

Case Report

Iatrogenic infection by atypical mycobacteria: a case report of *M. phlei* infection in an immunocompetent patient simulating breast malignancy

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Abstract

Introduction: Atypical nontuberculous mycobacteria (NTM) constitute a diverse group of environmental organisms capable of causing infections in immunocompromised patients. *Mycobacterium phlei* has limited documentation of clinical disease in the literature.

Case presentation: We present the case of a 68-year-old immunocompetent female with type II diabetes mellitus and a recent history of laparoscopic cholecystectomy. One month postoperatively, the patient developed localized wound complications followed by the appearance of a growing axillary mass. Imaging studies suggested possible malignancy (BIRADS-4), but histopathological evaluation revealed chronic granulomatous inflammation without malignant cells.

Results: the diagnosis was a rare case of lymphadenitis due to *M. phlei*, confirmed by histology and molecular diagnostics. The patient responded favorably to combination antibiotic therapy.

Conclusions: Through this report, we share our experience and expand the understanding of this entity, emphasizing the importance of considering this differential diagnosis and establishing appropriate guidelines for therapeutic decision-making, emphasizing in NTM.

Key words: Atypical mycobacteria; *Mycobacterium phlei*; iatrogenic infection; neoplasia.

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Introduction

Atypical mycobacteria, also known as nontuberculous mycobacteria (NTM), constitute a diverse group of bacteria of the genus *Mycobacterium* able of causing disease with a diverse set of manifestations. Currently, there is an increase in the number of infections related to this group of microorganisms, especially in immunocompromised patients. Unlike the more well-known pathogenic mycobacteria, atypical mycobacteria are generally not transmitted from person to person [1].

M. phlei has been a subject of research in industrial procedures due to its ability to degrade a wide variety of organic compounds, including hydrocarbons and environmental pollutants. Furthermore, it has been shown to have a therapeutic effect as a modulator of Regulatory T cells (TReg) in the treatment of asthma, making it an organism of interest in bioremediation, biotechnology, and medicine [2,3].

Clinical information associated with *M. phlei* disease is scarce in the literature due to the apparently very low incidence of this disease. This report presents a unique case of *Mycobacterium phlei* infection in a 68-year-old healthcare provider and related to a surgical procedure, offering a rare perspective on the behavior of this pathogen in the human host and contributing to the limited corpus of knowledge on atypical mycobacterial infections in immunocompetent individuals.

Case Report

We present the case of a 68-year-old female patient with a history of type II diabetes mellitus, in adequate control, and a recently resolved biliary pancreatitis through laparoscopic cholecystectomy. Approximately one month after this intervention, the patient began to show signs suggestive of infection, particularly difficulty in the healing of one of the ports used during

the laparoscopic procedure (Figure 1). This issue was accompanied by several complications, such as delayed healing, erythema, and the formation of a purulent collection. It is important to note that the patient did not report fever or other systemic symptoms during this period; No laboratory abnormalities were reported, except for hypertriglyceridemia (162.25 mg/dL), and a severe elevation on C-Reactive protein (101.47 mg/dL). Other signs on examination were unremarkable.

Two months after the surgery, a new eventuality emerged. The patient began to develop a lump in the axillary region on the same side as the initial wound complication. The lesion was characterized by rapid, painless, and firm growth. Given the suspicious nature of these symptoms and the family history of breast cancer in our patient (mother), an ultrasound and mammogram were performed. Imaging studies showed type C breast density, right breast with architectural distortion in R 10, and right axilla with data compatible with a mass-type lymph node with apparent extracapsular extension. Our patient was classified as BIRADS-4 type C, indicating findings with a high presumption of malignancy. An additional thoracoabdominal CT scan was performed, which was negative for associated lesions or metastasis.

To further evaluate these findings, a Tru-Cut biopsy of the lesion was performed. Surprisingly, the histopathological analysis of the sample did not corroborate the initial suspicion of malignancy. Instead, a chronic granulomatous reaction was observed, with negative stains for Periodic Acid-Schiff (PAS) and Ziehl-Neelsen (ZN).

Despite no changes observed in the size of the lymphadenopathy, the patient underwent additional

ultrasound studies due to the persistence of the lesion. These studies identified the emergence of new lymphadenopathies in the neck. This finding required a new biopsy to elucidate the nature of these new lesions. In this second biopsy, which was excisional and focused on the axillary lymph node, the findings reflected those of the initial biopsy: a chronic granulomatous lesion with a positive ZN stain showing scarce bacilli (Figure 2).

