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Case report

Mycobacterium xenopi native vertebral osteomyelitis and discitis: Case & review of published cases

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ABSTRACT

Mycobacterium xenopi is a rare cause of spinal osteomyelitis and discitis. Here we report the case of a 68-year-old woman with history of splenectomy for Felty's syndrome who developed *M. xenopi* lumbar discitis and osteomyelitis following repeated corticosteroid spinal injections for chronic back pain. Review of the 18 cases of *M. xenopi* spinal osteomyelitis cases described in the literature revealed common threads of immunocompromised hosts and prior spinal manipulation.

Case presentation

Our patient is a 68-year-old woman who had undergone a splenectomy for Felty's syndrome and who presented with one month of worsening lower back pain and fever. Her back pain was chronic and previously managed with intra-articular steroid injections over the course of several years but had recently worsened significantly. Spinal CT imaging revealed a stable compression deformity at the L1-L2 level and new L1-L2 discitis (Fig. 1). MRI showed L1-L2 discitis, vertebral body enhancement, and a contrast-enhancing anterior paraspinal soft tissue prominence (Fig. 2). An aerobic bacterial culture of the affected disc obtained via CT-guided aspiration was sterile, and she was treated empirically with intravenous (IV) vancomycin and ceftriaxone. Fever and back pain persisted while on antibacterial therapy, and repeat CT 4 weeks into treatment showed progression of the L1-L2 compression fracture without significant change in discitis.

She was transferred to our tertiary hospital and underwent an anterior L1 and L2 corpectomy with anterior T12 through L3 interbody fusion. The empiric antibiotics were held for three days preoperatively to improve the diagnostic yield of specimens obtained during surgery. Erythrocyte sedimentation rate (ESR) and C-reactive peptide (CRP) were elevated at $>$ 120 mm/hr (normal range 0–40 mm/hr) and 99.6 mg/L (normal range 0–4.9 mg/L), respectively.

Surgical pathology revealed acute and chronic osteomyelitis and osteonecrosis with necrotizing granulomas. Acid-fast bacilli (AFB) smear showed 10–99 AFB per field ("1+" designation), and aerobic and anaerobic bacterial tissue, bone, and blood cultures were negative for growth. Risk factors for exposure to MTB were absent. Induced sputum for AFB was smear and culture negative, and the patient had no respiratory symptoms. *M. tuberculosis* (MTB) interferon-gamma release assay (Quantiferon-TB®) was indeterminate due to low mitogen reactivity.

The patient was diagnosed with non-tuberculous mycobacterial (NTM) osteomyelitis/discitis and started on rifampin, ethambutol, moxifloxacin, and clarithromycin to cover broadly for the most common causes of NTM infection. The isolate was sent to the Maryland State Department of Health laboratory, where probes for MTB, M. *avium/intracellulare* complex (MAC), *M. kansasii* and *M. gordonae* were negative. It was then sent to a commercial laboratory for definitive identification and susceptibility testing. At approximately four weeks, growth was seen on the mycobacterial growth indicator tube (MGIT), presumptively identified as *M.fortuitum/chelonae* complex, though this species is a rapid grower, typically growing in 7–10 days. The regimen was switched to clarithromycin, moxifloxacin, and IV imipenem and amikacin. Subsequently 16 S sequencing was performed, and *M. xenopi* was identified. The isolate was reported as susceptible to amikacin, ciprofloxacin, clarithromycin, linezolid, moxifloxacin, and trimethoprim/sulfamethoxazole, and resistant to ethambutol, rifampin, and streptomycin (Table 1). Her regimen was changed to clarithromycin,

