Infection and Drug Resistance

Dovepress
Taylor & Francis Group

Open Access Full Text Article

CASE REPORT

A Case Report of Unusual Diagnosis of Melioidosis in a Non-Traveler: Implications for Transmission and Diagnosis

Chenliang Fan[1], Xiaosi Li[1], Baizhi Pi[2], Jiasheng Wu[3], Heping Shen[3], Yumiao Guo[3], Xiaoyan Wu[1]

[1]Department of Laboratory Medicine, the Second Affiliated Hospital of Jiaxing University, Jiaxing, 314001, People's Republic of China; [2]Department of Intensive Care, the Second Affiliated Hospital of Jiaxing University, Jiaxing, 314001, People's Republic of China; [3]Department of Infectious Diseases, the Second Affiliated Hospital of Jiaxing University, Jiaxing, 314001, People's Republic of China

Correspondence: Yumiao Guo, Department of Infectious Diseases, the Second Affiliated Hospital of Jiaxing University, Jiaxing, 314001, People's Republic of China, Email guoym0328@163.com; Xiaoyan Wu, Department of Laboratory Medicine, the Second Affiliated Hospital of Jiaxing University, Jiaxing, 314001, People's Republic of China, Email wxy87751@163.com

Abstract: Melioidosis is prevalent in Southeast Asia, acquired via breathing or skin contact with water or soil contaminated by *Burkholderia pseudomallei*. This article reports a 42-year-old male melioidosis patient without underlying diseases or travel history to epidemic areas, discussing its significance for epidemiology, diagnosis and treatment in non-epidemic areas. The patient's clinical manifestations, disease progression, previous treatment, admission examination, diagnostic process, treatment and follow-up results were retrospectively analyzed. tNGS, microbial culture and WGS were used for sample and pathogen identification and genetic analysis. The patient had recurrent fever with erythema nodosum on the left lower limb. Misdiagnosed and treated ineffectively in other hospitals, he was diagnosed with melioidosis in the Second Affiliated Hospital of Jiaxing University. The strain was identified as *Burkholderia pseudomallei*, type ST46. Appropriate antibiotic treatment was selected based on drug sensitivity test results. After 6 months of follow-up, most lesions were absorbed, laboratory indicators normalized and the clinical effect was good. Epidemiological investigations suggested ST46 might be transmitted via non-traditional routes related to the fact that 15 days before the onset of the disease, the patient had purchased live turtles and the soil for raising them online which were sourced from Yunnan, indicating the possibility of geographical transmission. This case enriches understanding of melioidosis' non-traditional transmission, strain transmission, clinical diagnosis and treatment, highlighting the importance of considering the disease in non-endemic areas' differential diagnosis and the need for further epidemiological surveillance and research.

Keywords: melioidosis, targeted next-generation sequencing, non-endemic areas, non-traditional transmission

Introduction

Melioidosis, an infectious disease caused by *Burkholderia pseudomallei (B. pseudomallei)*, poses a significant threat to public health in numerous regions. Humans and animals are infected through breathing or transdermal contact with water or soil contaminated with the *B. pseudomallei*.[1] It is predominantly endemic in tropical and subtropical zones, such as Southeast Asia, northern Australia.[2] In China, the highest incidence is mainly concentrated in southern cities such as Guangdong, Hainan and Guangxi.[3] Melioidosis is closely associated with occupation and contact with soil and water. Occupations involving frequent exposure to them, like farming and construction, are at higher risk as the pathogen lurks in such environments, facilitating its entry into the body. After melioidosis infection, there are usually various manifestations, including pneumonia, urinary and reproductive system infections, skin and soft tissue infections, visceral abscesses, suppurative arthritis, ocular and neurological melioidosis, as well as fulminant sepsis without obvious lesions.[4] Worldwide, there are 165,000 human cases of melioidosis each year, of which 89,000 die, for a global mortality rate of about 90,000 per year.[5]

Received: 14 April 2025
Accepted: 15 July 2025
Published: 22 July 2025

In recent years, with the exponential growth of global travel and trade, the geographical distribution of melioidosis has expanded. Although melioidosis has long been considered a disease of specific endemic regions, increasing cases have been reported in non-endemic areas.[6–8] These non-endemic cases often present diagnostic challenges due to limited local awareness and experience with the disease. Existing studies on non-endemic melioidosis cases have mainly focused on individual case reports and small-scale series, with a lack of comprehensive understanding of its epidemiological characteristics, transmission routes, and optimal diagnostic approaches in these regions.

