Suspected Occult Malignancy Revealing Pulmonary *Mycobacterium chimaera* Infection

Suspeita de Tumor Oculto a Revelar Infecção Pulmonar por *Mycobacterium chimaera*

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Abstract:

Mycobacterium chimaera is a slow-growing non-tuberculous mycobacterium of the *Mycobacterium avium* complex that may mimic malignancy or systemic inflammatory disease due to its non-specific presentation.

We report an elderly woman with significant weight loss (27% over two years), anorexia and asthenia, initially attributed to dementia and later suspected to represent an underlying occult malignancy. After exclusion of neoplastic and autoimmune causes, thoracic computed tomography showed bronchiectasis and a tree-in-bud pattern. Bronchoscopy confirmed *Mycobacterium chimaera* infection. She was treated with azithromycin, rifampicin and ethambutol for 12 months, with a favourable clinical and radiological response.

This case highlights the importance of considering non-tuberculous mycobacterial infection in unexplained weight loss, even in the absence of classical risk factors.

Keywords: Bronchiectasis; Mycobacterium chimaera; Mycobacterium Infection; Neoplasms/complications; Non-tuberculous Mycobacteria; Weight Loss.

Resumo:

Mycobacterium chimaera é uma micobactéria não tuberculosa de crescimento lento pertencente ao complexo *Mycobacterium avium*, cuja apresentação clínica é frequentemente inespecífica, podendo mimetizar doença maligna ou inflamatória sistémica.

Relata-se o caso de uma mulher octogenária com perda ponderal significativa (27% em dois anos), anorexia e astenia, inicialmente atribuídas a demência e posteriormente suspeitas de síndrome paraneoplásica. Após exclusão de neoplasia e doença autoimune, a tomografia torácica revelou bronquiectasias e padrão "*tree-in-bud*". A broncoscopia com estudo microbiológico confirmou infeção por *Mycobacterium chimaera*. A doente foi tratada com azitromicina, rifampicina e etambutol durante 12 meses, com resposta clínica e radiológica favorável.

Este caso reforça a necessidade de considerar micobactérias não tuberculosas no diagnóstico diferencial de perda ponderal inexplicada, mesmo sem fatores de risco clássicos.

Palavras-chave: Bronquiectasia; Infecção por Mycobacterium; Micobactérias não Tuberculosas; Mycobacterium chimaera; Neoplasias/complicações; Redução de Peso.

Learning Points

1. *Mycobacterium chimaera* can mimic an underlying occult malignancy, particularly in elderly patients presenting with unexplained weight loss and fatigue.
2. It should be considered even in the absence of known risk factors such as cardiac surgery or overt immunosuppression.
3. Underlying immunodeficiency, including HIV infection, must be excluded when constitutional symptoms are accompanied by lymphopenia or opportunistic infections.
4. Radiological findings (e.g., tree-in-bud pattern, bronchiectasis) may suggest mycobacterial infection but require microbiological confirmation.
5. Antimycobacterial therapy should be guided by susceptibility testing, as no standardised treatment regimen currently exists.
6. Early clinical suspicion and systematic evaluation are crucial for timely diagnosis and appropriate management.

Introduction

The *Mycobacterium avium* complex (MAC) is the most common group of non-tuberculous mycobacteria (NTM) in Central Europe and currently comprises twelve species, including *Mycobacterium chimaera* (MC), one of the most clinically relevant.[1] However, the pathogenic mechanisms of MC remain poorly understood. It acts as an opportunistic organism, with respiratory infections typically occurring through inhalation of aerosolised

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particles, particularly in immunocompromised patients or those with underlying structural lung disease.[2] MC was initially identified as a causative agent in outbreaks linked to cardiac surgery involving cardiopulmonary bypass, attributed to exposure to contaminated water systems.[2]

MC infection is characterised by a prolonged latency period, ranging from one to six years between exposure and the onset of clinical manifestations. Symptoms are often nonspecific and may include persistent fever, fatigue, weight loss, cough, myalgia, abdominal pain, and vomiting.[3] Due to the non-specific nature of its presentation, MC can closely mimic systemic conditions such as sarcoidosis, tuberculosis, or malignancy.[2]

If not diagnosed and treated in a timely manner, MC infection can be fatal. There is currently no standardised treatment regimen; antimicrobial therapy must be tailored based on susceptibility testing.[3]

Case Report

A woman in her eighties presented with a two-year history of progressive weight loss (approximately 27% of body weight), anorexia, and asthenia. These symptoms developed around the time of her diagnosis of Alzheimer's dementia and were initially attributed to cognitive decline. However, over the previous five months, there had been a further 13% weight loss, accompanied by episodes of presyncope, nausea, and vomiting, unrelated to food intake. There were no symptoms of dysphagia, gastrointestinal bleeding, respiratory complaints, or genitourinary disturbances.