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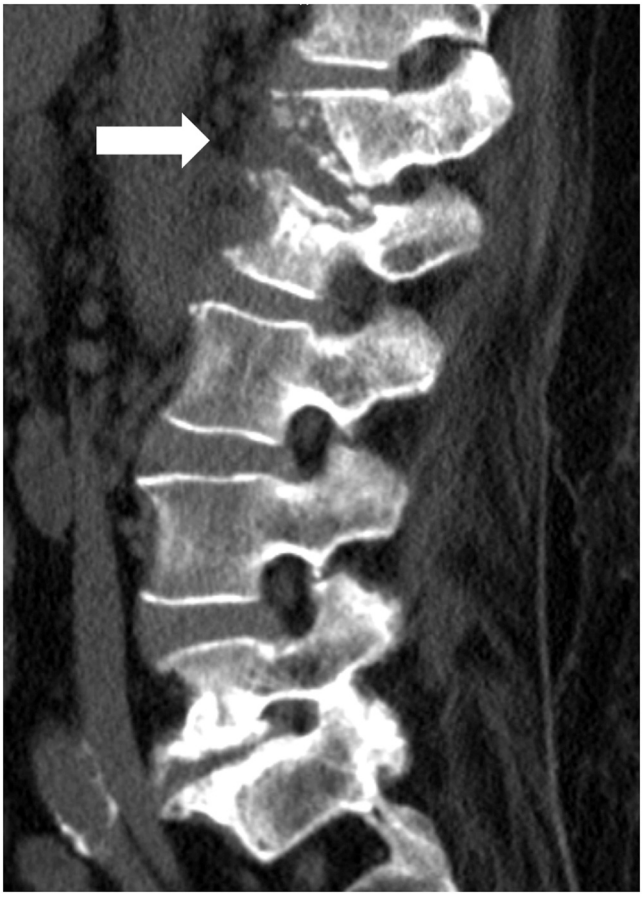

Fig. 1. CT of the lumbar spine showing stable compression deformity at the L1-L2 level and new L1-L2 discitis.

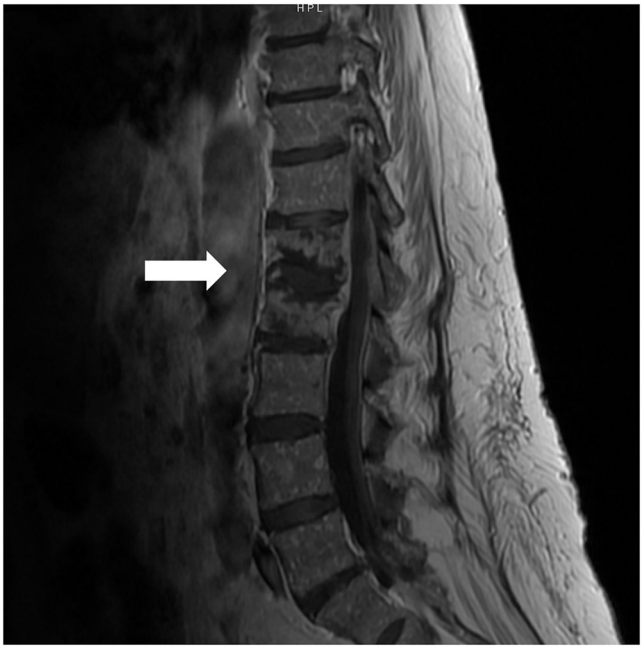

Fig. 2. MRI of the lumbar spine showing L1-L2 discitis, vertebral body enhancement, and contrast enhancing anterior paraspinal soft tissue prominence.

Table 1
M. xenopi drug susceptibility testing result.

Susceptible		Resistant	
Drug	MIC (mcg/mL)	Drug	MIC (mcg/mL)
Amikacin	8	Ethambutol	8
Ciprofloxacin	2	Rifampin	2
Clarithromycin	0.25	Streptomycin	32
Linezolid	8		
Moxifloxacin	0.25		
Trimethoprim/sulfamethoxazole	0.5/9.5		

moxifloxacin and linezolid based on susceptibility results, but severe nausea necessitated a switch from clarithromycin to azithromycin. The patient's back pain eventually subsided, and at a follow-up visit one month after beginning *M. xenopi* treatment, she was free of fever and other symptoms of infection. Objective data revealed a down-trending ESR and CRP with values of 52 mm/hr and 10.4 mg/L two months into treatment. Overall, she received approximately 4 months of appropriate treatment for *M. xenopi*, before dying of non-infectious causes related to her underlying illness.

Discussion

Mycobacterium xenopi is an NTM that was first discovered in 1959 from the skin lesions of *Xenopus laevis*, a species of toad [1]. It belongs to the slow-growing scotochromogenic NTM category and is highly resistant to extreme temperatures and a variety of disinfectants. *M. xenopi* has been found in water tanks, hospital water systems (cold and hot), and generators [2], and a small number of pseudo-outbreaks have been documented due to lab water contamination. [3,4] It is predominantly an opportunistic or iatrogenic pathogen, rarely causing lower respiratory tract infections in immunocompromised hosts. [5] Rarer still are cases of bone or joint infection.

