

## CASE REPORT

# Talaromyces Marneffei Infection Presenting with Cervical Lymphadenopathy as the Initial Manifestation

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### SUMMARY

**Background:** *Talaromyces marneffei* (TM) is an opportunistic pathogenic fungus primarily prevalent in Southeast Asia. It mainly infects immunocompromised individuals and is rarely observed in those with normal immune function. Additionally, patients infected with TM exhibit non-specific clinical manifestations, which significantly increase the difficulty of diagnosis. In this case, the final diagnosis of TM infection was confirmed through pathological examination following a cervical lymph node puncture and biopsy.

**Methods:** Lymph node biopsy.

**Results:** Pathological findings following cervical lymph node puncture and biopsy revealed hyperplastic lymphoid follicles of varying sizes, with some follicles exhibiting coagulative necrosis. Surrounding these areas were proliferative granulomas. The histological changes were consistent with granulomatous lymphadenitis, indicative of TM infection. Consequently, antifungal therapy with voriconazole was administered.

**Conclusions:** For patients with cervical lymphadenopathy, it is crucial to stabilize the condition while simultaneously identifying the underlying cause. Timely performance of relevant diagnostic procedures, such as cervical lymph node puncture and biopsy, is essential to establish a definitive diagnosis.

(Clin. Lab. 2025;71:xx-xx. DOI: 10.7754/Clin.Lab.2024.241228)

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#### KEYWORDS

*Talaromyces marneffei* infection, lymph node biopsy, lymphadenopathy

#### CASE REPORT

A 54-year-old female patient was admitted due to the discovery of a mass in the left neck and left occipital region for one month. She reported that about a month ago, without any obvious cause, she developed a mass in the left neck and left occipital area, approximately 5 x 5 mm in size, clustered together. The mass showed a tendency to grow, gradually increasing to about 10 x 10 mm, accompanied by pain and discomfort. It did not move up or down with swallowing and was not associated with low-grade fever, night sweats, cough, sputum production, or difficulty breathing. During her visit to our hospital's outpatient clinic, she underwent superficial ultrasound examination, which revealed multiple masses in the left neck with strong internal echoes and