Against this backdrop, we report a case of melioidosis in a 42-year-old male patient with no underlying diseases and with no history of traveling to endemic areas. This case adds to the scarce literature on non-endemic melioidosis and offers insights into potential non-traditional transmission routes, diagnosis in non-endemic settings, and effective treatment strategies. By sharing this case, we aim to heighten clinicians' awareness of melioidosis, even in areas where it was previously considered rare, and contribute to more informed decision-making in its diagnosis and treatment. The timeline of patient diagnosis and treatment is presented in Figure 1.

Case Presentation

A 42-year-old male patient, who had been in good health previously and had no history of underlying diseases or traveling to epidemic areas, was admitted to The Second Affiliated Hospital of Jiaxing University on August 22, 2024. He came to the hospital due to having experienced "recurrent fever accompanied by erythema nodosum on the left lower limb for more than half a month".

The onset happened suddenly in early August 2024 when he developed a high fever reaching up to 40°C without any obvious triggers. Along with the fever, he also suffered from chills, rigors, and headache. At the same time, painful erythema nodosum emerged above the outside of the left knee, and a painful abscess formed in the left inguinal area, with the local skin showing redness and swelling.

On the fifth day of the onset of the disease, the patient visited another hospital for the first time. At that time, due to skin manifestations such as erythema and nodules on the left lower extremity, the patient was diagnosed with "skin and soft tissue infection". Considering the existence of an inflammatory response, methylprednisolone (at a dose of 40mg/d) was given for anti-inflammatory treatment, and at the same time, nenoxacin (0.5g/d) was used in combination for anti-infection treatment. The course of treatment was 4 days. His body temperature dropped briefly and the skin symptoms were somewhat relieved. However, after discontinuing the hormone and continuing with nemonoxacin treatment for another 4 days, his body temperature rose again and the skin pain became even worse.

When it was the 13th day of the onset, the treatment was changed to ceftriaxone at 2 g/d for 3 days. Despite this, he still had recurrent fevers. In an attempt to bring down the fever, the patient took ibuprofen orally by himself, yet the effect was only temporary.

Upon admission to The Second Affiliated Hospital of Jiaxing University, a series of examinations were conducted for diagnosis. During the physical examination, his body temperature was measured at 38.8°C. There was a 2×3 cm erythema in the left inguinal area and a 1×1 cm tender erythema above the left knee, while the rest of the physical examination showed no abnormalities.

Laboratory tests were also carried out. For the infection indicators, the high-sensitivity C-reactive protein (hs-CRP) was 92.65 mg/L (0.00–8.00 mg/L), procalcitonin (PCT) was 0.170 ng/mL (0–0.046 ng/mL), white blood cell count (WBC) was 16.1×10^9/L ($3.50–9.50\times10^9$/L), and the percentage of neutrophils was 86.1% (40.0–75.0%) As for the exclusion tests, including blood culture, fungal antigens (G test, GM test), T cell detection for tuberculosis infection, and respiratory virus nucleic acids, all of them came back negative.

The patient's chest computed tomography (CT) scan revealed pneumonia in the left upper lobe, combined with the skin redness, levofloxacin was administered empirically to increase tissue penetration (Figure 2A). To clarify the pathological information, a skin lesion resection was performed on the erythema nodosum of the left lower limb. During the operation, purulent fluid was observed to flow out. Approximately 2×0.2 cm strip-shaped local skin tissue was excised and sent for pathological examination and tNGS. Pathology indicated fat necrosis accompanied by suppurative inflammation (Figure 2B). Tissue tNGS results showed *B. pseudomallei* (The normalized sequence count was 334 reads