A Pub-Med search for "Mycobacterium xenopi" plus "spinal" or "vertebral" in humans, published in English and French through August 2022 resulted in 18 unique cases of *M. xenopi* spine infections, dating between 1983 and 2022 (Table 2). [6–23] We found a report with 58 spinal infection cases during an outbreak in a French Sport Clinic, but since there was no clinical data describing the cases, we did not include that paper in the review of cases. [24].

The majority of *M. xenopi* spinal infections occurred in Europe (12), with four in USA, one in New Zealand, and one in China. The mean age of the patients was 48 years. Patient gender was identified in 17 of the 18 cases, with almost an even split between men and women (9 female and 8 male). Sites of infection were: cervical (1) thoracic (9), thoraco-lumbar (1), lumbar (5), lumbo-sacral (1), and sacral (1). One case described a patient with initial hip *M. xenopi* infection with recurrent infection of the spine, and another case had initial shoulder arthritis and subsequent spinal infection. Among these 18 cases, 12 were immunosuppressed individuals: five of them were people living with HIV, five with SLE and chronic corticosteroid use, one with pulmonary sarcoidosis and chronic corticosteroid use, and one with breast cancer on tamoxifen therapy. Four patients had prior spinal instrumentation (2 percutaneous nucleotomies, 1 laminectomy and corpectomy, 1 discectomy). Two of them also had intraspinal injections with corticosteroids.

There was substantial variation in the patients' treatment regimens. Multiple drug combinations were used: a 2-drug regimen was described in 2 cases, a 3-drug regimen was used in 6 cases, a 4-drug regimen was used in 8 cases, and a 5-drug regimen was used in 2 cases. The most common medications administered were rifamycins (13 cases), ethambutol (in 13 cases), clarithromycin (10 cases), isoniazid (8 cases), and fluoroquinolones (8 cases) in varying combinations. Patients received 9–24 months of treatment. The mean time between onset of symptoms and initiation of appropriate treatment for *M. xenopi* in reviewed cases

Table 2
M. xenopi spinal infection cases.

Year, location	Age, gender	Immune status	Infection site	Spinal history	Antimycobacterial regimen	Surgical Intervention	Outcome
1986, France [6]	45 M	Sarcoidosis, corticosteroids	S1-S2	S1-S2 laminectomy, corpectomy	INN, PCN-MTZ (6 ms)	Yes	Incomplete improvement
1986, UK [7]	55 F	SLE	L3	None	INH, PZA, RIF, STR	No	Incomplete improvement
1992, UK [8]	77 F	Competent	L1-L2	None	CPFX, ETH, INH, PZA, RIF	No	Incomplete improvement
1994, USA [9]	70 F	treatment)	T3-T4	None	CPFX, ETH, INH, PZA	Yes	Incomplete improvement
1995, USA [10]	? F	SLE, corticosteroids	T10-T12	NA	ETH, INH, PZA, RIF	Yes	Positive clinical and radiological outcome
1996, France [11]	28 M	Competent	L5	Percutaneous nucleotomy	CLR, ETH, PFLX	No	Positive clinical and radiological outcome
1997, France [12]	25 M	Competent	L5-S1	Percutaneous discectomy, injections	CLR, Sparfloxacine	Yes	Positive clinical and radiological outcome
1997, Netherlands [13]	56 F	azathioprine	T8, T9	None	CLR, CPFX, INH	No	Positive clinical and radiological outcome
1998, France [14]	41 F	HIV	C4-C5	None	CLR, CPFX, RFB	Yes	Unfavorable
2000, New Zealand [15]	73 F	Competent	T6-T7	None	ETH, RIF	Yes	Incomplete improvement
2001, UK [16]	35 M	HIV (ART)	T11-T12	None	ETH, INH, RIF	No	Positive clinical and radiological outcome
2005, France [17]	42 M	HIV (no ART)	T7-T8	None	CLR, ETH, RFB, INH	No	Incomplete improvement
2006, USA [18]	63 M	Competent	T12-L1	T9 & T12-L1 fracture	CLR, ETH, LVX, RIF	Yes	Unfavorable
2008, Germany [19]	28 ?	HIV (no ART)	T10	None	CLR, ETH, INH, RFB	Yes	Positive clinical and radiological outcome
2012, France [20]	61 M	Competent	L3-L4	Injections, percutaneous nucleotomy, fusion	CLR, ETH, RIF	No	Positive clinical and radiological outcome
2012, USA [21]	44 M	HIV (no ART)	T9-T10	None	CLR, ETH, MXF, RFB	No	Patient lost to follow up
2020, Italy [22]	46 F	SLE, corticosteroids	T8-T9	None	AZI, ETH, RFB	Yes	Positive clinical and radiological outcome
2022, China [23]	32 F	SLE, corticosteroids	L2-L4	None	CLR, ETH, LVX, LZD, RIF	No	Incomplete improvement
2023, US [this case]	68 F	RA, corticosteroids	L1-L2	Injections	CLR, MXF, LZD	Yes	Incomplete improvement