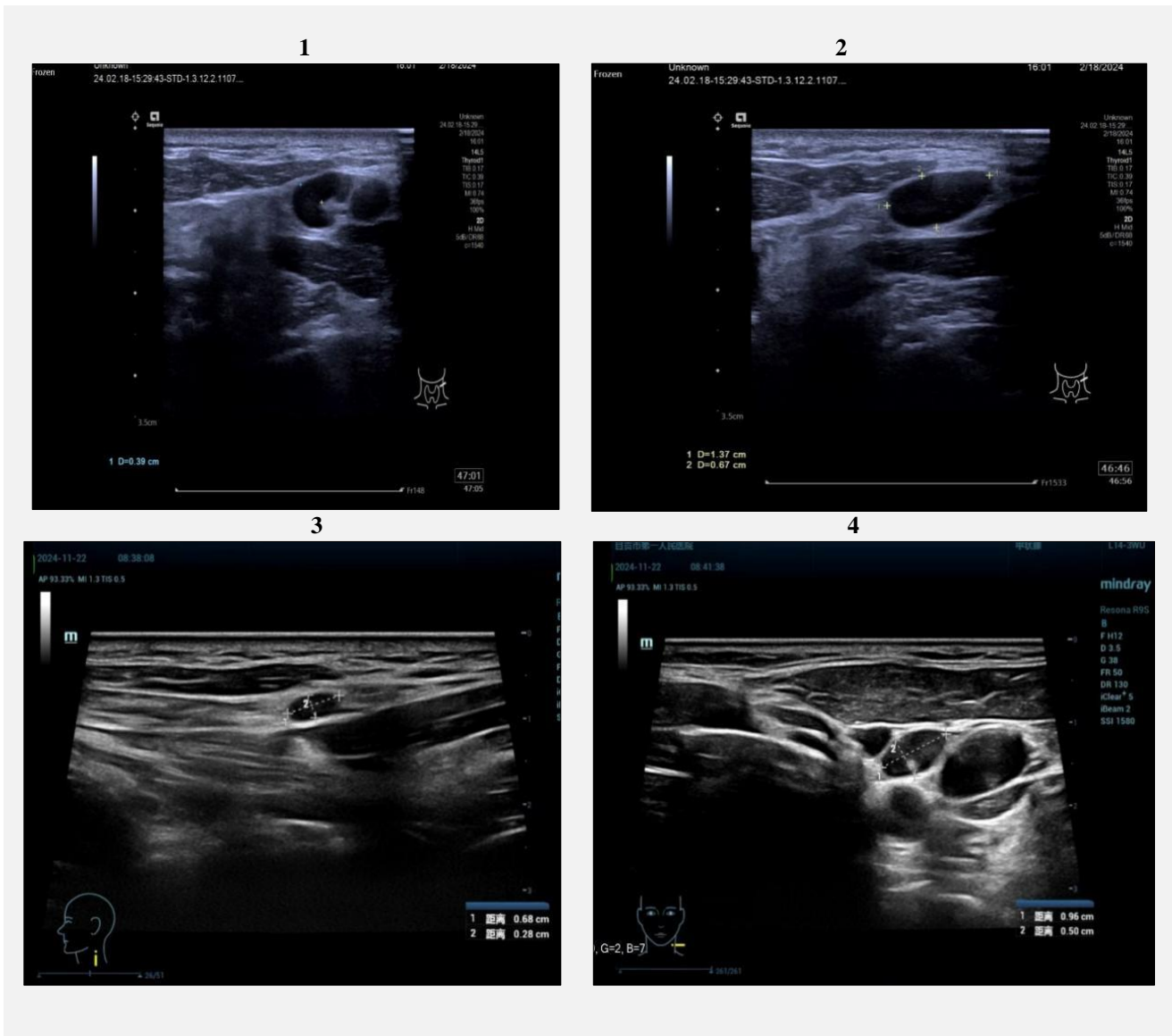
weak external echoes, some of which were round-shaped. The largest one was located in region V, measuring approximately 13.7 x 6.7 mm, with thickened cortex. In the subcutaneous fascia layer of the left posterior part of the head, there was a hypoechoic area, suggesting possible inflammation. No special treatment was given. Since the onset of the disease, the patient's weight has not changed significantly. She has no history of hypertension, diabetes, hepatitis, or tuberculosis. On admission, physical examination revealed a soft neck without jugular venous distension. There was a protruding mass in the left anterior neck, with the trachea in the midline. A hard mass could be palpated behind the left ear, measuring about 40 x 30 mm, with unclear borders, poor mobility, no masses palpable in both thyroid glands, and a protruding mass in the left occipital area, measuring about 30 x 25 mm, with fair mobility and no tenderness. After admission blood routine findings: RBC  $3.91 \times 10^{12}/L$  (reference value  $4 \times 10^{12}/L - 5.5 \times 10^{12}/L$ ), HGB 121 g/L (reference value 115 g/L - 150 g/L), WBC  $4.76 \times 10^9/L$  (reference value  $4 \times 10^9/L - 10 \times 10^9/L$ ), NEU  $2.69 \times 10^9/L$  (reference value  $1.8 \times 10^9/L - 6.3 \times 10^9/L$ ), LYM  $1.59 \times 10^9/L$  (reference value  $1.1 \times 10^9/L - 3.2 \times 10^9/L$ ), MON  $0.38 \times 10^9/L$  (reference value  $0.1 \times 10^9/L - 0.6 \times 10^9/L$ ), and improve the infection index tips: CRP 5 mg/L (reference value 0 mg/L - 8 mg/L), ESR 10 mm/hour (reference value 0 mm/hour - 15 mm/hour), fibrinogen 3.10 g/L (reference value 2 g/L - 4 g/L), no obvious abnormalities were found in biochemical detection. The EB virus antibody test was positive, while no abnormalities were detected in the subpopulation of lymphocytes, anti-tuberculosis antibody, and respiratory pathogen tests. Ultrasound of the cervical lymph nodes: Multiple hypoechoic lesions with strong internal echoes were observed on the left side of the neck, some of which were ovoid in shape. The largest lesion was located in zone V, measuring approximately 13.7 x 6.7 mm, with thickened cortex. Color Doppler Flow Imaging (CDFI) showed the presence of blood flow signals within the lesions. Initially, acute cervical lymphadenitis was suspected, and thymalfasin was administered to modulate the immune response; however, the treatment was ineffective. Therefore, a fine-needle aspiration biopsy of the lymph node was performed. Post-biopsy histopathology revealed variably sized hyperplastic lymphoid follicles, with some follicles showing coagulative necrosis, and granulomas with hyperplasia surrounding the follicles. The histopathological changes were consistent with granulomatous lymphadenitis, and *Talaromyces marneffeii* (TM) was suspected. The final diagnosis was TM infection, and the patient was treated with voriconazole for antifungal therapy. The patient's condition improved, and she was discharged. A follow-up ultrasound of the cervical lymph nodes after discharge showed a reduction in the size of the left cervical lymph nodes.