Her past medical history included dyslipidemia, chronic gastritis, allergic rhinosinusitis and osteoporosis. She had no history of cardiac surgery or cardiopulmonary bypass procedures. She was functionally independent and lived at home with family support.

On hospital admission, physical examination was unremarkable. Initial laboratory investigations showed an elevated erythrocyte sedimentation rate (ESR) of 42 mm/h and ferritin of 390 ng/mL. White blood cell count revealed neutrophilia (8.65 G/L), marked lymphopenia (0.39 G/L), and mild monocytopenia (0.33 G/L), with no anaemia.

Chest radiography demonstrated a bilateral reticulonodular pattern, predominantly in the mid-lung zones, and signs of hyperinflation. Chest computed tomography (CT) revealed bronchiectasis in the middle lobe and lingula with parenchymal retraction, suggestive of atelectasis. A tree-in--bud pattern (Fig. 1) was noted in both lower lobes, along with consolidation in the posterior segment of the left lower lobe and a small left-sided pleural effusion, findings consistent with a possible infectious or inflammatory process.

Flexible bronchoscopy revealed moderate bilateral purulent secretions and mucosal friability, particularly in the upper left segmental bronchi, with visible architectural disorganisation.

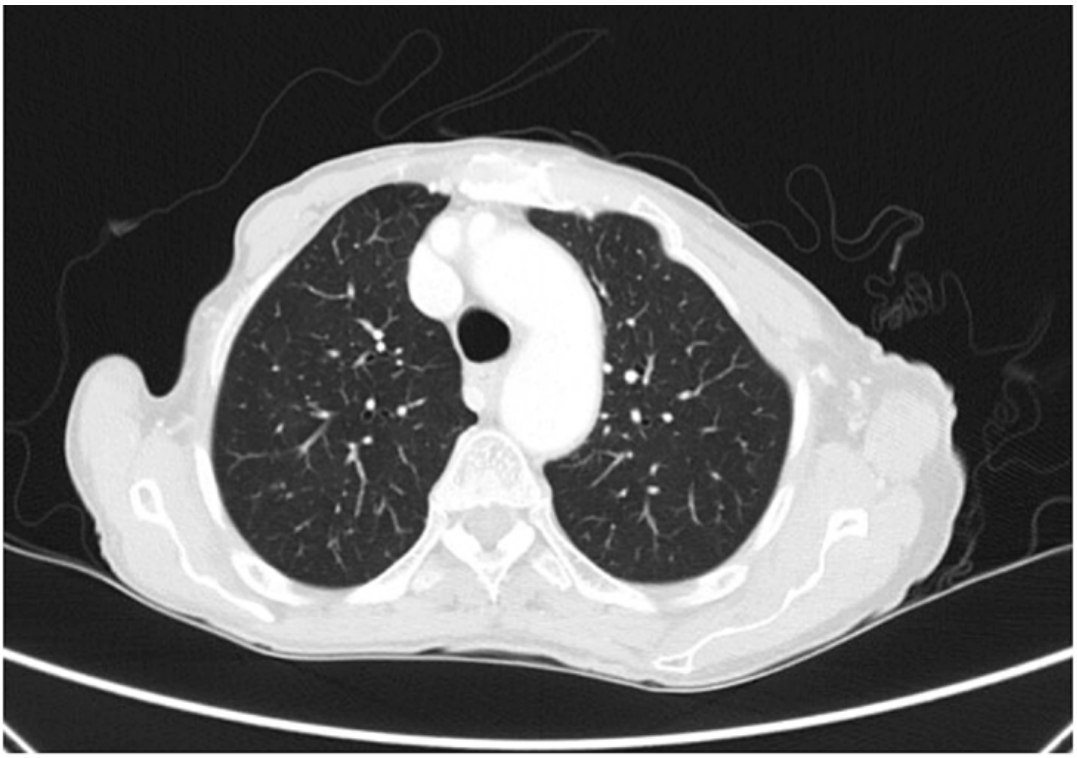

Figure 1: Axial chest computed tomography (lung window) demonstrating multiple bilateral centrilobular nodules with branching linear opacities, consistent with a tree-in-bud pattern. These findings are suggestive of bronchiolar inflammation and endobronchial spread of infection.