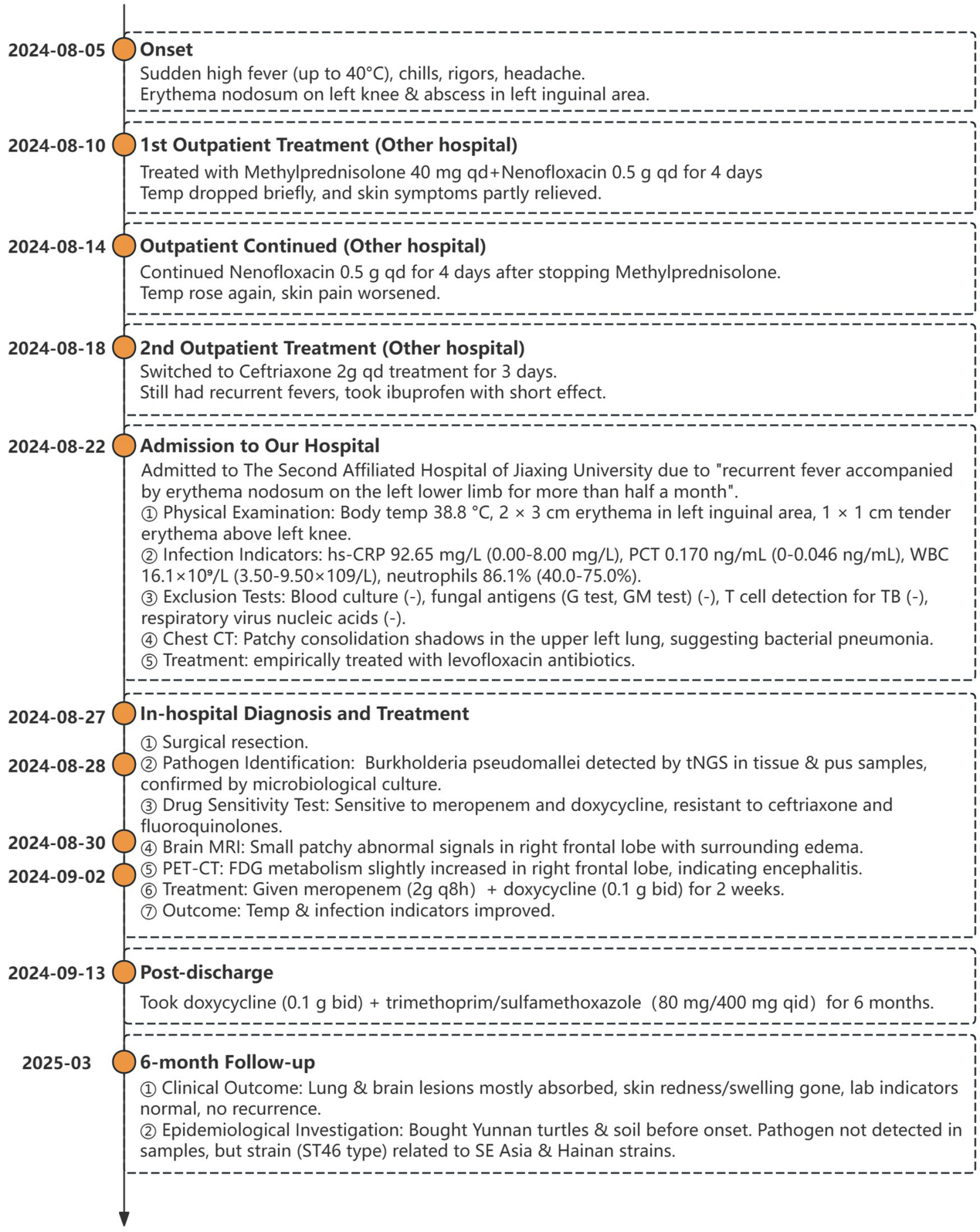

Figure 1 The timeline shows the entire diagnosis and treatment process of this case.

https://doi.org/10.2147/IDR.S528971

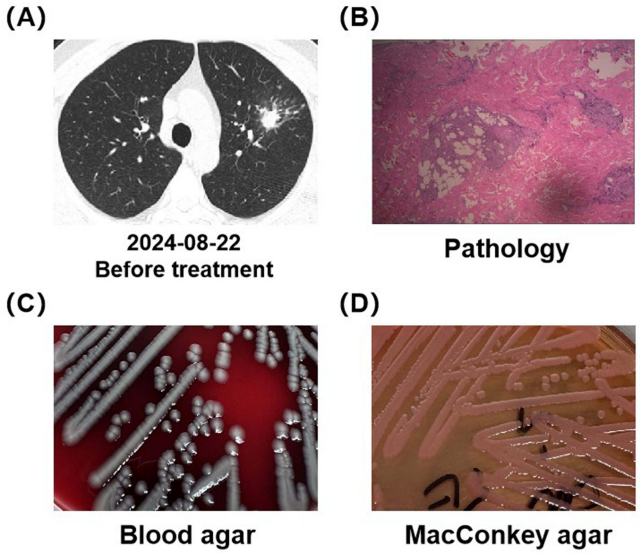

Figure 2 (**A**) The chest CT image before treatment. (**B**) The histological pathology image stained to visualize tissue structures. (**C**) The growth of *B. pseudomallei* on blood agar and (**D**) MacConkey agar.

