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Pott's Disease? AIDS-Associated *Mycobacterium heckeshornense* Spinal Osteomyelitis and Diskitis

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Acid-fast bacillus (AFB) spinal osteomyelitis in a patient with AIDS is often presumed to be caused by reactivated *Mycobacterium tuberculosis*. However, other AFB pathogens can mimic *M. tuberculosis* and, to ensure appropriate and adequate therapy, should be considered by clinicians. We present a case of aggressive spinal osteomyelitis caused by *Mycobacterium heckeshornense* in an AIDS patient; a review of the literature is also included.

CASE REPORT

A 45-year-old man with AIDS presented with a 3-week history of mid-back pain. There was no history of trauma or constitutional or neurologic symptoms. He also had a history of pulmonary cryptococcosis, Kaposi's sarcoma, squamous cell carcinoma of the skull and face, chronic hepatitis B infection, and medication nonadherence. Medications included fosamprenavir, ritonavir, tenofovir, lamivudine/zidovudine, rilpivarine, prophylactic atovaquone and azithromycin, and fluconazole. Physical examination revealed normal vital signs without fever, low thoracic spine midline tenderness without overlying edema, erythema, ecchymosis, or mass lesion, and normal neurologic exam. Laboratory data included a total white blood count of $3.5 \times 10^3/\mu l$, hemoglobin of 11.4 g/dl, hematocrit of 36.4%, platelet count of $297 \times 10^6/\mu l$, creatinine of 0.7 mg/dl, normal liver enzymes, an HIV load of 25 copies/ml, and a CD4 lymphocyte count of 65 cells/μl (3%). Magnetic resonance imaging revealed a 2.1-cm by 2.5-cm by 2.0-cm low T1 and bright T2 bone marrow lesion of the T12 and L1 vertebral bodies involving the T12/L1 disk (Fig. 1). A computerized tomography (CT)-guided biopsy of the L1 lesion was obtained; aerobic, anaerobic, and fungal cultures showed no growth, but an acid-fast bacillus (AFB) smear was positive. For presumed diagnosis of spinal tuberculosis, rifabutin (dosed by blood levels), isoniazid, pyrazinamide, and ethambutol (RHZE) were initiated; the rilpivarine dose was doubled. Eighteen days later, an orange-pigmented growth was noted in a BacT/Alert MP bottle (bioMérieux, Durham, NC) incubated at 37°C on the BacT/Alert 3D system. Preliminary rRNA-DNA hybridization of the bottle sediment (AccuProbe, Gen-Probe, Inc., San Diego, CA) was positive for *Mycobacterium gordonae* (36,271 relative light units) and negative for *Mycobacterium avium* complex (MAC) (<10,000 RLU). Given the clinical presentation consistent with tuberculous mycobacterium disease and a probe value just above the assay cutoff (30,000 RLU), DNA probes were repeated on growth on Lowenstein-Jensen (LJ) slants and were negative for *M. gordonae* (<10,000 RLU) and also negative for *M. tuberculosis* (MTB) complex. A final probe set of the bottle sediment was negative for *M. gordonae*, MTB complex, and MAC, suggesting that the initial result was a false-positive result for *M. gordonae*. Biochemically, the isolate was scotochromogenic, reactive for aryl sulfatase at 14 days, and nonreactive for nitrate reduction, semiquantitative catalase, heat-stable (68°C) catalase, urease, and Tween hy-

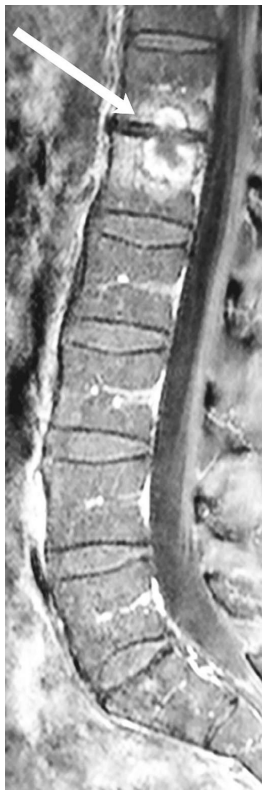

FIG 1 MRI (T1 postgadolinium with fat suppression). Sagittal lumbar spine showing T12/L1 lesion.

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TABLE 1 Summary of English-language literature search results[a]

