immunodeficiency syndrome (AIDS)-defining diseases, the mortality

and morbidity rates of talaromycosis are preceded only by HIV-related tuberculosis and cryptococcosis in Thailand [3]. Although the incidence of talaromycosis in people living with HIV has decreased because of the widespread use of antiretroviral therapy, its mortality is still as high as 20% [4]. The infection usually starts as a subacute disease: patients commonly develop fever, weight loss, hepatosplenomegaly, lymphadenopathy, and abnormal symptoms of respiratory and gastrointestinal diseases [5]. Skin bumps with a small dent in the center are a common manifestation, in addition to fever and other infection-related presentations [6]. Herein, we describe the diagnostic workup for a patient with an upper abdominal mass derived from *T. marneffe*i-infected lymphadenopathy.

## Case presentation

A 29-year-old man presented with abdominal distension, which had lasted for more than 2 months, accompanied by a weight loss of 10 kg. No complaints of chills and fever, nausea, vomiting, abdominal pain, or diarrhea were

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reported by this patient. Physical examination revealed a swollen abdomen with a mass of 10 cm in diameter in the upper abdomen and multiple swollen lymph nodes in the neck. HIV antibody test was positive, and HIV-1 infection was confirmed with only 8 CD4<sup>+</sup> cells/ $\mu$ L. Laboratory tests revealed that he had anemia and leukopenia, in addition to elevated erythrocyte sedimentation rate, C-reactive protein and procalcitonin levels (Table 1). Abdominal computed tomography (CT) scan showed a giant mass in the upper abdomen (Fig. 1a). Based on the clinical and imaging findings, lymphoma was suspected. Subsequently, a cervical lymph node biopsy was performed, which demonstrated large areas of tissue necrosis in the lymph nodes, along with a large number of foam cell reactions around them as well as numerous yeast-like cells in the cytoplasm, suggesting a fungal infection (Fig. 2). The *T. marneffe*i infection was initially diagnosed

by NGS of the retroperitoneal lymph node tissue, which revealed a *T. marneffe*i fungemia of 39,185 unique reads with 96.42% coverage of identified fungal genes in 72 h (Fig. 3). The blood and tissue culture grew *T. marneffe*i in 11 and 5 days, respectively, confirming the diagnosis of *T. marneffe*i infection.

After the diagnosis was considered to be a fungal infection following neck lymph node biopsy, treatment with intravenous amphotericin B was initiated. When the diagnosis of *T. marneffe*i was confirmed by NGS, the current treatment was continued. After 2 weeks, oral itraconazole for consolidation therapy along with antiretroviral therapy was started, resulting in a favorable clinical response in 1 month and shrinkage of the abdominal mass (Fig. 1b). The patient was discharged from the hospital in a stable condition.

