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Case report

Disseminated *Mycobacterium colombiense* infection mimicking malignancy: A case report

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ABSTRACT

Mycobacterium colombiense, an infrequently reported non-tuberculous mycobacterium, is characterized by its slow-growing nature and capacity to simulate malignancies in clinical presentation. This report details a case of disseminated *M. colombiense* infection initially misidentified as cancer due to atypical symptoms, negative etiological tests, and imaging suggestive of a neoplastic disease. However, comprehensive diagnostic investigations, including a bone marrow biopsy and flow cytometry analysis, excluded malignancy as the diagnosis. The patient subsequently developed palpable masses, from which a definitive diagnosis was made using metagenomic Next-Generation Sequencing (mNGS) and culture of aspirate. A regimen of clarithromycin, ethambutol, rifampin, and amikacin was administered, leading to substantial improvement and resumption of activities at the eight-month follow-up. This case highlights the diagnostic challenges posed by the nonspecific clinical presentation of disseminated *M. colombiense* infection and the importance of rigorous investigation to avoid grave misdiagnosis and treatment delays.

1. Introduction

Non-tuberculous mycobacteria (NTM) encompass a diverse group of mycobacterial species, excluding *Mycobacterium tuberculosis* and *Mycobacterium leprae*, and are recognized as opportunistic pathogens [1]. Notably, the *Mycobacterium avium* complex (MAC), predominantly comprising *Mycobacterium avium* and *Mycobacterium intracellulare* [2], now also includes *M. colombiense* [3,4], due to advancement in molecular diagnostics that facilitate its identification and attract substantial scientific interest. NTM are known to manifest a spectrum of clinical forms, including pulmonary, lymph nodal, cutaneous, soft tissue, and disseminated diseases [5,6]. Disseminated NTM infections present substantial diagnostic challenges, often masquerading as metastatic malignancies, myeloma, or lymphomas and consequently affecting prognosis [6]. We detail the first well-documented case of disseminated *M. colombiense* infection, which clinically mimicked a malignant neoplastic process, emphasizing the intricacies involved in the accurate diagnosis of such pathogens.

2. Case presentation

A 52-year-old female with well-controlled HIV, undergoing treatment with albuvirtide and dolutegravir, presented with symptoms

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of unexplained fever and lower back pain persisting for one week. She has no other underlying diseases, no hereditary family diseases, and is in good socio-psychological health. Despite prior extensive diagnostic efforts, which included negative serologic tests, blood and bronchoalveolar lavage cultures, comprehensive chest and lumbar spine imaging, and mNGS, no causative pathology was identified. Her effective HIV management was indicated by undetectable viral loads and a $CD4^+$ T-cell count of 255 cells/μL. After empirical anti-tuberculous therapy failed to alleviate her symptoms, she was subsequently referred to the specialized infectious disease clinic at West China Hospital, Sichuan University, for further evaluation.

Upon presentation at our infectious disease clinic, the patient's physical examination was unremarkable. Extensive laboratory assessments, including complete blood count and procalcitonin, revealed no significant abnormalities except for a slight elevation in C-reactive protein (Table 1). Assays for galactomannan, (1,3)-β-D-Glucan assays, TB-interferon-gamma release assays, *Cryptococcus neoformans* and *Pneumocystis jirovecii* DNA, as well as screening for respiratory viruses, all returned negative results. Ultrasound of the superficial lymph nodes and echocardiography showed no significant findings. However, further imaging presented concerning findings: MRI of the lumbar spine revealed multiple patchy lesions in the lumbar and sacral regions, with appearances suggesting neoplastic changes (Fig. 1A). Moreover, PET/CT revealed widespread osteolytic damage and heightened glucose metabolism throughout the skeleton, heightening the suspicion of an underlying malignancy (Fig. 1B). However, no evidence supporting a primary or hematological malignancy was discovered after detailed exploration, including imaging studies failing to identify a primary tumor. Immunofixation electrophoresis and immunoglobulin light chain measurement were within normal limits. Furthermore, bone marrow biopsy and flow cytometry showed no abnormal findings (Fig. 1C), effectively excluding malignancy, our primary differential at presentation.