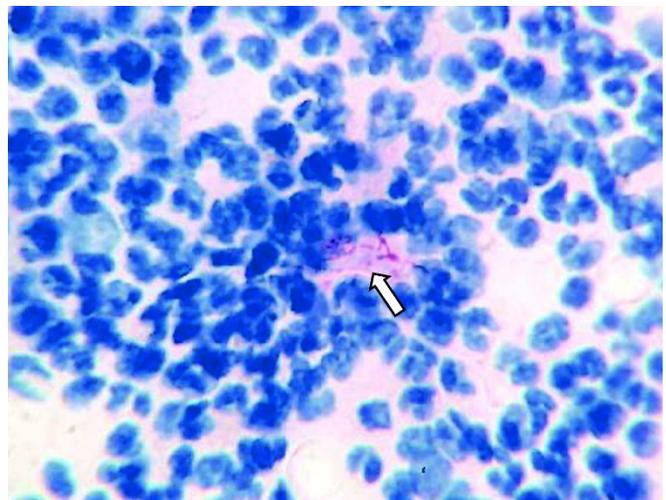
Additional molecular diagnostic tests were performed, including a PCR assay for mycobacteria (using GeneXpert® for tuberculosis mycobacteria and Seegene® for non-tuberculous mycobacteria) on the lymph node sample. The results were negative for *M. tuberculosis* complex but positive for *Mycobacterium spp.* For further confirmation and validation, the patient's slides were sent to a reference laboratory for a panel of atypical mycobacteria by PCR (using PCR-LCD Array MYCO®) showing positivity for *Mycobacterium phlei*. The preferred method was PCR, as it provides superior performance for this type of sample [4]. Additionally, the use of culture, identification, and susceptibility testing for mycobacteria is not commonly practiced in our region.

An empirical antibiotic regimen was initiated, including doxycycline, clarithromycin, and amikacin, this last one was suspended due to creatinine elevation after 21 days of treatment, but the rest of the drugs were continued. The patient presented a total resolution of her symptoms after two months of treatment, but the medication was continued for six months. In a follow-up consult one year after the infection the patient did not present recurrence of the disease.

Figure 1. Right upper quadrant abdominal injury secondary to trocar insertion.



Figure 2. Chronic granulomatous lesion with a positive ZN stain showing scarce bacilli.



Discussion

Mycobacterium phlei is a species of mycobacteria that belongs to the group of non-tuberculous mycobacteria (NTM). It's a rapidly growing mycobacterium classified in Runyon group IV and phylogenetically related to *Mycobacterium fortuitum* and *Mycobacterium smegmatis* [5]. This group of pathogens was once considered innocuous to humans, but in recent years a diverse range of infections has been reported in individuals with underlying health conditions. Although it has been isolated in various environmental conditions and human microbiota, its pathogenic role is not as well defined as that of other species in the *Mycobacterium* genus [5]. Humans acquire this pathogen by exposure to environmental reservoirs or as we suspect in the case of our patient by nosocomial inoculation via unsterilized instrumentation [6]. Documented clinical cases of infections caused by *Mycobacterium phlei* are remarkably scarce, with less than 10 cases reported (Table 1). This literature includes various clinical manifestations, such as peritonitis due to Tenckhoff catheter infections, septic

arthritis, soft tissue infections, and cardiac infections associated with the use of pacemakers [6-11]. Each of these cases provides invaluable information, as the rarity of these infections offers unique learning opportunities for healthcare professionals. Likewise, Ming *et al.* have described its effectiveness in medical therapeutics as an effective asthma symptom reliever, bronchial hyperreactivity reducer, and lung function improver similar to Seretide [2]. In this report, we describe an unusual case of lymphadenitis caused by *Mycobacterium phlei* in a 68-year-old immunocompetent patient without a history of immunosuppression, resembling a possible breast malignancy. To our knowledge, this represents the first report of lymphadenitis caused by *Mycobacterium phlei* in an individual without underlying immunosuppressive conditions. Tanaka *et al.* reported a similar clinical case of an immunocompetent adult with disseminated infection caused by *Mycobacterium phlei*, suggesting a possible relationship between the disease and the presence of anti-IFN- γ autoantibodies [7]. Understanding the particularities of infections

Table 1. Summary of all reported cases of infection due to *Mycobacterium phlei*.