Bronchial specimens were cultured in liquid medium using the Mycobacteria Growth Indicator Tube (MGIT) system. Acid-fast bacilli were detected on direct microscopy. Species identification was performed using a nucleic acid amplification assay.

Drug susceptibility testing was carried out according to Clinical and Laboratory Standards Institute (CLSI) guidelines for slow-growing non-tuberculous mycobacteria, confirming susceptibility to azithromycin, rifampicin and ethambutol.

The diagnosis fulfilled ATS/ERS/IDSA criteria for non-tuberculous mycobacterial pulmonary disease, including compatible constitutional symptoms, radiological abnormalities (bronchiectasis and tree-in-bud pattern), and microbiological confirmation from bronchial specimens. The presence of systemic manifestations and subsequent clinical and radiological improvement following targeted antimycobacterial therapy strongly supports true infection rather than airway colonisation.

DIFFERENTIAL DIAGNOSIS

The patient's constitutional symptoms and significant weight loss raised concern for several systemic conditions.

OCCULT MALIGNANCY

Given the progressive 27% weight loss, anorexia and asthenia, an occult malignancy was initially suspected. Age and constitutional symptoms strengthened this hypothesis. However, gastrointestinal endoscopy and imaging studies revealed no evidence of neoplasia, and no mass lesions were identified on thoracic imaging.

PRIMARY LUNG CANCER AND LYMPHOMA

Pulmonary malignancy and lymphoma were considered due to constitutional symptoms and radiological abnormalities. However, imaging did not demonstrate a suspicious mass, and bronchoscopic findings were not suggestive of neoplastic disease. Cytological analysis was negative for malignancy.

TUBERCULOSIS AND OTHER NON-TUBERCULOUS MYCOBACTERIA

The presence of bronchiectasis and a tree-in-bud pattern strongly suggested mycobacterial infection. Direct microscopy revealed acid-fast bacilli, and culture ultimately identified MC.

HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION

Given the marked lymphopenia and the diagnosis of an opportunistic mycobacterial infection, underlying HIV infection was considered. Serological testing for HIV was performed and returned negative, excluding acquired immunodeficiency as a contributing factor.

SARCOIDOSIS

Sarcoidosis was considered due to overlapping radiological findings and constitutional symptoms. However, microbiological confirmation of MC infection and the absence of compatible systemic involvement excluded this diagnosis.

AUTOIMMUNE AND CHRONIC INFLAMMATORY DISORDERS

Systemic autoimmune diseases were also considered but were excluded based on negative serological markers and lack of extrapulmonary manifestations.

THERAPEUTIC INTERVENTION

Following confirmation of MC infection through culture of bronchial secretions, the patient was started on combination antimycobacterial therapy. Given the absence of standardised treatment protocols specifically for MC, the therapeutic approach was based on guidelines for the management of non-tuberculous mycobacterial (NTM) pulmonary disease, particularly those outlined by the American Thoracic Society, Infectious Diseases Society of America, and European Respiratory Society (ATS/IDSA/ERS),[4] as well as Portuguese national guidance from the Direção-Geral da Saúde.[5]

The selected regimen included ethambutol 600 mg/day, rifampicin 300 mg/day and azithromycin 250 mg/day.

This macrolide-based combination was chosen for its intracellular activity against slow-growing mycobacteria and its proven efficacy in treating pulmonary MAC infections. Drug susceptibility testing confirmed sensitivity to all three agents.

The planned treatment duration was 12 months, as recommended for NTM pulmonary disease with radiographic and microbiological response.[4] The patient was monitored through regular clinical and laboratory assessments, including liver function tests and visual screening for ethambutol toxicity.

Treatment was well tolerated, with no reported adverse effects and no need for dose modification or interruption.

FOLLOW-UP AND OUTCOMES

The patient was followed up regularly throughout the 12-month course of antimycobacterial therapy. Clinical response was evident within the first few months, with progressive improvement in appetite, energy levels, and functional status. She experienced a gradual recovery of body weight and overall well-being.

No adverse drug reactions or treatment-related toxicities were observed. Serial liver function tests and ophthalmological evaluations remained within normal limits.

Inflammatory parameters normalised after treatment.