As the patient's condition progressed, palpable masses emerged on her body surface (Fig. 1D). Acid-fast bacillus staining of a surface mass sample was positive (Fig. 1E). Subsequently, a puncture aspiration of the surface mass was performed from which all microbial DNA was extracted. The DNA was then fragmented, a library was constructed, and high-throughput sequencing was conducted on a sequencing platform. The sequencing results were compared with a high-quality, clinical-grade database, revealing the presence of *M. colombiense* in the surface mass (Sequence 768), establishing a diagnosis of disseminated *M. colombiense* infection. Further testing for anti-interferon gamma autoantibodies was negative. The patient was administered a quadruple anti-infective regimen consisting of clarithromycin 500 mg twice daily, ethambutol 750 mg once daily, rifampin 600 mg once daily, and amikacin 400 mg once daily. After one month of anti-infection treatment, the patient's body temperature normalized, and her lower back pain gradually alleviated. Repeated complete blood count and procalcitonin were normal, with C-reactive protein slightly elevated. The $CD4^+$ T-cell count was 265 cells/μL, maintaining an undetectable HIV viral load (Table 1). This led to clinical improvement and the subsequent discharge of the patient. Five weeks later, a culture of the mass aspirate grew *M. colombiense*. Antibiotic susceptibility testing was performed using a Drug Susceptibility Test Kit for Mycobacteria (Encode, Zhuhai, China), according to the manufacturer's instructions. The results were interpreted according to Clinical and Laboratory Standards Institute guidelines M62 1st Edition [7]. The strain exhibited sensitivity to ethambutol (minimum inhibitory concentration [MIC] 5 μg/mL), clarithromycin (MIC 4 μg/mL), rifampin (MIC $\leq$1 μg/mL), and amikacin (MIC 16 μg/mL), but resistance to moxifloxacin (MIC 4 μg/mL) (Table 2).

Post-discharge, the patient underwent monthly follow-ups at the outpatient clinic. Open communication was maintained to ensure the patient understood the treatment process. In accordance with treatment guidelines, after three months of continued therapy, amikacin was discontinued, and treatment was maintained with clarithromycin, ethambutol, and rifampin. Five months post-discharge, a repeat thoracic and lumbar spine CT scan was performed (Fig. 2A). The results indicated an increase in vertebral bone density compared to that observed in the initial post-discharge CT scans (Fig. 2B), suggesting improvement. During an eight-month follow-up, no drug-related adverse reactions occurred, the patient's condition remained stable, and she resumed normal daily activities.

3. Discussion

M. colombiense, a member of the MAC, is a non-tuberculous mycobacterium initially identified in 2006 from an HIV-positive individual in Colombia [3]. Cases of *M. colombiense* infection are rarely reported, likely due to previous diagnostic challenges in distinguishing between MAC species [8]. Recent studies suggest that *M. colombiense* infections predominantly afflict immunocompromised individuals, with those who are severely immunocompromised at an increased risk of developing life-threatening disease [8–12]. This case involved a patient with well-controlled HIV infection, characterized by undetectable levels of HIV RNA and a $CD4^+$ T-cell count of 255 cells/μL. The presentation of an aggressive, systemic *M. colombiense* infection in such a patient is both atypical and concerning, as it challenges the prevailing assumption that significant morbidity is unlikely in the absence of marked immunodeficiency.

Table 1
Routine laboratory test results at admission and discharge.

Time Point	White Blood Cells (× 10^9/L)	Neutrophils (× 10^9/L)	Lymphocytes (× 10^9/L)	C-Reactive Protein (mg/L)	Procalcitonin (ng/mL)	$CD4^+$ T-cell (cells/μL)	HIV Viral Load
Admission	8.26	6.37	1.25	44.2	0.05	255	Amplification Negative
Discharge	7.87	5.88	1.41	79.7	0.04	265	Amplification Negative

