Infection and Drug Resistance

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ORIGINAL RESEARCH

Clinical Characteristics and Drug Resistance Profile of *Mycobacterium colombiense* Infection: A Study of 22 Cases

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Purpose: *Mycobacterium colombiense*, a rare yet clinically significant species within the *Mycobacterium avium* complex, demonstrates a marked propensity for disseminated disease and is associated with high mortality. However, data on its clinical characteristics and drug resistance profiles remain scarce. This study aims to conduct an in-depth analysis of the clinical characteristics and drug resistance profile of *Mycobacterium colombiense* disease, providing insights for optimizing its diagnosis and treatment strategies.

Patients and Methods: We retrospectively analyzed the clinical data of 22 HIV-negative patients diagnosed with *Mycobacterium colombiense* disease at Guangzhou Chest Hospital from April 2021 to April 2024. Data included clinical manifestations, laboratory findings, and treatment regimens.

Results: Among the 22 confirmed cases, disseminated *Mycobacterium colombiense* disease accounted for 63.6% (14/22), primarily involving the lungs, bones and joints, serous cavities, and lymph nodes. Common symptoms included cough/sputum production, fatigue/weight loss, fever, bone pain, and subcutaneous abscesses/skin ulcers. All patients tested positive for *Mycobacterium colombiense* via tNGS, while 19 cases were concurrently confirmed through culture of sputum or bronchoalveolar lavage fluid as part of the *Mycobacterium avium* complex. All patients received combined anti-nontuberculous mycobacterial therapy. Drug susceptibility testing performed in 11 cases revealed high sensitivity to bedaquiline, clofazimine, rifabutin, ethambutol, and rifampin.

Conclusion: *Mycobacterium colombiense* infection is prone to causing disseminated disease, affecting multiple organ systems with diverse clinical presentations. Timely therapeutic intervention can improve patient prognosis to some extent. This study offers valuable references for the clinical diagnosis and treatment of *Mycobacterium colombiense* infection, underscoring its practical significance in clinical practice.

Keywords: *Mycobacterium colombiense*, disseminated infection, drug susceptibility testing, nontuberculous mycobacteria, clinical characteristics

Introduction

Nontuberculous mycobacteria (NTM) refer to a broad category of mycobacteria excluding the *Mycobacterium tuberculosis* complex and *Mycobacterium leprae*. To date, approximately 200 species of NTM have been identified.[1–6] The incidence of NTM infections has been increasing annually. Among these, *Mycobacterium colombiense*, a rare species within the *Mycobacterium avium complex* (MAC), has been infrequently reported in the literature and is associated with a higher mortality rate compared to other MAC species.[6–9] This pathogen is characterized by its tendency to cause disseminated infections, involving multiple organs even in immunocompetent hosts, and it is difficult to differentiate from other MAC species using conventional culture methods.[7–9] Current treatment strategies generally follow MAC guidelines, but the drug resistance profile of *Mycobacterium colombiense* has not been systematically evaluated, leading to considerable challenges in clinical management and high mortality rates.[6,10]

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Due to the rarity of *Mycobacterium colombiense*, previous studies have been limited to case reports with small sample sizes, lacking comprehensive analyses of clinical features and drug resistance patterns. These studies have primarily focused on immunocompromised populations.[7–11] This study retrospectively analyzes the clinical characteristics and drug resistance profiles of 22 clinically confirmed HIV-negative patients with *Mycobacterium colombiense* infection, aiming to provide insights for the diagnosis and treatment of this disease.

Materials and Methods

Study Subjects

Patients hospitalized or visiting the outpatient department of Guangzhou Chest Hospital from April 2021 to April 2024 were enrolled. Those suspected of mycobacterial infection underwent targeted next-generation sequencing (tNGS) of specimens such as sputum, bronchoalveolar lavage fluid (BALF), or bone aspirates to identify *Mycobacterium colombiense* infection. This retrospective study was conducted using clinical data obtained from previously hospitalized patients. All data were anonymized before analysis. The study was approved by the Ethics Committee of Guangzhou Chest Hospital (Approval No. KY-2024-046). Due to the use of anonymized data and the study's retrospective design, the ethics committee granted an exemption from obtaining informed consent. Accordingly, this investigation was designed as a retrospective study utilizing anonymized electronic health record data.

Research Methods

Analysis of Clinical Characteristics

Inclusion Criteria: (1) Patients diagnosed with nontuberculous mycobacterial (NTM) disease according to the Diagnosis and Treatment Guidelines for Nontuberculous Mycobacterial Diseases;[2,3] (2) Detection of *Mycobacterium colombiense*-specific nucleic acid sequences via NGS in ≥1 specimen site (after excluding contamination), (3) adults of either gender presenting with relevant symptoms and confirmed by *M. colombiense* diagnostic method, (4) For patients with multiple positive cultures (eg, sputum, BALF, bone aspirate, skin pus, lymph node biopsy, blood) identified as the same species, only data from the initial diagnosis were analyzed.

Exclusion Criteria: (1) Patients with incomplete clinical data; (2) Those with NTM colonization (ie, meeting bacteriological criteria but not clinical diagnostic standards); (3) Key data missing (eg, lack of etiological confirmation or treatment follow-up records).