and pathogen load 282 copies/mL). Bacterial culture of pus revealed gram-negative bacilli (Figure 2C and D), which were detected by mNGS both as *B. pseudomallei*. The blood tNGS testing result was negative.

Subsequently, drug susceptibility tests showed that the strain was sensitive to a variety of antimicrobial agents, including imipenem, ceftazidime, amoxicillin/clavulanate, tetracycline, sulfamethoxazole-trimethoprim (Table 1). The drug susceptibility testing was performed by methods for antimicrobial dilution and disk susceptibility testing of infrequently isolated or fastidious bacteria (CLSI guideline M45-A3).

After a comprehensive physical examination, the magnetic resonance imaging (MRI) of the brain showed small patchy abnormal signals in the right frontal lobe (Figure 3A).

Considering that melioidosis has the characteristic of being able to disseminate, a positron emission tomography/computed tomography (PET/CT) scan was performed to further clarify the condition. The results of the PET/CT examination indicated a patchy low-density edema shadow in the right frontal lobe, and the fluorodeoxyglucose (FDG) metabolism in the adjacent gyri was slightly increased symmetrically (Figure 3B). Based on all the above imaging findings, the possibility of encephalitis was taken into account.

Based on the melioidosis guidelines and drug sensitivity results, a treatment plan was formulated.[9] The patient was treated with intravenous injection of meropenem at 2 g q8h combined with oral doxycycline at 0.1 g bid for 2 weeks.

Table 1 Antimicrobial Drug Susceptibility Testing of *B. pseudomallei*

Antibiotics	MIC for Category (ug/mL)			MIC (μg/mL)	Interpretation
	Susceptible	Intermediate	Resistant		
Imipenem	≤4	8	≥16	2	S
Meropenem	–	–	–	≤1	–
Ceftazidime	≤8	16	≥32	0.5	S
Cefepime	–	–	–	≤1	–
Amoxicillin/clavulanic acid	≤8/4	16/8	≥32/16	2/1	S
Peracillin/Tazobactam	–	–	–	2	–
Tetracycline	≤4	8	≥16	1	S
Sulfamethoxazole-Trimethoprim	≤2/38	-	≥4/76	<0.25/4.75	S
Levofloxacin	-	-	-	≤1	-

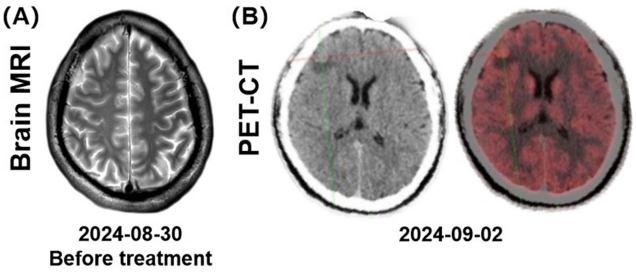

Figure 3 (**A**) The brain MRI image before treatment and (**B**) the PET-CT images.

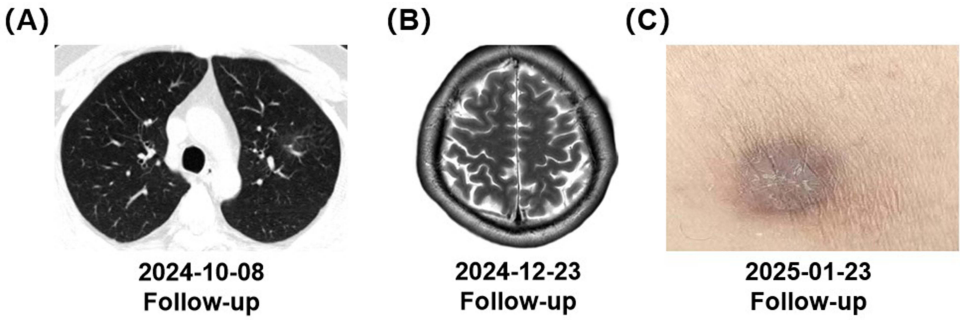

Figure 4 (**A**) The follow-up chest CT image and (**B**) the brain MRI image. (**C**) The follow-up appearance of the same area.