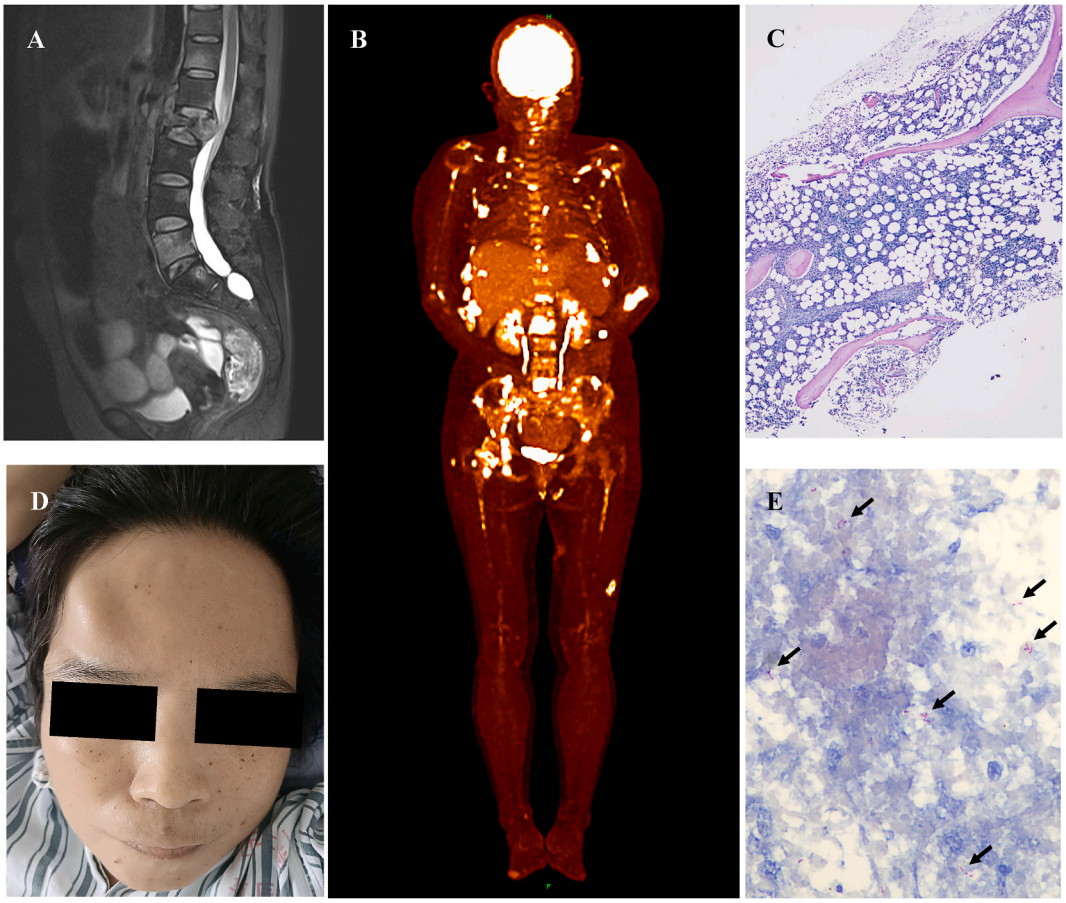

Fig. 1. Disseminated *M. colombiense* infection.
(A) Lumbar spine MRI suggests multiple lumbar and sacral vertebrae lesions, indicative of neoplastic changes. (B) PET/CT shows extensive osteolytic destruction and increased glucose uptake across the skeleton, suggesting malignancy. (C) Bone marrow biopsy demonstrates active proliferation of hematopoietic cells. (D) Visible mass on the forehead. (E). Acid-fast stain of the surface mass with a positive result (black arrow).

M. colombiense infections can result from ingestion or direct cutaneous inoculation through skin injury, leading to a wide range of clinical manifestations that aptly earn it the moniker "great mimicker" [12,13]. As reported by Tang et al., among nine documented disseminated *M. colombiense* infection cases, the majority primarily involved the lungs, lymph nodes, and skin, with fewer cases affecting visceral organs [12]. The present case features extensive skeletal lesions atypical of *M. colombiense* infection. The Initial negative screenings and malignancy-mimicking imaging led to an erroneous focus on potential neoplasia. It is important to note that the occurrence of non-tuberculous mycobacteria (NTM) mimicking malignancy is relatively rare (3.6 %) yet carries a high risk of severe, sometimes fatal consequences [14]. This case highlights the clinical challenges in accurately diagnosing NTM infections.

The definitive diagnosis of NTM infection hinges on microbiological confirmation. In the presented case, acid-fast bacillus staining of the surface mass aspirate yielded positive results, but this method alone cannot differentiate NTM from *M. tuberculosis*. With its ability to identify pathogens rapidly and accurately at the species level, mNGS has emerged as a valuable diagnostic tool [15]. In this instance, mNGS of the aspirate pinpointed *M. colombiense* within two days, providing critical insights for an accurate diagnosis. While NTM culture is integral for species confirmation and in vitro susceptibility testing to guide treatment, it's often protracted and susceptible to false negatives [16]. In this case, it took five weeks to culture *M. colombiense* from the aspirate. However, the subsequent susceptibility tests did play a crucial role in shaping the therapeutic approach. Therefore, both mNGS and cultures are indispensable, serving as complementary modalities in effectively diagnosing and managing NTM infections.