**Table 1** Laboratory test results on admission

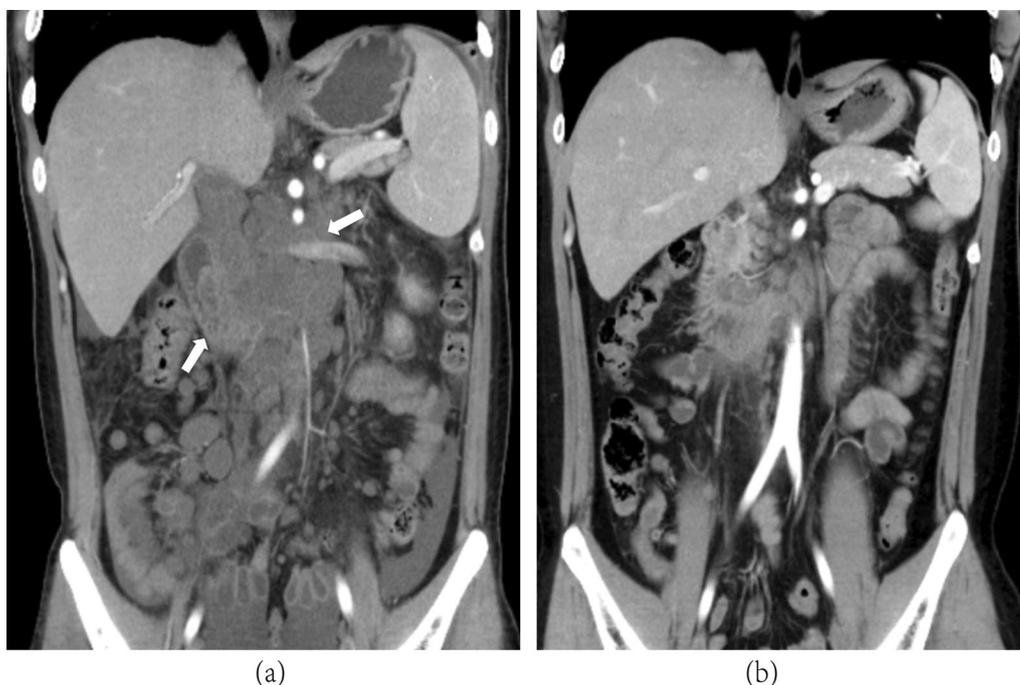
| Test item                                  | Test value         | Normal range |
|--|--------------------|--------------|
| White blood cell counts ( $10^9$ /L)       | 2.44               | 3.5–9.5      |
| Neutrophils percentage (%)                 | 80.8               | 40–75        |
| Red blood cell counts ( $10^{12}$ /L)      | 3.5                | 4.3–5.8      |
| Hemoglobin (g/L)                           | 81.0               | 130–175      |
| Platelets ( $10^9$ /L)                     | 269                | 125–350      |
| Blood urea nitrogen (mmol/L)               | 4.14               | 2.29–7.0     |
| Creatinine ( $\mu$ mol/L)                  | 57                 | 53–106       |
| Alanine transaminase (U/L)                 | 45                 | 9–50         |
| Glutamic-oxal acetic transaminase (U/L)    | 80                 | 15–40        |
| Total protein (g/L)                        | 63.7               | 65–85        |
| Albumin (g/L)                              | 27.9               | 40–55        |
| Creatine kinase (U/L)                      | 34                 | 50–310       |
| Lactate dehydrogenase (U/L)                | 288                | 120–250      |
| CD4 cell counts (cells/ $\mu$ L)           | 8                  | 600–800      |
| Erythrocyte sedimentation rate (mm/h)      | 85                 | < 15         |
| High-sensitivity C-reactive protein (mg/L) | 78.6               | 0–3          |
| Procalcitonin (ng/mL)                      | 0.21               | < 0.1        |
| Plasma (1,3) beta-D-glucan (pg/mL)         | 72.1               | < 60         |
| Serum galactomannan antigen                | Negative           | Negative     |
| Cryptococcus antigen                       | Negative           | Negative     |
| Anti-EBV-EA immunoglobulin M antibody      | Negative           | Negative     |
| Anti-EBV-VCA immunoglobulin M antibody     | Negative           | Negative     |
| Anti-CMV immunoglobulin M antibody         | Negative           | Negative     |
| Anti-CMV immunoglobulin G antibody         | Positive           | Negative     |
| Anti-TOX immunoglobulin M antibody         | Negative           | Negative     |
| Anti-TOX immunoglobulin G antibody         | Negative           | Negative     |
| EBV DNA (copies/mL)                        | < 500              | < 500        |
| CMV DNA (copies/mL)                        | $2.33 \times 10^3$ | < 500        |
| HIV RNA loads (copies/mL)                  | $10 \times 10^6$   | < 500        |

EBV Epstein–Barr virus, CMV cytomegalo virus, EA early antigen, VCA viral capsid antigen, HIV human immunodeficiency virus, Tox toxoplasma