After this period of treatment, his body temperature and infection indicators improved significantly. After being discharged from the hospital, he was given sequential oral doxycycline at 0.1 g bid and trimethoprim/sulfamethoxazole at 80 mg/400 mg qid for 6 months for consolidation.

During the 6-month follow-up after treatment, the lesions in the lungs and brain were mostly absorbed (Figure 4A and 4B), the skin redness and swelling subsided (Figure 4C), and the laboratory indicators remained normal without recurrence.

In terms of the epidemiological investigation, it was discovered that the patient had purchased live turtles and the soil for raising them online which were sourced from Yunnan 15 days before the onset. Although the pathogen was not detected in the environmental samples (turtle surface, soil) through culture and tNGS, whole-genome sequencing (WGS) showed that the isolated strain (ST46 type) had a close genetic relationship with the strains from Southeast Asia (Vietnam YB16 strain) and Hainan, China (Figure 5). Specifically, phylogenetic analysis revealed a genetic distance of 30 between ST46 and *B. pseudomallei*, which is notably shorter than the average distance of 87.9 between ST46 and other *Burkholderia species*, highlighting its closer evolutionary proximity to *B. pseudomallei*. Written informed consent was obtained from the patients to publish this paper. This study was conducted in accordance with the Declaration of Helsinki and approved by the Medical Ethics Committee of the Second Affiliated Hospital of Jiaxing University (Num: 2023JX132-01).

Discussion

Melioidosis has diverse clinical manifestations that lack specificity, making it extremely prone to misdiagnosis.[10] The difficulty in diagnosing this disease in non-endemic areas was particularly prominent, as clinicians often lack awareness of its manifestations and have limited experience with such cases. In this case, the patient lived in Pinghu, Zhejiang Province, China, which is a non-endemic area far from Hainan Province (endemic area in China). The patient was an office employee of a company, primarily engaged in indoor work with no occupational requirement for outdoor activities or contact with soil/water before the onset of symptoms, which helps rule out the traditional transmission of melioidosis from soil and water, further highlighting the importance of this case. The patient mainly presented with recurrent fever, erythema nodosum and abscesses on the skin, and infections in multiple sites (encephalitis and pneumonia), which made it easily misdiagnosed as a common bacterial infection. The early empirical antibiotic treatments (such as nemonoxacin