Clinical data including gender, age, symptoms, signs, comorbidities, imaging findings, and laboratory results were recorded.

Bacterial Identification and Drug Susceptibility Testing

Bacterial Identification

Culture and Identification Method. In accordance with the *Technical Guidelines for Tuberculosis Laboratory Testing*, mycobacterial culture was performed using the BD BACTEC MGIT 960 system (Becton, Dickinson and Company, USA).[12] Isolates obtained from culture were further identified to species or complex level using the *Mycobacterium Species Identification Kit* (DNA microarray method) manufactured by Chengdu Boao Jingxin Biotechnology Co., Ltd. All experimental procedures strictly followed the manufacturer's instructions for both instruments and reagents. The routine quality control included the use of negative controls (sterile medium) and positive controls with the reference strain *Mycobacterium avium* (ATCC 700898) and *Mycobacterium tuberculosis* H37Rv (ATCC 27294) in each batch.

tNGS Identification Method. Specimens were processed and analyzed using the Guangzhou KingMed Clinical Laboratory's KM MiniSeqDx-CN system (Guangzhou Jinqi Ruí Biotechnology Co., Ltd). The procedure involved sample processing, nucleic acid extraction, library construction, and sequencing to generate valid data. Valid sequencing data refers to the data generated when the cluster density on the sequencing instrument interface is between 590 and 800 K/mm^2, the Q30 score is ≥85%, and the data output (in million reads) calculated based on the instrument's final data yield (in MB) and the sequencing read length (76 bp) meets or exceeds 90% of the expected yield. This included the use of a non-template control (deionized, sterile, nuclease-free water) during the nucleic acid extraction step to monitor for

contamination. Library quality was assessed via agarose gel electrophoresis, with the target fragment size approximately 350 bp, and quantified using a Qubit 4.0 Fluorometer. Dual-indexed barcodes were employed for detection during the sequencing run.

Drug Susceptibility Testing

The *p-nitrobenzoic acid (PNB) method* was used to differentiate between *Mycobacterium tuberculosis* complex and NTM. For strains identified as MTBC, drug susceptibility testing was conducted using the liquid culture method. The following 12 drugs were tested: isoniazid (INH), rifampicin (RFP), ethambutol (EMB), amikacin (AMK), rifabutin (RFB), capreomycin (CPM), levofloxacin (LEV), linezolid (LZD), prothionamide (PTO), clofazimine (CFZ), moxifloxacin (MFX), and bedaquiline (BDQ). Interpretation criteria followed the guidelines provided in the drug susceptibility testing kit. The reference strain *Mycobacterium avium* (ATCC 700898) was included in each batch to validate drug potency, following standard laboratory protocols.[12]

Statistical Analysis

Data analysis was performed using SPSS software (version 24.0). Categorical variables were expressed as frequency, percentage (%), or proportion.

Results

General Characteristics

A total of 22 patients with *Mycobacterium colombiense* disease were included after excluding cases of colonization and those with incomplete data. Among them, 14 cases (63.6%) had disseminated infection, and 8 cases (36.4%) had isolated pulmonary disease, as shown in Table 1. The cohort consisted of 12 females (54.5%) and 10 males (45.5%), with an age range of 22–73 years. The mean age was 55.36 years, and the median age was 58 years. Nine patients (40.9%) were over 60 years old. Geographically, 18 patients (81.8%) were from Guangdong Province, 2 from Guangxi, and 1 each from Fujian and Zhejiang Province.

The involved anatomical sites included the lungs (22 cases), bones and joints (12 cases), serous cavities (pleural, pericardial, peritoneal, and meningeal; 12 cases), lymph nodes (superficial or mediastinal lymphadenopathy; 9 cases), skin (subcutaneous abscesses/skin ulcers; 6 cases), and liver (1 case), as given in Table 2.

All 22 patients tested positive for *Mycobacterium colombiense* via tNGS. Additionally, 19 patients were concurrently confirmed through culture as part of the MAC.

Table 1 Demographic Data of Disseminated and Non-Disseminated Infections

Characteristic	Disseminated Infection N = 14, n (%)	Non-Disseminated Infection N = 8, n (%)
Gender		
Male	5 (35.7%)	5 (62.5%)
Female	9 (64.3%)	3 (37.5%)
Age		
20-39	3 (21.4%)	0 (0%)
40-59	4 (28.6%)	6 (75.0%)
≥60	7 (50.0%)	2 (25.0%)

Note: Data are presented as n (%), where n indicates the number of patients/events.

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Table 2 Involved Sites of Mycobacterial Infection

Affected Organ/System	N=22, n (%)
Lungs	22 (100.0%)
Bones and Joints	12 (54.5%)
Serous Cavities (Pleural, Pericardial, Peritoneal, Meningeal)	12 (54.5%)
Lymph Nodes	9 (40.9%)
Skin	5 (22.7%)
Liver	1 (4.5%)

Note: Data are presented as n (%), where n indicates the number of patients/events.