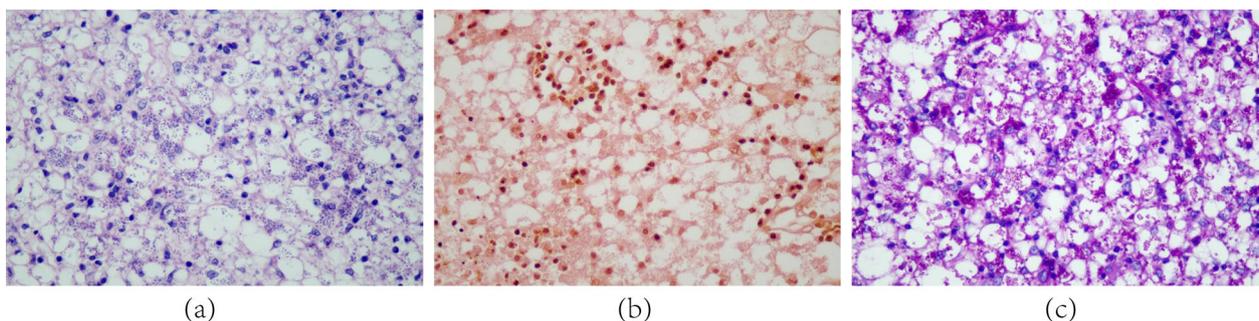
## Discussion and conclusions

Lymphadenopathy is extremely common in patients with HIV infection and has several possible causes, including the generalized lymphadenopathy of HIV-infection, malignancy, and single or multiple co-infections [7]. As with the case that we reported, HIV-infected person with abdominal lymphadenopathy as the main clinical symptom may be finally diagnosed with *T. marneffe*i infection. *T. marneffe*i can cause infection in immunocompromised individuals with, or without, a history of residence in, or travel to, an endemic region [8]. It is the most important thermally dimorphic fungus, which can cause respiratory, skin, and systemic mycosis in China and Southeast Asia [9]; it is also a life-threatening mycosis that primarily affects immunocompromised individuals [1]. The main risk factor for *T. marneffe*i infection is cell-mediated immune dysfunction, which is usually secondary to HIV infection, especially in people with CD4<sup>+</sup> cell counts below 100 cells/ $\mu$ L [10]. The symptoms of *T. marneffe*i infection vary. The most common symptoms include fever, weight loss, malaise and anemia. There may also be fungemia, lymphadenopathy, hepatomegaly, lung disease (non-productive cough and dyspnea), diarrhea, splenomegaly, and systemic skin lesions [11]. Skin lesions are present in 60–70% of patients, which are often the early manifestations of disseminated cases, and more common on the face, trunk and upper limbs [6]. The common laboratory findings of *T. marneffe*i infection include anemia, thrombocytopenia, and elevated transaminases [12]. The laboratory examination results of the patient we reported suggest anemia and leukopenia in addition to elevated erythrocyte sedimentation rate, C-reactive protein, and procalcitonin levels. These were helpful in making the early diagnosis of *T. marneffe*i infection.

Microscopic findings of intramacrophage and extramacrophage yeast organisms in smears of skin lesions,



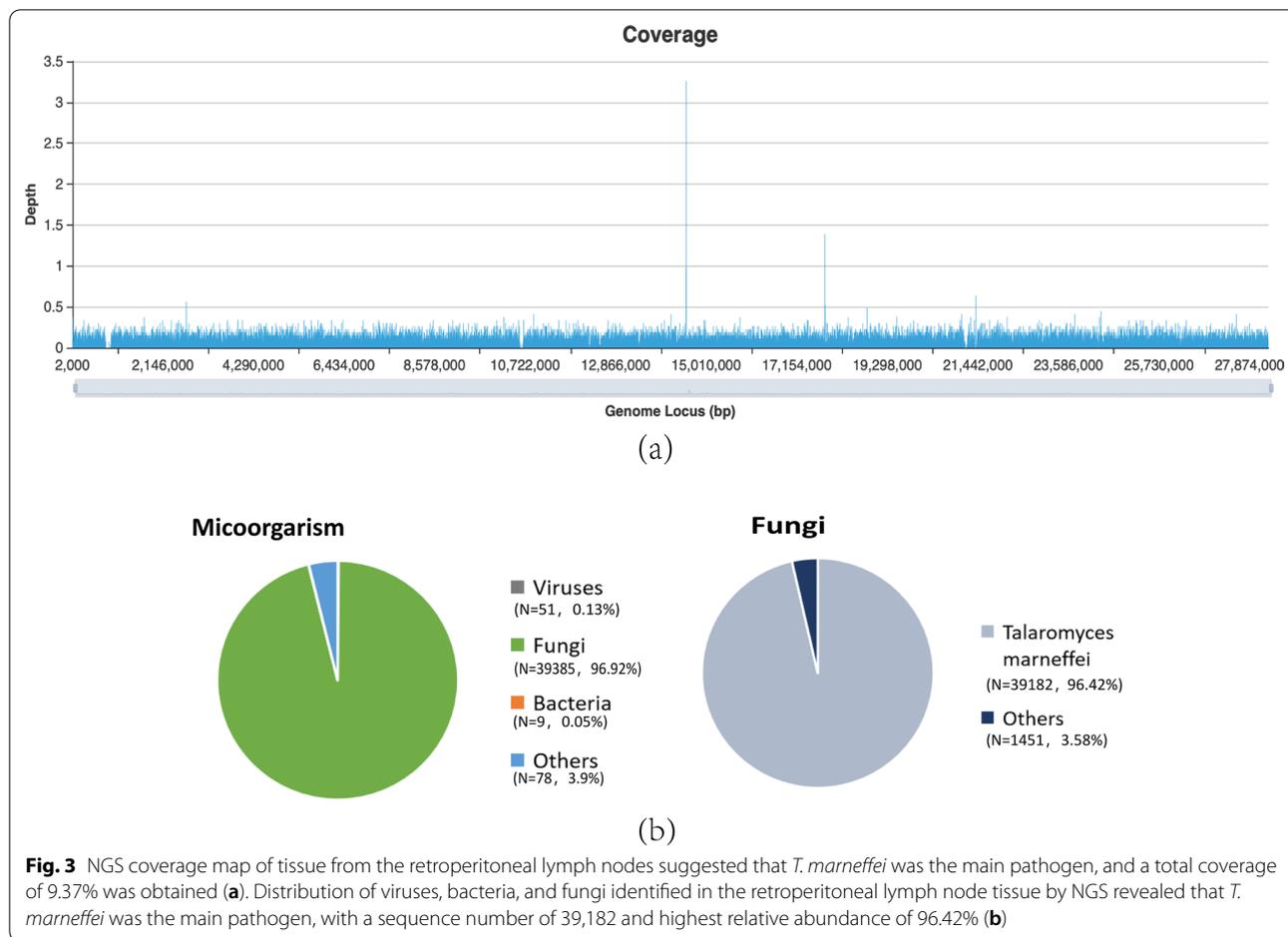
**Fig. 1** Abdominal CT scan (a) shows a giant mass in the upper abdomen, which demonstrated shrinkage after treatment (b)