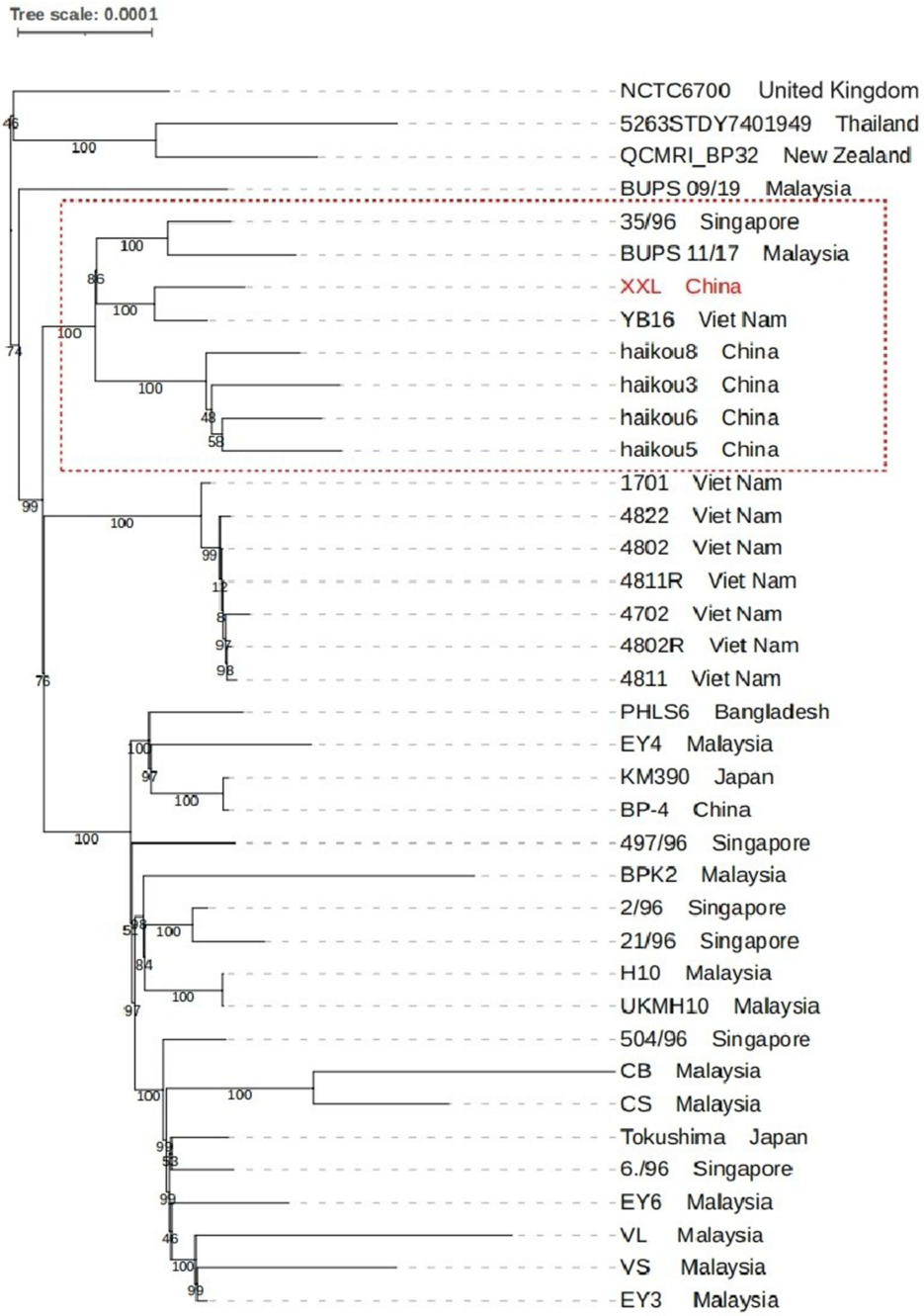

Figure 5 The phylogenetic tree. The red-boxed area highlights samples mainly from China and Vietnam. The XXL represents isolated strain (ST46 type) as shown in red text.

and ceftriaxone) were ineffective, highlighting the limitations of conventional antibacterial regimens against *B. pseudomallei*.

Studies have shown that diabetes, alcoholism, chronic pulmonary diseases, chronic kidney diseases, long-term use of hormonal drugs, or immunodeficiency caused by other diseases are high-risk factors for the occurrence of melioidosis.[11,12] However, the patient reported in this case had no underlying diseases but suffered from infections in multiple sites, revealing the transmission and infection risks of this disease among healthy populations, which should draw more attention from clinicians in non-endemic areas.

The inability to identify *Bacillus pseudomallei* using conventional identification instruments and mass spectrometers further exacerbates the difficulty of diagnosis. A systematic review comparing different diagnostic methods for melioidosis showed that traditional methods have significant limitations, while tNGS has unique advantages in pathogen detection.[13] tNGS detection has the advantages of fast speed, wide coverage and high accuracy compared with mNGS detection, but its cost is only one-fourth. The diagnosis in our report relied on the combined application of tNGS and microbiological culture, demonstrating the necessity of using molecular detection techniques for precise pathogen detection in cases of unexplained infections.

Based on the drug sensitivity test results, the appropriate antibiotic combination achieved a good therapeutic effect, suggesting the significance of individualized treatment. A meta-analysis on the optimal antibiotic treatment duration for melioidosis can also provide a reference for the treatment duration in this case, ensuring the effectiveness of treatment.[14]