Author	Sex	Age	Clinical presentation	Diagnostic Methods	Radiological findings	Laboratory abnormalities	Treatment	Outcome
Aguilar <i>et al.</i> , 1989	M	7 Y	Conjunctivitis, urethritis and arthritis.	PCR	No abnormalities.	No abnormalities.	INH, RFP, and SM	Cured
Spiegl & Feiner, 1994	M	49 Y	Localized infection of the foot.	PCR	MRI revealed peripherally enhancing lobulated cystic lesions centered around the tibialis posterior and flexor digitorum longus tendons.	No abnormalities	CLR, LVX/surgery	Lost in follow up
Paul & Devarajan, 1998	M	17 Y	Dialysis-associated peritonitis.	N/S	CT revealed a fecalith in the right iliac fossa.	Peritoneal fluid WBC count was elevated at 760 cells/ml	AMK, CFX, DOX	Cured
McGee Jr <i>et al.</i> , 2019	M	45 Y	Vertebral osteomyelitis.	PCR	CT of the lumbar spine demonstrated a solid fusion at the L4-5 level.	No abnormalities	AZM, MC/surgery	Cured
Tanaka <i>et al.</i> , 2019	F	79 Y	Disseminated infection.	PCR	Chest CT showed a nodule in the left S1+2 segment, thickening of the interlobular septum in the left lower lobe, lymphadenopathy of the cervical lymph nodes, and osteolysis of the sternum and left second rib.	Leukocytosis, elevated CRP, elevated ESR	RIF, CLR, LVX, EMB	Cured
Ramos <i>et al.</i> , 2021	F	70 Y	Tumor on the anterior side of the right thigh	MALDI-TOF	Soft tissue ultrasound revealed a collection of subcutaneous cellular tissue in the thigh, with irregular walls and avascular pseudo nodular echogenic areas within.	Elevated ESR and CRP	MFX, CLR/surgery	Cured
Tang <i>et al.</i> , 2022	F	68 Y	Sweet's syndrome accompanied by disseminated infection.	Gene chip	Chest CT showed increasing lung lesions with multiple patchy exudations, fibrous proliferation and ground glass opacity in both lungs. Bone CT revealed bone destruction in the C7-T2 vertebral bodies.	Leukocytosis, Elevated ESR, anemia, elevated IgA antibodies	INH, RPT, EMB, LVX, CLR	Cured
Echeverria <i>et al.</i> , 2023	M	57 Y	Recurrent pulmonary tuberculosis.	PCR	No radiological findings.	No abnormalities	SXT, CLR, RIF, EMB, DC	Deceased

M: male; EM: erythromycin; PCR: polymerase chain reaction; MC: minocycline; AZM: azithromycin; DC: doxycycline; F: female; IgA: immunoglobulin A; Y: years; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; MALDI-TOF: Matrix-Assisted Laser Desorption/Ionization; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; RIF: rifampicin; CLR: clarithromycin; LVX: levofloxacin; EMB: ethambutol; SXT: trimethoprim-sulfamethoxazole; INH: isoniazid; MFX: moxifloxacin; SM: Streptomycin; AMK: Amikacin; CFX: cefoxitin; DOX: Doxycycline; WBC: white blood cells; N/S: not specified.

caused by *Mycobacterium phlei* is crucial, as these can be confused with neoplasms or other infections due to their uncommon nature and the lack of distinctive clinical characteristics of NTM; As mentioned by Ramos *et al.*, this pathogen can go unnoticed by showing minimal impact on acute phase reactants such as CRP and ESR, and minimal symptomatology [12]. The chronic granulomatous reactions observed in the histopathological analysis of our patient required meticulous diagnostic processes to differentiate these infections from other conditions that presented similar histological findings, such as Granulomatous lobular mastitis or neoplasia [13]. The use of various diagnostic tools, including PCR, histopathology, and additional laboratory tests, was fundamental in reaching our diagnosis [6-9,12,14]. In our patient, the initial radiological findings were consistent with a BIRADS 4 category, which is highly suggestive of malignancy. A Tru-cut biopsy was subsequently performed, which ruled out malignancy and confirmed the diagnosis as infectious. It is established that NTM organisms can cause acute, subacute, or late-onset infections, most common microorganisms found in these infections included *Mycobacterium fortuitum*, *M. avium*, *M. abscessus*, *M. chelonae* [15], and recently the introduction of *M. phlei*. Our case report highlights the challenges that physicians may encounter during the diagnostic and therapeutic process of NTM and emphasizes the importance of considering this type of infection in the differential diagnosis. Echevarria *et al.*, suggest that, given the increasing number of reported cases, it is recommended that local authorities register and monitor NTM disease, a difficult step for underdeveloped countries and their limitations [16]. Additionally, our case sheds light on therapeutic approaches for managing infections caused by *M. phlei*. Although no consensus exists on NTM therapy, these pathogens remain sensitive to amikacin, fluoroquinolones, and clarithromycin, with intrinsic resistance to macrolides and cefotaxime. Treatment choice depends on the clinical presentation, mycobacterial species, and the patient's immune status. A key consideration is removing any foreign body, as these mycobacteria can form biofilms [17]. Our patient showed a positive clinical response after initiating a regimen of doxycycline and clarithromycin, suggesting that these antibiotics can be effective in treating infections caused by these atypical mycobacterial infections, providing an important reference point for similar cases in the future. In conclusion, this case highlights the importance of considering atypical Mycobacteria in the differential diagnosis of infections

resistant to conventional antibiotics. Implementing precise diagnostic procedures, including proper sampling of the infection site and AFB cultures is essential, along with the establishment of effective treatment protocols to ensure timely management and optimal patient outcomes. Further research and documentation of additional cases are crucial to enhance our knowledge and management of NTM infections.

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Conflict of interests

No conflict of interests is declared.

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