Authors (reference)	Yr published	Infection	Therapy	Outcome
Roth et al. (4)	2000	Cavitary lung disease (immunocompetent)	RHE, protionamide, CIPRO and lobectomy	Infection eradicated
van Hest et al. (7)	2004	Nodular lung disease and pneumothorax (immunocompetent)	RHZE, then RE	Infection eradicated
van Hest et al. (7)	2004	Cavitary lung disease	RH, CLARI, LEVO	Unknown
Godreuil et al. (8)	2006	Flexor tenosynovitis of hand (immunocompetent)	Flexor tenosynovectomy; no medical therapy	Infection eradicated
Jaureguy et al. (9)	2007	Cavitary and nodular lung disease (immunocompetent)	RHZ, then CLARI, E, and MOX	Infection eradicated
Elyousfi et al. (10)	2009	RA-associated lumbar spondylodiskitis	RHZE, then CLARI, MOX, R	Unknown
McBride et al. (11)	2009	Axillary lymphadenitis (immunocompetent)	Axillary node dissection; no medical therapy	Infection eradicated
Ahmed et al. (12)	2010	HIV-associated dissemination (blood culture)	INH, CLARI, MOX, R, ART	Infection eradicated
van Ingen et al. (2)	2010	Porcine lymphadenitis	NA	NA
Chan et al. (13)	2011	PD-associated peritonitis	PD catheter removal and fluid drainage; no medical therapy	Infection eradicated
Morimoto et al. (14)	2011	Pneumonia (immunocompetent)	MER, then MOX, then CLARI	Infection eradicated
Elze et al. (1)	2013	Feline disseminated disease	NA	NA
Carpenter and Graf (this study)	2015	AIDS-associated lumbar osteomyelitis and diskitis	RHZE, then RH	Favorable clinical response with ongoing therapy

[a] R, rifampin/rifabutin; H, isoniazid; Z, pyrazinamide; E, ethambutol; CIPRO, ciprofloxacin; CLARI, clarithromycin; LEVO, levofloxacin; MOX, moxifloxacin; ART, antiretroviral therapy; PD, peritoneal dialysis; MER, meropenem; RA, rheumatoid arthritis; NA, not applicable.

drolysis. Despite strong biochemical similarity to *Mycobacterium xenopi*, the isolate grew equally well at 37°C and 42°C. The isolate was sent for molecular identification by 16S rRNA gene sequencing and identified as *Mycobacterium heckeshornense*; there was 100% identity with *M. heckeshornense* over a match length of 986 bp, while there were 30 mismatches with the next closest match, *M. xenopi*. The identification was performed at a large commercial reference laboratory using CLSI guidelines for percent match with the SmartGene *Mycobacterium* database. Drug susceptibility data using the Sensititre plate for slow-growing mycobacteria (Trek, Oakwood Village, OH), also performed by the same large commercial reference laboratory, was available at time of isolate identification (ID), showing susceptibility to isoniazid (MIC, 0.2 μg/ml), rifampin (MIC, 1.0 μg/ml), ethambutol (MIC, 5.0 μg/ml), and clarithromycin (MIC, 1.0 μg/ml) but resistance to pyrazinamide (MIC, 100 μg/ml). Interpretations were made using CLSI breakpoints. At this time, 5 weeks after antimycobacterial therapy was started, there had been remarkable clinical response with resolution of spinal pain. Due to potential drug interactions and since azithromycin had already been administered at 1,250 mg weekly, RHZE was continued through 8 weeks, with a plan to continue rifabutin and isoniazid for at least 18 months.

We report the first case of AIDS-associated *M. heckeshornense* spinal disease. *M. heckeshornense* is a nontuberculous mycobacterium (NTM) that rarely causes human disease and has also been associated with feline and porcine illness (1–3). NTM are present in the environment, may be especially prevalent in tap water, and rarely cause osteomyelitis. *M. heckeshornense* is thought to be a very rare cause of bronchopulmonary disease in humans, but not osteomyelitis (3).

First described in 2000, *M. heckeshornense* is a scotochromogenic NTM closely related to *M. xenopi* that grows at 37°C, 40°C, and 45°C; biochemically, it is often heat-stable-catalase positive but negative for all other standard mycobacterial biochemical tests (4). However, our isolate was negative for heat-stable catalase activity. Very limited drug susceptibility data show that the species has variable susceptibility to first-line antituberculosis drugs (4).

We searched the English-language literature using Pub-Med with search term "heckeshornense" and found 15 articles and 11 cases of human infection with *M. heckeshornense* (Table 1). Interestingly, 55% of these patients were thought to be immunocompetent. Due to an aggressive clinical presentation, most cases were initially treated as reactivated *M. tuberculosis* with standard four-drug therapy, which was later modified to target *M. heckeshornense*. Given its close phylogenetic relationship to *M. xenopi*, some authors advocate treating it as such with isoniazid, rifamycin, ethambutol, and clarithromycin, with or without an initial course of streptomycin; however, as with any infection, drug interactions must be considered when therapy is being selected for individual patients (5). *In vitro* drug susceptibility data can be difficult to interpret for NTM due to the knowledge that some do not predict clinical response. Due to their variable susceptibility to first-line antituberculous drugs, *M. heckeshornense* isolates should be tested for drug susceptibility and this information considered when a treatment regimen is being selected (5, 6).

Given our experience with positive and then negative *M. gordonae* hybridization probe results, we urge clinicians to pursue definitive methods of mycobacterial identification when the clinical syndrome is not consistent with rapid diagnostic test results. The RLU value for the *M. gordonae* probe was just above the assay cutoff, suggesting a possible false-positive result. The results for two repeat tests of the isolate, one from growth on an LJ slant and the other from the broth sediment, were negative. Morphologically and biochemically, *M. heckeshornense* resembles and may be commonly misidentified as *M. xenopi* in the absence of careful growth temperature studies or gene sequencing.

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