In conclusion, compared to existing studies [5,6,8,9,11,12], our research emphasizes that disseminated *M. colombiense* infections can occur even in patients without marked immunodeficiency. Disseminated *M. colombiense* infections can mimic the presentation of malignant tumors, earning the nickname "great mimicker" and posing significant diagnostic challenges. Modern diagnostic techniques such as mNGS play a pivotal role in diagnosing challenging cases of infectious diseases, while traditional culture remains irreplaceable for guiding treatment. A notable limitation of our study is that despite an extensive eight-month follow-up, the treatment regimen's long-term effects and safety warrant further observation and evaluation.

Table 2
Susceptibility of *M. colombiense* to antibiotics.

Antibiotic	Doxycycline	Ethambutol	Rifabutin	Moxifloxacin	Clarithromycin	Linezolid	Minocycline	Amikacin	Rifampin
MIC (μg/mL)	64	5	≤0.5	4	4	32	32	16	≤1
Susceptibility (S, I, R)	R	S	S	R	S	R	R	S	S

MIC (Minimum Inhibitory Concentration). Interpretation: S (Susceptible), I (Intermediate), R (Resistant).

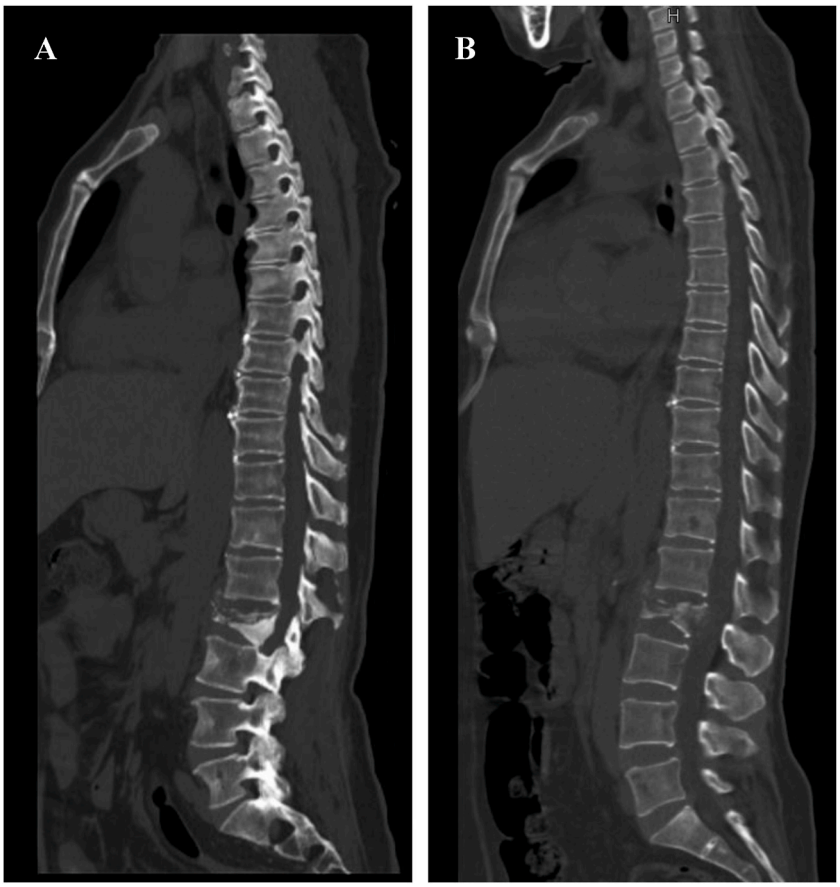

Fig. 2. CT scans of the thoracic and lumbar spine.
(A) CT scan of the thoracic and lumbar spine five months after discharge. (B) CT scan of the thoracic and lumbar spine at discharge.

4. Conclusion

We present a case of disseminated *M. colombiense* infection, with initial clinical manifestations that closely mimicked malignancy. This case underscores the critical roles of mNGS for rapid pathogen identification and the vital importance of pathogen culture combined with susceptibility testing for effective treatment strategies. Given the demographic shifts toward a larger elderly population and the increasing prevalence of secondary immunodeficiency conditions, the incidence of *M. colombiense* infections may rise. Clinicians should maintain vigilance for *M. colombiense* as a potential causative agent in similar clinical presentations to avoid misdiagnoses and subsequent delays in administering appropriate therapy.

Ethics statement

The authors affirm that they have obtained all required consent from the patient. In the consent form, the patient consented to her images and other clinical information being reported in the journal. All authors complied with the journal's ethics and policy.

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Data availability statement

The data associated with this study have not been deposited in a publicly available repository. Instead, all data were included in the article.

Additional information

No additional information is available for this paper.

CRediT authorship contribution statement

Jiayuan Qin: Writing – original draft, Validation, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Guangmin Tang:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Not applicable.

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