Clinical Features

Comorbidities

Among the 14 patients with disseminated infection, extrapulmonary comorbidities included sepsis (7 cases), cardiac/hepatic/renal dysfunction (4 cases), anti-interferon-γ autoantibody positivity (3 cases), systemic lupus erythematosus (2 cases), hemophagocytic syndrome (1 case), thalassemia (1 case), multiple osteomyelitis (1 case), and lacunar cerebral infarction (1 case), as shown in Table 3. Pulmonary comorbidities included pneumoconiosis (1 case, 4.5%), *Scedosporium prolificansinfection* (1 case, 4.5%), and disseminated *Talaromyces marneffei* infection (2 cases, 9.1%). Among the 8 patients with isolated pulmonary infection, extrapulmonary comorbidities included ankylosing spondylitis (1 case) and hypertension (1 case). Pulmonary comorbidities included pulmonary aspergillosis (1 case).

Clinical Manifestations and Signs

The clinical symptoms of *Mycobacterium colombiense* infection are nonspecific, primarily manifesting as cough, expectoration, fatigue/weight loss, fever, and others, as shown in Table 3. Among the 22 patients, cough/expectoration was observed in 18 cases, fatigue/weight loss in 10 cases, fever in 6 cases, subcutaneous abscesses/skin ulcers in 5 cases, bone pain in 5 cases, chest tightness in 5 cases, hemoptysis/blood-tinged sputum in 4 cases, and headache in 1 case. Of these 22 patients, 12 exhibited bone and joint involvement, primarily presenting as bone destruction and/or abscess formation, with involvement of the ribs (6 cases), vertebrae (5 cases), clavicles (4 cases), scapulae (2 cases), and radius (1 case), either concurrently or in isolation. Lymph node involvement was noted in 9 cases, mainly presenting as superficial and mediastinal lymphadenopathy, including mediastinal lymphadenopathy (6 cases) and superficial lymphadenopathy (3 cases). Serous cavity involvement with effusion (pleural/pericardial/abdominal) was observed in 6 cases, pericardial/pleural thickening in 5 cases, and subcutaneous abscesses/skin ulcers in 5 cases. One patient developed disseminated

Table 3 Clinical Characteristics of Patients with *Mycobacterium colombiense* Infection

Clinical Characteristics	Disseminated Infection N = 14, n (%)	Non-Disseminated Infection N = 8, n (%)
Clinical Symptoms		
Cough/Sputum Production	1 (7.1%)	8 (100.0%)
Fever	5 (35.7%)	1 (12.5%)
Bone Pain	5 (35.7%)	0 (0%)
Chest Tightness	3 (21.4%)	2 (25%)
Hemoptysis/Blood-streaked Sputum	1 (7.1%)	3 (37.5%)

(*Continued*)

Table 3 (Continued).

Clinical Characteristics		Disseminated Infection N = 14, n (%)	Non-Disseminated Infection N = 8, n (%)
Comorbidities			
Extrapulmonary	Sepsis	7 (50.0%)	0 (0%)
	Cardiac/Hepatic/Renal Dysfunction	4 (28.6%)	0 (0%)
	Systemic Lupus Erythematosus	2 (14.3%)	0 (0%)
	Hemophagocytic Syndrome	1 (7.1%)	0 (0%)
	Thalassemia	1 (7.1%)	0 (0%)
	Pneumoconiosis	1 (7.1%)	0 (0%)
	Multiple Osteomyelitis	1 (7.1%)	0 (0%)
	Lacunar Cerebral Infarction	1 (7.1%)	0 (0%)
	Hypertension	0 (0%)	1 (12.5%)
	Ankylosing Spondylitis	0 (0%)	1 (12.5%)
Pulmonary	Disseminated *Talaromyces marneffei* Infection	2 (14.3%)	0 (0%)
	Scedosporium prolificans	1 (7.1%)	0 (0%)
	Pneumoconiosis	1 (7.1%)	0 (0%)
	Pulmonary Aspergillosis	0 (0%)	1 (12.5%)
Imaging Findings and Laboratory Findings			
Lung Imaging	Patchy Shadows	1 (7.1%)	8 (100.0%)
	Nodules	6 (42.9%)	4 (50%)
	Bronchiectasis	3 (21.4%)	4 (50%)
	Mediastinal Lymphadenopathy	6 (42.9%)	0 (0%)
	Pleural/Pericardial Effusion	6 (42.9%)	0 (0%)
	Pleural/Pericardial Thickening	2 (14.3%)	3 (37.5%)
	Fibrous Strips	4 (28.6%)	2 (25%)
	Cavitation	1 (7.1%)	3 (37.5%)
	Atelectasis	1 (7.1%)	0 (0%)
Bone and Joint Imaging	Patchy Bone Destruction	8 (57.1%)	0 (0%)
	Peripheral Soft Tissue Swelling	5 (35.7%)	0 (0%)
	Cystic Bone Destruction	4 (28.6%)	0 (0%)
	Bone Sclerosis	4 (28.6%)	0 (0%)

(*Continued*)

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Table 3 (Continued).

Clinical Characteristics		Disseminated Infection N = 14, n (%)	Non-Disseminated Infection N = 8, n (%)
Laboratory Findings	Decreased Absolute CD4+ T-cell Count	6 (42.9%)	0 (0%)
	Elevated Leukocyte and Neutrophil Count	1 (7.1%)	1 (12.5%)
	Hypoalbuminemia/Anemia	9 (64.3%)	4 (50%)
	Positive Anti-Interferon-γ Autoantibody (Negative reference value <6.8 μg/mL)	3 (21.4%)	0 (0%)

Note: Data are presented as n (%), where n indicates the number of patients/events.

infection involving the liver and meninges, and another presented with bone destruction accompanied by the formation of a cold abscess that ruptured through the body surface.