## DISCUSSION

*Talaromyces marneffeii* (TM) is a thermally dimorphic fungus that can cause life-threatening opportunistic infections in humans [1,2]. In 1956, the Capponi team at the Pasteur Institute in Vietnam first isolated TM from the liver of a bamboo rat and subsequently confirmed its virulence in rodents [3,4]. TM causes human fungal infections affecting the respiratory tract, skin and subcutaneous tissues, and even disseminated disease [5,6]. TM infection is endemic in tropical regions, particularly in Thailand, Vietnam, northeast India, southern China, Hong Kong, Taiwan, Laos, Malaysia, Myanmar, Cambodia, and Laos [4]. TM is a highly pathogenic fungus that can cause life-threatening systemic mycosis. Ranking as the third most common opportunistic infection among HIV-positive individuals living in endemic areas after tuberculosis and cryptococcosis, TM poses a significant threat. Notably, in recent years, there has been an increase in the number of TM infections occurring in individuals without HIV infection [7-9]. Patients with HIV-negative TM infections often exhibit severe immunosuppression, particularly those undergoing solid organ transplantation, bone marrow transplantation, or long-term steroid use [10]. However, in this case, the patient did not present with pronounced immunosuppression; instead, the initial symptoms were masses in the neck and occipital regions, ultimately confirmed to be due to TM via lymph node biopsy.

The severity of TM infection varies depending on the degree of underlying immune dysfunction and the timing of diagnosis. The symptoms and signs of TM infection are atypical and include fever, weight loss, fatigue, hepatosplenomegaly, lymphadenopathy, and abnormalities in the respiratory and gastrointestinal systems [11]. Compared to HIV-infected individuals, those with HIV-negative TM infection have a longer diagnostic interval, a higher proportion experiencing dyspnea, significantly older age, and lower proportions of fever, splenomegaly, and umbilicated cutaneous lesions. Non-HIV infected patients also show higher leukocyte counts, CD4 lymphocyte counts, and platelet counts, as well as lower alanine aminotransferase (ALT) levels and blood culture positivity rates [12,13]. However, in this case, the patient only presented with cervical lymphadenopathy without exhibiting other significant clinical manifestations or signs, which posed challenges to our initial diagnosis.

TM exhibits thermally dimorphic characteristics, producing molds at 25 - 30°C and yeast forms at 37°C. The ability to switch from mold to yeast may be one of the key virulence factors of this organism, enabling it to evade host immune defenses. At 37°C, TM yeast grows as segmented, yeast-like cells that produce daughter cells through division, resulting in the characteristic transverse septa formation unique to TM. Finally, recent DNA sequence analyses suggest reclassifying TM from the genus *Penicillium*, subgenus *Biverticillium*, to the genus *Talaromyces* [14,15]. TM proliferates within