Traditionally, melioidosis is transmitted through contact with soil or water in endemic areas.[15] Although the pathogen was not detected in the direct environmental samples (turtles and soil), considering the patient's exposure history of purchasing live animals from Yunnan online, it is speculated that the pathogen might have been indirectly introduced into non-endemic areas through unmonitored environmental carriers (such as soil or biological products).[16] This case implies the existence of potential non - traditional transmission routes, which requires further investigation. Previous studies have demonstrated that *B. pseudomallei* can spread over long distances through contaminated water sources, soil, or animals.[17–19] This case presents a novel scenario where cross-border pet trade might emerge as a new transmission chain. Animals may also be important vectors for *B. pseudomallei* to extend its presence beyond traditional endemic areas.[20,21] This highlights the need for greater awareness of such non - traditional transmission routes in the context of increasing global trade. As people can easily access items from different regions through online platforms, the risk of introducing infectious agents from endemic areas to non-endemic ones is rising. Authorities should consider implementing measures to monitor and regulate the trade of potentially infectious items, such as live animals and plants, to prevent the spread of diseases like melioidosis.

The ST46 strain is commonly found in Southeast Asia and Hainan, China.[22] In our case, the isolated strain showed high homology with the Vietnamese strain (with a single nucleotide polymorphism difference≤5). It is hypothesized that it might have been introduced into Yunnan through trade activities along the Lancang-Mekong River Basin. Although Yunnan is not a traditional melioidosis endemic area, its tropical climate provides conditions that could potentially make it a source of the pathogen. Therefore, it is essential to conduct environmental pathogen screening in such regions to better understand the distribution and prevalence of the pathogen. A study on the phylogenetic analysis of *B. pseudomallei* strains from different regions can help us better understand the genetic relationship between the strains in this case and those in other regions, providing a basis for tracing the spread of the pathogen.[23] This would not only help in early detection and prevention of local outbreaks but also contribute to tracing the spread of specific strains across different regions. Moreover, it emphasizes the importance of international cooperation in monitoring and controlling the spread of infectious diseases, especially those with the potential for geographical expansion through trade and other human activities.

In conclusion, the occurrence of cases in non-endemic areas like in our presented case indicates that the spread pattern might be changing due to various factors such as global trade. Clinicians should be more vigilant about this disease even in areas where it was previously rarely seen. This case enriches our understanding of melioidosis in terms of clinical, diagnostic, treatment, and epidemiological aspects and can serve as a reference for clinicians in dealing with similar cases in the future.