Imaging Features

All patients demonstrated pulmonary involvement. Chest CT findings primarily included patchy opacities, nodular shadows, bronchiectasis, mediastinal lymphadenopathy, pleural effusion, and others (Figure 1A–D). Among the 14 patients with disseminated infection, 12 underwent CT/MRI examinations of bones and joints, which mainly revealed patchy bone destruction, cystic bone destruction, and surrounding soft tissue swelling (Figure 1G–I). Electronic bronchoscopy was performed in 12 of the 22 patients, revealing mild chronic bronchitis in 7 cases, luminal stenosis (due to edematous narrowing, neoplastic obstruction, or granulomatous necrotic material) in 7 cases (Figure 1E and F), and essentially normal findings in 1 case.

Laboratory Findings

Elevated inflammatory markers were observed as follows: CRP >10 mg/L in 19 cases (86.4%), elevated white blood cell count (>10×109/L) in 16 cases (72.7%), neutrophil count >6.3×10^9/L in 15 cases (68.2%), and markedly elevated white blood cell count (>20×10^9/L) in 4 cases (18.2%). Hemoglobin and albumin levels were reduced in all 18 patients tested, with 4 patients exhibiting severe anemia (hemoglobin >30 g/L and ≤60 g/L), and 3 patients having moderate anemia (hemoglobin >60 g/L and ≤90 g/L). Lymphocyte subset analysis was performed in 18 patients, showing CD4+ T-cell counts ranging from 172 to 1168 cells/μL (median: 482 cells/μL). Only 2 patients had CD4+ T-cell counts <300 cells/μL, 7 patients had counts between 300 and 500 cells/μL, and 9 patients had counts >500 cells/μL. Notably, the two deceased patients had CD4+ T-cell counts of 1168 and 816 cells/μL, respectively. Anti-interferon-γ antibody testing was performed in 3 patients, all of whom tested positive.

Drug Resistance Analysis

Drug susceptibility testing was performed in 11 patients, as shown in Table 4. The results showed susceptible to bedaquiline (0%), clofazimine (9.1%), rifabutin (18.2%), ethambutol (18.2%), and rifampin (27.3%). Notably, no resistance to bedaquiline was observed, and only one case (9.1%) exhibited resistance to clofazimine.

In contrast, the results showed resistant to levofloxacin (100%), linezolid (100%), amikacin (100%), isoniazid (100%), capreomycin (100%), moxifloxacin (90.9%), and prothionamide (81.8%). Specifically, the results of drug resistance indicate that the majority of patients (≥90.9%) were resistant to levofloxacin, linezolid, amikacin, isoniazid, and capreomycin and moxifloxacin.

Treatment and Outcomes

All enrolled patients received anti-nontuberculous mycobacterial therapy, primarily consisting of combination regimens, as shown in Table 5. The selection of therapeutic agents, including macrolides (eg, clarithromycin or azithromycin),