Radiological follow-up showed partial resolution of the tree-in-bud pattern and consolidation, with stability of the bronchiectatic changes. Although post-treatment sputum samples were not collected due to minimal productive cough, the absence of clinical relapse and sustained weight gain supported a favourable microbiological outcome.

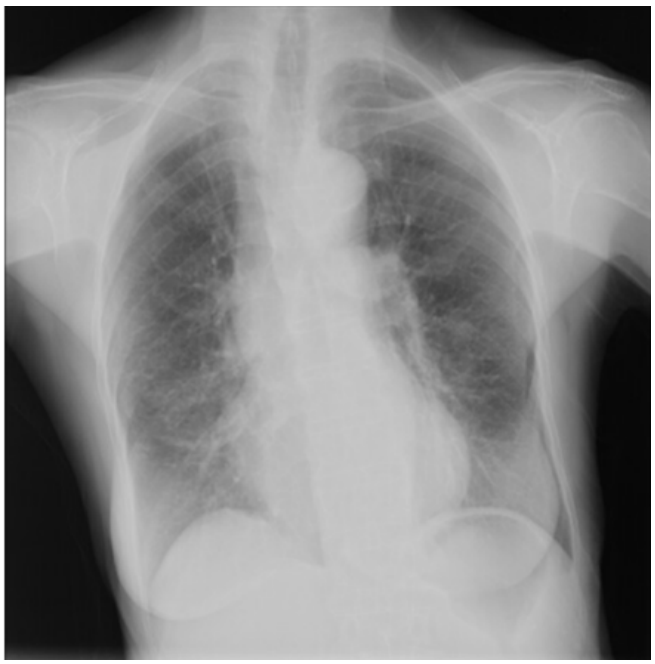

Figure 2: Chest radiograph following completion of 12 months of antimycobacterial therapy. There is partial resolution of the previously noted infiltrates and no evidence of progression. Bronchial markings remain prominent, consistent with stable underlying bronchiectasis.

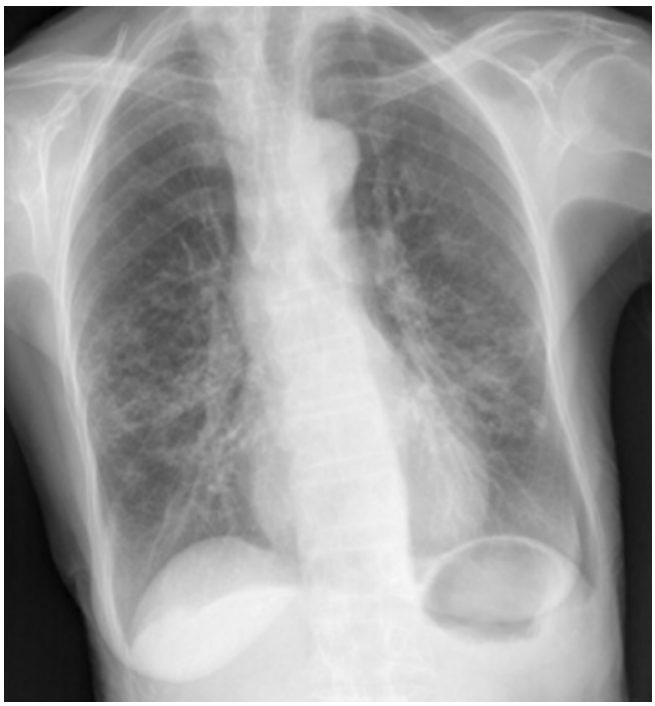

Figure 3: Chest radiograph at the time of diagnosis, prior to treatment. Bilateral reticulonodular opacities are visible, predominantly in the mid-lung zones, along with signs of hyperinflation. These findings were suggestive of a possible infectious or inflammatory process and prompted further investigation.

Her cognitive function, as assessed by serial Mini-Mental State Examinations (MMSE), remained stable throughout the treatment period.

This case illustrates the importance of close monitoring and long-term follow-up in patients with NTM pulmonary infections, both to assess therapeutic response and to detect potential complications or relapse.

Follow-up chest radiography (Fig. 2) demonstrated partial resolution of the initial infiltrates seen on presentation (Fig. 3), consistent with a favourable therapeutic response.