Notes: UK, United Kingdom; USA, United States of America; M, male; F, female; NA, not available; SLE, systemic lupus erythematosus; HIV, human immunodeficiency virus; ART, antiretroviral therapy; RA, rheumatoid arthritis; CPFX, ciprofloxacin; ETH, ethambutol; INH, isoniazid; PZA, pyrazinamide; RIF, rifampicin; CLR, clarithromycin; PFLX, pefloxacin; RFB, rifabutin; LVX, levofloxacin; MXF, moxifloxacin; AZI, azithromycin; LZD, linezolid.

was 38 weeks. The microbial culture identification time was 55 days (SD 7.5). [23] Only in 10 published cases was surgical treatment described as a part of management. The following outcomes were reported: 2 unfavorable, 8 complete recovery, and 7 incomplete improvements; 1 patient left against medical advice.

Very limited data is available to aid in the diagnosis and management of *M. xenopi* spinal infections. Cases are most prevalent in Europe (France, Italy, Netherlands and UK), with only 4 cases reported in the United States.

Per our review of published cases, most (66.7 %) *M. xenopi* spinal infections are seen in immunocompromised patients. Prior manipulation of the site of infection was also common, suggesting iatrogenic inoculation. Therefore, the combination of a compromised host plus inoculation of a usually avirulent pathogen is likely the usual pathway for infection. This was the case in our patient as well, as she was immunocompromised due to asplenia and had received spinal corticosteroid injections.

Clinically *M. xenopi* osteomyelitis presents very similarly to tuberculosis, which makes it challenging to differentiate. [26] Patients usually present with chronic local pain, swelling, fever, weight loss, malaise, and fatigue. [6,25] The clinical course of *M. xenopi* seems to be more indolent than tuberculosis, as the mean time between the presumed iatrogenic introduction of mycobacteria from a procedure and diagnosis was 5.6 years. [7] Other diagnoses that should also be considered in patients with these symptoms are metastases of an underlying neoplasm, lymphoma, sarcoidosis, actinomycosis [6], echinococcosis, and brucellosis. [26].

Blood tests may show leukocytosis and elevated ESR and CRP. AFB blood cultures are usually sterile. Imaging (X-ray, CT and MRI) should be performed to identify the level of involvement, rule out cord compression, and assess vertebral stability. Definitive diagnosis is made by biopsy (needle or open) with histological, cultural and molecular testing. In vitro susceptibility testing might be difficult to interpret and does not always correlate clinically. [27] For slow-growing mycobacterium like *M. xenopi*, the most challenging aspects of patient management are establishing a definitive diagnosis and treatment plan. In our case only molecular testing was able to provide us with an accurate diagnosis, but targeted therapy for *M. xenopi* was not initiated until almost 20 weeks had elapsed from her initial hospitalization and 25 weeks from the onset of her symptoms. Our review confirms that delays in definitive diagnosis are commonplace.

Clinical practice guidelines for any extrapulmonary sites of NTM infection are absent due to the rarity of these infections, but guidelines on pulmonary NTM recommend use of at least a 3-drug regimen including rifampicin, ethambutol, and moxifloxacin or macrolides, for at least 12 months. [27] These recommendations are conditional and with low certainty in estimates of effect.

Conclusion

Although *M. xenopi* osteomyelitis is increasingly reported in the literature, data to guide diagnosis and treatment are lacking. More trials, studies, and case reports are needed to expand knowledge of this rare but serious infection, to ultimately improve management of the patients with *M. xenopi* osteomyelitis.

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CRediT authorship contribution statement

Daria Bekina-Sreenivasan: Data collection, Writing – original draft, Writing – review & editing. Sarah A. Schmalzle: Patient management, Conceptualization, Data collection, Writing – original draft, Writing – review & editing, approved the final manuscript. Paul Saleeb: Writing – review & editing, approved the final manuscript.

Ethical approval

This was not an interventional study and did not require ethical approval.

Consent

Written informed consent was obtained and is on file with the corresponding author.

Conflict of interest

All authors declare no conflicts of interest that the editors consider relevant to the content of the manuscript.

Data Availability

There is no supplementary data.

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