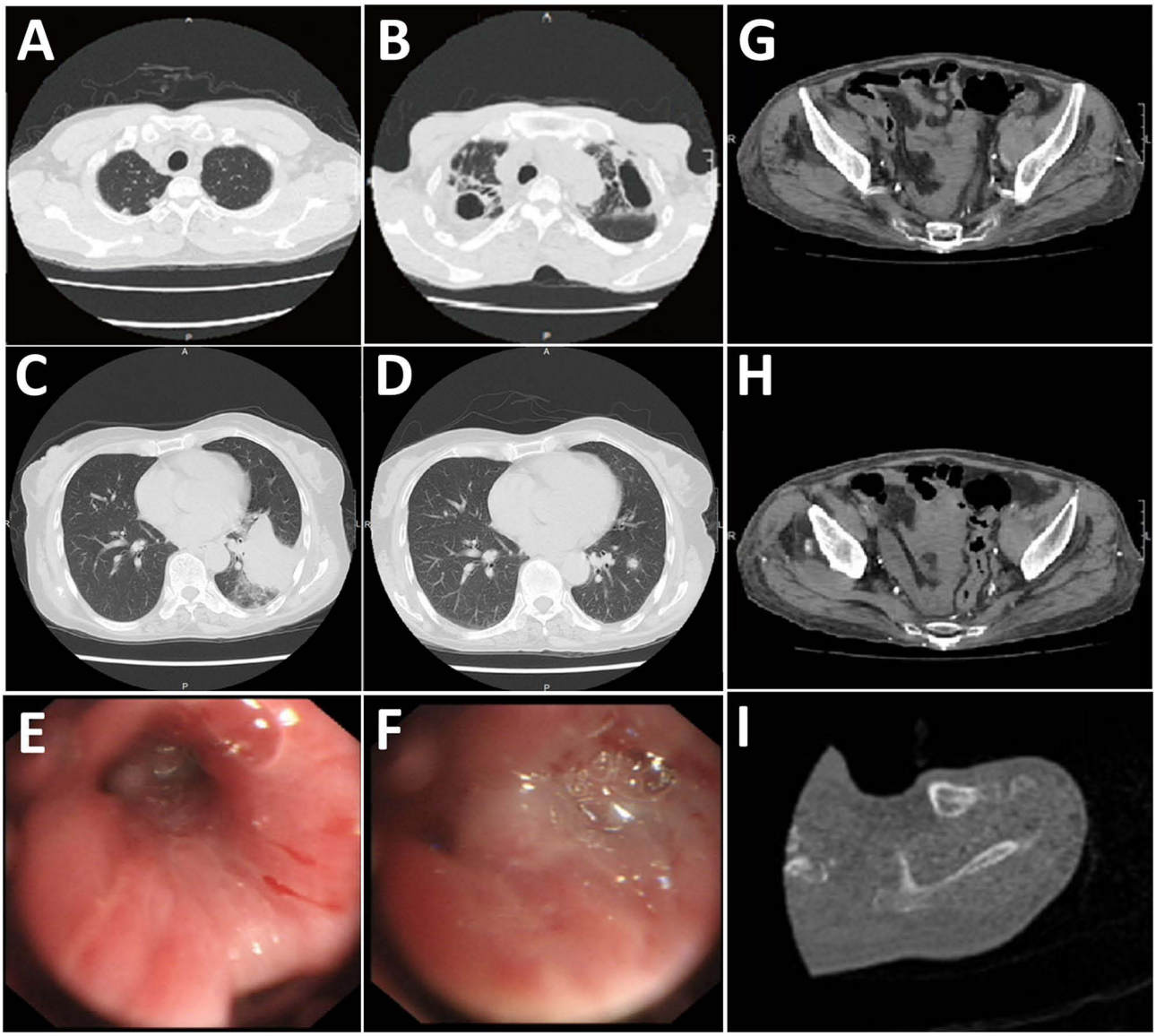

Figure 1 Imaging Findings of the Patients (**A**–**D**) Chest CT scans demonstrate varied pulmonary abnormalities. (**A**) Patient 1 exhibits a pulmonary nodule. (**B**) Patient 2 shows cavities in both upper lobes accompanied by cylindric bronchiectasis. (**C**) Patient 3 presents scattered patchy opacities in both lungs. (**D**) Patient 4 reveals an irregular soft tissue mass at the anterior basal segment of the left lower lobe, extending across the fissure. (**E** and **F**) Bronchoscopy of Patient 3 identifies swelling in the apical segment of the left upper lobe with the formation of viscous purulent secretions. (**G** and **H**) Abdominopelvic CT scans reveal thickening of the peritoneum, omentum, and mesentery, with strand-like opacities within the abdominal cavity and retroperitoneal fat spaces. Subcutaneous edema of the thoracic, abdominal, and pelvic walls is noted, along with multiple abscesses in the right anterior pelvic wall, bilateral sacroiliac muscles, and the muscle groups surrounding the femora and within intermuscular spaces, suspected to be caused by non-tuberculous mycobacterial infection. (**I**) CT of the acromioclavicular joint demonstrates multiple bony destructions in the proximal clavicle and scapula, with relatively well-defined margins and sclerotic rims observed in most lesions.

ethambutol, rifampin, amikacin, levofloxacin, and linezolid. Currently, there is no unified international treatment consensus specifically for *Mycobacterium colombiense* infections. In our study, the treatment regimens were primarily formulated with reference to the guidelines for slow-growing nontuberculous mycobacteria outlined in the ATS/ERS/ESCMID/IDSA clinical practice guidelines and the Chinese Guideline for the Diagnosis and Treatment of Nontuberculous Mycobacterial Diseases (2020 Edition) issued by the Tuberculosis Branch of the Chinese Medical Association.[2,3] Eight patients with disseminated infection underwent surgical interventions, such as excision of subcutaneous masses, debridement of skin ulcers, and vertebral fixation. Following the treatment, clinical improvement was achieved in 20 patients, while two patients died. Regarding the two patient fatalities, both individuals were of advanced age and presented with disseminated infections complicated by severe comorbidities; we posit that this clinical profile

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Table 4 Results of Drug Resistance Testing

Drug (Abbreviation)		Disseminated Infection, N = 8, n (%)	Non-Disseminated Infection, N = 3, n (%)	Total Strains, N = 11, n (%)
The first-line anti-tubercular drug	Isoniazid (INH)	8 (100.0%)	3 (100.0%)	11 (100.0%)
	Rifampicin (RFP)	2 (25.0%)	1 (33.3%)	3 (27.3%)
	Ethambutol (EMB)	1 (12.5%)	1 (33.3%)	2 (18.2%)
	Rifabutin (RFB)	0 (0%)	2 (66.7%)	2 (18.2%)
The second-line anti-tubercular drug	Levofloxacin (LEV)	8 (100.0%)	3 (100.0%)	11 (100.0%)
	Linezolid (LZD)	8 (100.0%)	3 (100.0%)	11 (100.0%)
	Amikacin (AMK)	8 (100.0%)	3 (100.0%)	11 (100.0%)
	Capreomycin (CPM)	8 (100.0%)	3 (100.0%)	11 (100.0%)
	Moxifloxacin (MFX)	8 (100.0%)	2 (66.7%)	10 (90.9%)
	Prothionamide (PTO)	6 (75.0%)	3 (100.0%)	9 (81.8%)
	Clofazimine (CLO)	0 (0%)	1 (33.3%)	1 (9.1%)
	Bedaquiline (BDQ)	0 (0%)	0 (0%)	0 (0%)

Note: Data are presented as n (%), where n indicates the number of patients/events.