**Fig. 2** Hematoxylin–eosin staining (a magnification,  $\times 400$ ), Gomori methenamine silver staining (b magnification,  $\times 400$ ), and periodic acid schiff staining (c magnification,  $\times 400$ ), show large areas of soft tissue necrosis in the cervical lymph nodes accompanied with a large number of foam cell reactions around them, along with multiple yeast-like cells gathered in the cytoplasm, suggesting a fungal infection

lymph nodes, and bone marrow aspirate can lead to a rapid presumptive diagnosis [6]. In addition, *T. marneffei* is a dimorphic fungus, and a diffusible red pigment that can be seen on culture can confirm the diagnosis. However, the very long time for culture, can lead to delays in diagnosis and increased mortality, especially in patients without skin lesions [8]. The histopathologic finding of intracellular and extracellular yeast forms and the characteristic cross-septation of *T. marneffei* highlighted by Gomori methenamine silver staining from specimens obtained from the affected tissue or *T. marneffei* grew in cultures that could identified the

diagnosis [13]. In atypical and severe cases, it is difficult to establish a rapid diagnosis using traditional assays. The patient whose case we reported, was characterized mainly with an abdominal mass, but without the typical *T. marneffei* symptoms, such as skin lesions. Finally, the nucleotide sequence of *T. marneffei* in the abdominal mass samples from our patient, was identified quickly by NGS. It can be seen that NGS testing brings the dawn of diagnosis detect rare pathogen and takes a shorter time [14]. Actually, The current gold standard for the diagnosis of *T. marneffei* infection is pathogen culture, but culture generally takes 7–10 days, making



early diagnosis difficult. In contrast, NGS diagnosis only takes 24–72 h [15].

Antifungal therapy is the first choice of treatment for *T. marneffeii*, and it is classified into induction, consolidation, and maintenance stages. International guidelines recommend the use of amphotericin B deoxycholate for initial (induction) treatment at a dose of 0.7 to 1 mg per kilogram of body weight per day for 2 weeks, followed by itraconazole at a daily dose of 400 mg for 10 weeks [16]. A recent randomized controlled trial on itraconazole versus amphotericin B in the treatment of penicilliosis in Vietnam suggests that amphotericin B is superior to itraconazole at induction stage in HIV related *T. marneffeii* infection [17].

Unlike previously reported cases, we reported an unusual case of *T. marneffeii* infection in a patient with AIDS, the principal clinical manifestations of abdominal distension and abdominal mass. Due to the lack of specific clinical manifestations, *T. marneffeii* infection could likely be misdiagnosed as tuberculosis, histoplasmosis, cryptococcosis, and lymphoma in patients with

systemic lymphadenopathy. Accordingly, it is necessary to emphasize the need to diagnose this disease. In the case of atypical talaromycosis, the diagnosis is more rapid by NGS than by biopsy or culture, allowing rapid initiation of therapy, which is particularly important in immunocompromised patients. Hence, rapid diagnosis is of significant benefit to these patients.

#### Abbreviations

HIV: Human immunodeficiency virus; AIDS: Acquired immunodeficiency syndrome; CT: Computed tomography; NGS: Next-generation sequencing.

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#### Authors' contributions

XC: Study conception and design; drafting of manuscript; review, analysis and interpretation of scientific literature. LJ: critical revision of the manuscript and analysis of the analysis of NGS data and production of sequencing coverage map; YW: acquisition clinical data; JC: performing the pathological diagnosis and analyzing the result of the pathological examination; TZ and YM: providing important intellectual content; YZ: study conception and design, obtaining funding and study supervision. All authors have contributed to the manuscript and ensure that this is the case. All authors read and approved the final manuscript.

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### Availability of data and materials

All data generated or analyzed during this study are included in this published article. The data that support the findings of this study are available from the corresponding author upon reasonable request.

### Declarations

#### Ethics approval and consent to participate

The study was approved by the Ethics Committee of Beijing You An Hospital, Capital Medical University.

#### Consent to publish

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

#### Competing interests

The authors declare that they have no competing interests.

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