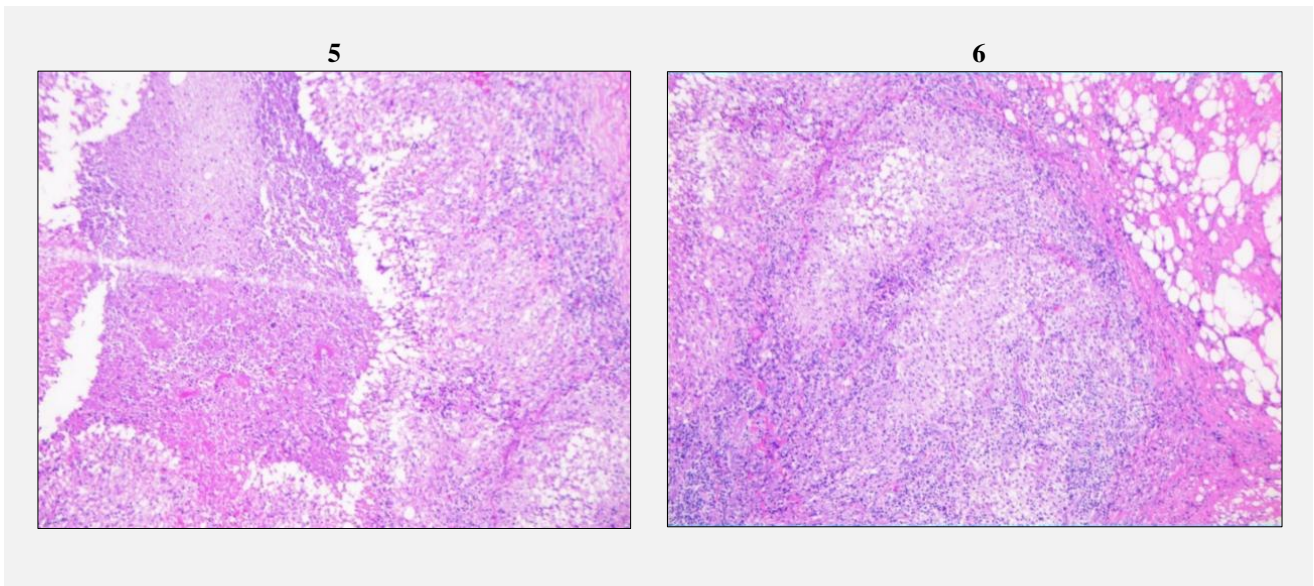
**Figure 1, 2.** Left neck: Multiple hypoechoic areas with internal hyperintensity and external weakness, some of which are round or oval in shape. The largest lesion is located in the V region, measuring approximately 13.7 x 6.7 mm. The cortical layer is thickened. CDFI reveals visible blood flow signals within the lesion.

**Figure 3, 4** After 9 months of treatment: Multiple hypoechoic areas with internal hyperintensity and external weakness are observed in regions II, III, and V of the left neck. The largest lesion measures approximately 9.6 x 5.0 mm, with clear boundaries. CDFI reveals visible blood flow signals within the lesion.

macrophages and spreads through the reticuloendothelial system [16]. Phagocytic cells likely serve as the primary host defense against this fungus, and T-cell-derived cytokines that activate macrophages are essential for the macrophage-mediated killing of intracellular yeast cells. TM can elicit three types of host reactions in tissues: granulomatous reactions, suppurative reactions, and non-reactive necrosis. It can affect major organs of the body, with the most common sites being the trachea, lung parenchyma, hematopoietic and lymphatic systems, skin, mucosa, bones, and soft tissues [1]. Due to

the lack of specific clinical manifestations, misdiagnosis often occurs. Cultures from bone marrow and lymph node tissues have a high positive rate for diagnosing TM and are considered the most reliable methods. We ultimately diagnosed the presence of TM based on a lymph node biopsy, which showed granulomatous inflammation in the lymph node.

Current research indicates that itraconazole and ketoconazole are the best choices for treating mild to moderate TM infections, while amphotericin B may be an effective drug for severe cases of TM infection [17]. In this



**Figure 5, 6.** Visible hyperplastic lymphoid follicles of various sizes are present, some of which show coagulation necrosis. Hyperplastic granulomas are observed in the surrounding area. The histological changes indicate granulomatous inflammation of the lymph nodes, suggesting a possible infection of TM.

particular patient's case, we used voriconazole for treatment, and subsequent follow-up neck lymph node ultrasound showed a reduction in the size of the left cervical lymph nodes.

### CONCLUSION

Our case demonstrates that for patients with enlarged cervical lymph nodes, even those with normal immune function, it is important to be vigilant for the possibility of TM infection. When necessary, timely lymph node biopsy and other relevant examinations should be performed to establish a definitive diagnosis. Formulating an appropriate treatment plan early in the disease process can provide the best possible treatment in the initial stages, thereby improving patient outcomes.

### Acknowledgment:

We would like to thank other members of the Department of Respiratory Medicine, Zigong First People's Hospital of Technology for the constructive criticism.

### Source of Support:

This work was supported by Zigong Science and Technology Program Project (2023YKY07 and 2023YLWS 21).

### Ethical Approval:

This study was approved by the ethics committee of Zigong First People's Hospital. All procedures performed in studies were in accordance with the ethical standards. Informed consent was obtained.

### Declaration of Interest:

No conflicts of interest.

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