Table 5 Results of Medication and Surgery Treatment Regimen for the 22 Patients

No.	Gender	Age	Disseminated Infection	Medication Regimen and Dosage	Treatment Duration	Surgical Regimen	Outcome
1	Male	73	Y	Rifampicin 450 mg/d, Ethambutol 750mg/d, Clarithromycin 500 mg/bid, Amikacin 400mg/d	15 months	Excision of Right Subclavian Mass	Improvement
2	Male	70	Y	Rifampicin 450 mg/d, Ethambutol 750mg/d, Amikacin 400mg/d, Azithromycin 500 mg/d	12 months	Excision of Left Scapular Lesion	Improvement
3	Male	51	N	Rifabutin 300 mg/d, Azithromycin 500 mg/d, Ethambutol 750mg/d	12 months	/	Improvement
4	Male	37	Y	Rifabutin 300 mg/d, Clarithromycin 500 mg bid, Ethambutol 750mg/d, Linezolid 600 mg/d	18 months	Excision of Thoracic Vertebral Lesion and Instrumentation	Improvement
5	Female	71	Y	Rifampicin 450 mg/d, Ethambutol 750 mg/d, Clarithromycin 500 mg bid, Amikacin 400 mg/d, Linezolid 600 mg/d	6 months	/	Death
6	Female	60	Y	Clarithromycin 500 mg/bid, Ethambutol 750mg/d, Amikacin 400mg/d, Linezolid 600 mg/d	13 months	/	Improvement
7	Male	66	Y	Rifampicin 300 mg/d, Ethambutol 750mg/d, Amikacin 400mg/d, Azithromycin 500 mg/d	12 months	/	Improvement

(*Continued*)

Table 5 (Continued).

No.	Gender	Age	Disseminated Infection	Medication Regimen and Dosage	Treatment Duration	Surgical Regimen	Outcome
8	Female	56	Y	Rifabutin 300 mg/d, Clarithromycin 500 mg/bid, Ethambutol 750mg/d, Prothionamide 250 mg/bid	12 months	Surgical incision and drainage of abscess in the left hand	Improvement
9	Female	22	Y	Clarithromycin 500 mg bid, Ethambutol 750mg/d, Linezolid 600 mg/d, Amikacin 400mg/d	12 months	/	Improvement
10	Female	66	N	Rifampicin 300 mg/d, Ethambutol 750mg/d, Clarithromycin 500 mg bid, Amikacin 400mg/d, Linezolid 600 mg/d	12 months	/	Improvement
11	Male	57	Y	Amikacin 400mg/d, Rifabutin 300 mg/d, Linezolid 600 mg/d, Azithromycin 500 mg/d	9 months	Bilateral Cervical Lymph Node Excision (Including Level I Nodes)	Death
12	Female	64	Y	Rifampicin 300 mg/d, Ethambutol 750mg/d, Clarithromycin 500 mg bid, Linezolid 600 mg/d	18 months	Excision of a parotid lesion/mass	Improvement
13	Female	54	Y	Rifampicin 300 mg/d, Ethambutol 750mg/d, Clarithromycin 500 mg bid	15 months	Excision of Gluteal Soft Tissue Lesion	Improvement
14	Male	65	N	Rifabutin 300 mg/d, Clarithromycin 500 mg/bid, Ethambutol 750mg/d, Amikacin 400mg/d	12 months	/	Improvement
15	Female	53	Y	Linezolid 600 mg/d, Clarithromycin 500 mg/bid, Moxifloxacin 400 mg/d, Doxycycline 100 mg/d, Ethambutol 750mg/d	12 months	/	Improvement
16	Female	66	Y	Rifampicin 300 mg/d, Ethambutol 750mg/d, Clarithromycin 500 mg/bid	12 months	/	Improvement
17	Female	25	Y	Rifampicin 600 mg/d, Ethambutol 750mg/d, Levofloxacin 500 mg/d, Clarithromycin 500 mg/bid	16 months	Anterior Cervical and Anterior Superior Mediastinal Lymph Node Excision	Improvement
18	Female	59	N	Rifabutin 300 mg/d, Ethambutol 750mg/d, Clarithromycin 500 mg bid, Levofloxacin 500 mg/d, Amikacin 400mg/d	12 months	/	Improvement
19	Female	42	N	Isoniazid 300 mg/d, Rifampicin 600 mg/d, Ethambutol 750mg/d, Clarithromycin 500 mg/bid	12 months	/	Improvement
20	Male	57	N	Rifampicin 300 mg/d, Ethambutol 750mg/d, Clarithromycin 500 mg/bid, Amikacin 400mg/d, Levofloxacin 500 mg/d	12 months	/	Improvement

(*Continued*)

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Table 5 (Continued).