Discussion

Unintentional weight loss in adults over 65 years of age is associated with increased morbidity and mortality and warrants a structured diagnostic approach, including detailed history, physical examination, and targeted investigation of common causes such as malignancy, psychiatric disorders, and infection.[4,6] Because malignancy accounts for up to one-third of cases, the initial work-up should include age-appropriate cancer screening, laboratory testing, and additional imaging or endoscopic evaluation when clinically indicated.[6] Nevertheless, even after extensive assessment, no cause is identified in 6%–28% of cases.[6]

In our patient, stable MMSE scores throughout the period of weight loss argued against a cognitive or behavioural cause, despite the recognised association between low body mass index, weight loss, and depressive or cognitive disorders in older adults.[7-9] Marked lymphopenia also raised suspicion of an underlying immunodeficiency; however, HIV serology was negative, prompting further investigation for alternative infectious causes.

Abnormal chest radiography led to thoracic CT and subsequent bronchoscopy. CT demonstrated tree-in-bud opacities, bronchiectasis, and parenchymal consolidation, findings suggestive of an infectious process, while culture of bronchial secretions confirmed *Mycobacterium chimaera* (MC). Although mycobacteria are often difficult to isolate, advances in molecular diagnostic techniques have improved the detection and characterisation of slow-growing non-tuberculous mycobacteria such as MC.[10]

MC, a member of the *Mycobacterium avium* complex, has increasingly been recognised as a cause of both pulmonary and disseminated infection. It is most commonly associated with contaminated heater–cooler units used during cardiac surgery involving cardiopulmonary bypass.[2,11] Most reported cases have involved prosthetic valve endocarditis, vascular graft infection, or disseminated disease following surgical exposure. In contrast, our patient had no history of cardiac surgery or extracorporeal circulation, supporting the hypothesis that MC may also behave as an environmental opportunistic pathogen in elderly or immunosenescent individuals.[12,13]

Several reports have described mycobacterial infections mimicking malignancy,[14-19] but only one previous case specifically involved MC. In that report, a healthcare worker

presented with cough, fever, weight loss, and a pulmonary mass initially interpreted as neoplastic; partial lobectomy was performed before histology and culture established the diagnosis of MC infection.[10] By contrast, in our case, the diagnosis was achieved bronchoscopically, allowing successful treatment without surgery.

Non-tuberculous mycobacteria may persist in domestic water systems and biofilms despite standard chlorination, and aerosolisation during showering has been proposed as a possible route of exposure in susceptible individuals. Although no environmental investigation was performed in this case, community water exposure remains a plausible source of infection.

The patient responded well to a 12-month course of rifampicin, ethambutol, and azithromycin, consistent with ATS/IDSA/ERS recommendations for pulmonary NTM infection[3] and with Portuguese national guidance from the Direção-Geral da Saúde[5] for pulmonary disease caused by members of the Mycobacterium avium complex, with no adverse effects and clear clinical and radiological improvement. This case highlights the diagnostic challenge posed by MC when constitutional symptoms raise suspicion of occult malignancy. To our knowledge, this is the second published report of MC mimicking an underlying neoplastic process and the first managed without surgical intervention. ■

Awards and Previous Presentations

The manuscript was previously presented in 31º CNMI (Congresso Nacional de Medicina Interna).

Contributorship Statement

SB - Conducted the literature review and drafted the manuscript. She also participated in the clinical follow-up of the patient.
JC - Contributed to the interpretation of diagnostic findings and critical revision of the manuscript.
CC - Contributed to the literature review, assisted in drafting and performed the comprehensive English language revision of the manuscript.
JVV - Contributed to data collection and clinical documentation and participated in the revision of the manuscript.
JSB - Contributed to the discussion of the case and critically revised the manuscript for important intellectual content.
JRG - Was directly involved in the clinical management and follow-up of the patient and provided senior clinical supervision, also contributed to data interpretation and critical revision of the manuscript

Declaração de Contribuição

SB - Revisão da literartura e elaboração do manuscrito. Acompanhamento clínico do paciente.
JC - Interpretação dos resultados dos exames diagnósticos.Revisão crítica do manuscrito..
CC - Revisão da literatura. Redação do manuscirto. Revisão abrangente do manuscrito em língua inglesa
JVV - Recolha de dados e documentação clínica. Revisão do manuscrito.
JSB - Discussão do caso e revisão crítica do caso. Revisão crítica do manuscrito. Discussão do conteúdo intelectual relevante do manuscrito.
JRG - Esteve diretamente envolvido na gestão clínica e no acompanhamento do paciente, tendo prestado supervisão clínica senior. Interpretação dos dados. Revisão crítica do manuscrito.

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