Ethics Approval and Informed Consent

This study was conducted in accordance with the Declaration of Helsinki and approved by the Medical Ethics Committee of the Second Affiliated Hospital of Jiaxing University (Num: 2023JX132-01). Institutional approval was also required and obtained from the Second Affiliated Hospital of Jiaxing University for the publication of the case details. Written informed consent was obtained from the patients to publish this paper.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; have drafted, revised or critically reviewed the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This research was funded by Science and Technology Bureau of Jiaxing City (Num: 2023AD11018).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Mou S, Savchenko V, Filz V, Böttcher T, DeShazer D. Burkholderia pseudomallei produces 2-alkylquinolone derivatives important for host virulence and competition with bacteria that employ naphthoquinones for aerobic respiration. *Front Microbiol*. 2024;15:1474033. doi:10.3389/fmicb.2024.1474033
2. Jenkins CH, Scott AE, O'Neill PA, Norville IH, Prior JL, Ireland PM. The arabinose 5-phosphate isomerase KdsD is required for virulence in Burkholderia pseudomallei. *J Bacteriol*. 2023;205(8):e0003423. doi:10.1128/jb.00034-23
3. Meumann EM, Limmathurotsakul D, Dunachie SJ, et al. Burkholderia pseudomallei and melioidosis. *Nat Rev Microbiol*. 2024;22(3):155–169. doi:10.1038/s41579-023-00972-5
4. Chang CY. Periorbital cellulitis and eyelid abscess as ocular manifestations of melioidosis: a report of three cases in Sarawak, Malaysian Borneo. *IDCases*. 2019;19:e00683.
5. Zheng W, Kuang S, Zhong C, et al. Risk factors for melioidosis mortality and epidemics: a multicentre, 10-year retrospective cohort study in Northern Hainan. *Infect Dis Ther*. 2023;12(3):951–964. doi:10.1007/s40121-023-00768-3
6. Limmathurotsakul D, Golding N, Dance DA, et al. Predicted global distribution of Burkholderia pseudomallei and burden of melioidosis. *Nat Microbiol*. 2016;1(1):15008. doi:10.1038/nmicrobiol.2015.8
7. Ni HY, Zhang Y, Huang DH, et al. Multi-systemic melioidosis in a patient with type 2 diabetes in non-endemic areas: a case report and review of literature. *World J Clin Cases*. 2024;12:1669–1676.
8. Norman FF, Blair BM, Chamorro-Tojeiro S, et al. The evolving global epidemiology of human melioidosis: a narrative review. *Pathogens*. 2024;13(11):926. doi:10.3390/pathogens13110926
9. Currie BJ, Janson S, Meumann EM, Martin GE, Ewin T, Marshall CS. The 2024 revised Darwin melioidosis treatment guideline. The Northern territory disease control. *Bulletin*. 2023;30(4):3–12.
10. Wiersinga J, Currie B, Peacock S. Melioidosis. *N Engl J Med*. 2012;13(11):1035–1044. doi:10.1056/NEJMra1204699
11. Raj S, Sistla S, Sadanandan DM, Kadhiravan T, Rameesh BMS, Amalnath D. Clinical profile and predictors of mortality among patients with melioidosis. *J Glob Infect Dis*. 2023;15(2):72–78. doi:10.4103/jgid.jgid_134_22
12. Basheer A, Iqbal N, S C, Kanungo R, Kandasamy R. Melioidosis: distinctive clinico-epidemiological characteristics in southern India. *Trop Doct*. 2021;51(2):174–177. doi:10.1177/0049475520943698
13. Fairley L, Smith S, Maisrikrod S, et al. Systematic review and meta-analysis of diagnostic tests for diagnosis of melioidosis. *Acta Trop*. 2021;214:105784. doi:10.1016/j.actatropica.2020.105784
14. Anothaisintawee T, Harncharoenkul K, Poramathikul K, et al. Efficacy of drug treatment for severe melioidosis and eradication treatment of melioidosis: a systematic review and network meta-analysis. *PLoS Negl Trop Dis*. 2023;17:e0011382.
15. Mayo M, Kaesti M, Harrington G, et al. Burkholderia pseudomallei in unchlorinated domestic bore water, Tropical Northern Australia. *Emerg Infect Dis*. 2011;17(7):1283–1285. doi:10.3201/eid1707.100614
16. Shaw T, Assig K, Tellapragada C, et al. Environmental factors associated with soil prevalence of the melioidosis pathogen Burkholderia pseudomallei: a longitudinal seasonal study from South West India. *Front Microbiol*. 2022;13:902996. doi:10.3389/fmicb.2022.902996
17. Baker AL, Warner JM. Burkholderia pseudomallei is frequently detected in groundwater that discharges to major watercourses in northern Australia. *Folia Microbiol*. 2016;61(4):301–305. doi:10.1007/s12223-015-0438-3
18. Chapple SN, Price EP, Sarovich DS, et al. Burkholderia pseudomallei genotype distribution in the Northern Territory, Australia. *Am J Trop Med Hyg*. 2016;94(1):68–72. doi:10.4269/ajtmh.15-0627
19. Sermswan RW, Royros P, Khakhum N, et al. Direct detection of Burkholderia pseudomallei and biological factors in soil. *Trans R Soc Trop Med Hyg*. 2015;109(7):462–468. doi:10.1093/trstmh/trv040
20. Höger AC, Mayo M, Price EP, et al. The melioidosis agent Burkholderia pseudomallei and related opportunistic pathogens detected in faecal matter of wildlife and livestock in northern Australia. *Epidemiol Infect*. 2016;144(9):1924–1932. doi:10.1017/S0950268816000285
21. Sprague LD, Neubauer H. Melioidosis in animals: a review on epizootiology, diagnosis and clinical presentation. *J Vet Med B Infect Dis Vet Public Health*. 2004;51(7):305–320. doi:10.1111/j.1439-0450.2004.00797.x
22. Zheng H, Qin J, Chen H, et al. Genetic diversity and transmission patterns of Burkholderia pseudomallei on Hainan island, China, revealed by a population genomics analysis. *Microb Genom*. 2021;7(11):000659. doi:10.1099/mgen.0.000659
23. Kamthan A, Shaw T, Mukhopadhyay C, et al. Molecular analysis of clinical Burkholderia pseudomallei isolates from southwestern coastal region of India, using multi-locus sequence typing. *PLoS Negl Trop Dis*. 2018;12:e0006915.