No.	Gender	Age	Disseminated Infection	Medication Regimen and Dosage	Treatment Duration	Surgical Regimen	Outcome
21	Male	58	N	Rifampicin 600 mg/d, Clofazimine 100 mg/d, Ethambutol 750mg/d, Clarithromycin 500 mg/bid	12 months	/	Improvement
22	Male	46	N	Clarithromycin 500 mg/bid, Rifapentine 450 mg/biw, Ethambutol 750mg/d	12 months	/	Improvement

substantially contributed to their mortality. Conversely, the clinical improvement observed in the remaining 20 patients can be primarily attributed to the implementation of personalized multidrug regimens and a comprehensive therapeutic strategy, which included surgical intervention where indicated.

Discussion

Mycobacterium colombiense is a rare subspecies within the MAC. In 2006, Murcia et al first isolated *M. colombiense* from sputum and blood samples, though no clinical characteristics or drug susceptibility data were provided.[3] Since then, only a few cases of *M. colombiense* infection have been reported.[4–7] A 2012 French study identified 6 cases of *M. colombiense* among 67 MAC isolates, accounting for 9.0%.[13] A 2022 study in mainland China reported 14 cases of *M. colombiense* out of 287 MAC isolates, representing 4.9%.[14] A 2024 European multicenter study found 1 case of *M. colombiense* among 386 MAC isolates, accounting for 0.2%.[15] A 2025 Thai study identified 5 cases of *M. colombiense* out of 66 MAC isolates, representing 7.6%.[12] Although the incidence of *M. colombiense* is low, it is associated with high mortality. A 2017 study reported a higher mortality rate for *M. colombiense* infection compared to M. aviumsubsp. Hominissuis (MAH) infection (50% vs 4%).[14] The present study demonstrates that *M. colombiense* carries a high risk of disseminated infection. A 2024 European study of 187 MAC patients reported 40 cases of disseminated infection, accounting for 21.4%, which is significantly lower than the 63.6% (14/22) observed in our study.[15] This distinctive feature significantly differs from other MAC subtypes, suggesting that *M. colombiense* may possess unique invasive properties and specific virulence factors.[13–15]

Demographic characteristics revealed a median age of 58 years (40.9% ≥60 years), which is consistent with the typical age distribution of MAC-infected populations.[1,10,14] The predominant symptoms observed in this study included cough/expectoration (18 cases), fatigue/weight loss (10 cases), fever (6 cases), subcutaneous abscesses/skin ulcers (5 cases), and bone pain (5 cases), among others. The diversity of these clinical manifestations reflects the multi-system invasiveness of *M. colombiense* infection.[3–9] Notably, bone and joint involvement was prominent (54.54%, 12/22 cases), a characteristic feature that may be associated with the pathogen's specific pathogenic mechanisms. Previous studies have suggested that certain NTM strains can produce specific enzymes or toxins that disrupt normal bone tissue structure, leading to osteolysis and destruction.[13–15] However, the exact mechanism by which *M. colombiense* causes skeletal lesions requires further investigation.

Chest CT imaging revealed pulmonary involvement in all 22 patients, with common radiological findings including patchy opacities, nodular shadows, bronchiectasis, mediastinal lymphadenopathy, and pleural effusion. These manifestations are nonspecific and difficult to distinguish from other pulmonary infectious diseases or tuberculosis.[8–10] Additionally, bone CT/MRI examinations of patients with skeletal involvement showed that the ribs, vertebrae, and clavicles were the most frequently affected sites, with imaging features such as patchy low-density lesions, cystic low-density shadows, sclerotic margins, surrounding soft tissue swelling, and the formation of cold abscesses.[13–15] These thoracic and osteoarticular imaging characteristics closely resemble those of tuberculosis, indicating that imaging alone cannot reliably distinguish between tuberculosis and nontuberculous mycobacterial diseases.[16]

As for laboratory findings, according to existing reports, the clearance of NTM primarily relies on CD4+ T cell-mediated Th1 immune responses, with interferon-gamma (IFN-γ) serving as the key effector molecule.[1,3,10] IFN-γ

activates macrophages, promoting lysosomal fusion and reactive oxygen species generation, thereby eliminating intracellular mycobacteria.[1,3,10] In this study, the average CD4+ count among 18 patients was 546 cells/μL (only one case <200 cells/μL), ruling out severe cellular immunodeficiency. However, three patients with disseminated infection tested positive for anti-interferon-gamma autoantibodies (AIGA). AIGA neutralizes IFN-γ, impairs macrophage activation, and disrupts the Th1 immune pathway, consistent with previously reported cases of AIGA-associated disseminated NTM disease.[15,17] Therefore, patients with disseminated *M. colombiense* infection, particularly those with normal CD4+ T-cell counts, should undergo testing for AIGA.

In this study, 54.5% of patients exhibited bone and joint destruction/abscesses, a proportion significantly higher than that observed in other disseminated nontuberculous mycobacterial (NTM) infections.[17–20] The most frequently involved extrapulmonary sites in disseminated *M. colombiense* infection were bone and joint (54.5%) and poly-serositis (31.8%), distinguishing it from other NTM species.[17–20] All patients with bone and joint infections in this study received combined surgical and pharmacological intervention. Consistent with existing literature on NTM osteoarticular infections, a 13-year Korean study of 29 patients reported that all cases required surgical intervention in addition to antibiotic therapy.[21] Moreover, relevant guidelines and studies recommend that NTM skeletal infections generally require combined pharmacological and surgical management. A minimum of 6 months of multidrug antibiotic therapy is typically advised, with the exact duration dependent on the antibiotic susceptibility of the pathogen. Surgical treatment involves resection of all infected tissue and may require repeated debridement and/or continuous drainage.[21–24]

As for bacterial identification, conventional mycobacterial culture methods can only identify isolates to the MAC level, without further speciation. In molecular identification, 16S rRNA gene sequencing alone can only classify isolates to the MAC complex level; additional analysis of hsp65 or rpoB genes is required for accurate subspecies identification.[1,3,10] In this study, the average turnaround time for tNGS was 2 days, demonstrating its value in facilitating rapid diagnosis and subspecies-level identification of NTM.

As for drug resistance, different subspecies within MAC exhibit variations in both virulence and drug susceptibility. Highly virulent strains may demonstrate higher innate drug sensitivity.[25] Studies have shown that virulence differs among various MAC subspecies.[26–29] Even within the same subspecies, genetic diversity may exist—a Japanese study reported distinct genetic profiles between isolates from patients with pulmonary disease and those with disseminated disease.[30] Therefore, accurate subspecies-level identification of MAC and individualized drug susceptibility testing are crucial. Currently, most studies only compare drug susceptibility between *M. avium* and *M. intracellulare*, with limited research on the differential drug susceptibility patterns among various MAC subspecies. Consequently, the latest 2020 treatment guidelines for MAC pulmonary disease recommend a uniform treatment approach for all MAC pulmonary disease patients, without subspecies-specific stratification.[2]

This study revealed that a resistance rate of below 27.3% was observed for bedaquiline, clofazimine, rifabutin, ethambutol, and rifampin. In contrast, over 90% resistance rates was observed for levofloxacin, linezolid, amikacin, isoniazid, capreomycin, and moxifloxacin. Specifically, the lowest resistance rates were noted for bedaquiline (0%) and clofazimine (9.1%). According to previous studies, the low resistance to bedaquiline and clofazimine in *M. colombiense* may be attributed to the absence of pre-existing resistance mutations in target genes (eg, atpE) or regulatory regions (eg, Rv0678), which are typically associated with drug resistance in *Mycobacterium tuberculosis*. Furthermore, the limited clinical exposure to these drugs due to the rarity of *M. colombiense* infections may have reduced the evolutionary pressure for resistance development.[31–34] Previous studies on overall drug resistance patterns in MAC isolates reported resistance rates of 10.8% for amikacin, 47.84% for linezolid, and 53.60% for moxifloxacin.[14] While linezolid and moxifloxacin showed 100% resistance rates, amikacin and clarithromycin demonstrated relatively lower resistance.[14] These differential resistance profiles suggest distinct characteristics between *M. colombiense* and other MAC subspecies.[12–15,35] This retrospective study of 22 patients with *Mycobacterium colombiense* infection demonstrated low rates of resistance to both bedaquiline and clofazimine in vitro, observed consistently across patients with both disseminated and non-disseminated disease. These findings suggest that bedaquiline and clofazimine may represent viable therapeutic alternatives for inclusion in treatment regimens when first-line options recommended by current guidelines prove ineffective or are poorly tolerated.

In summary, the study of 22 patients with *Mycobacterium colombiense* disease indicates that this disease primarily affects the elderly. Patients mostly presented with disseminated infection. Besides pulmonary involvement, bone and joint as well as serous cavities were the most commonly affected sites. Due to the limited sample size, comprehensive statistical analysis was not possible. It is preliminarily inferred that advanced age and multiple underlying diseases may be significant risk factors for *Mycobacterium colombiense* infection.

Conclusion

This study analyzed the clinical characteristics and drug resistance profiles of 22 patients with *M. colombiense* infection. The findings indicate that *M. colombiense* infection is prone to disseminated disease, involving multiple organ systems with diverse clinical manifestations. Targeted next-generation sequencing played a valuable role in early and accurate pathogen identification. In this study, in vitro drug susceptibility testing revealed a unique resistance profile for *Mycobacterium colombiense*, characterized by near-universal resistance to fluoroquinolones (levofloxacin, moxifloxacin), linezolid, and aminoglycosides (amikacin), but comparatively high susceptibility to bedaquiline, clofazimine, and rifamycins (rifampin, rifabutin). Treatment of this disease remains challenging, with few reported cases achieving complete clinical cure. Individualized therapy based on drug susceptibility testing (prioritizing regimens containing clofazimine and bedaquiline) may improve outcomes. This study provides valuable insights for future prevention and treatment strategies against *M. colombiense* infection.

Nevertheless, this study has inherent limitations as a single-center, retrospective investigation with a limited sample size, which may constrain the generalizability of the findings. Future multicenter studies with larger cohorts are warranted for further validation.

Data Sharing Statement

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

Ethics Approval and Consent to Participate

This research adhered to the ethical principles outlined in the Declaration of Helsinki and followed applicable guidelines. Ethical approval was obtained from the Ethics Committee of Guangzhou Chest Hospital (Approval No. KY-2024-046). In this retrospective investigation, which utilized de-identified patient data extracted from medical records, participant confidentiality was thoroughly protected, and the study did not present any additional risks to subjects. As the analysis was based on anonymized data and followed a retrospective design, the ethics committee granted an exemption from obtaining informed consent.

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Disclosure

The authors report no conflicts of interest in this work.

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