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Case report

Intramedullary spinal cord lesions in an immunocompromised host due to *Mycobacterium haemophilum*

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ABSTRACT

Mycobacterium haemophilum is a slow growing acid-fast bacillus (AFB) in the nontuberculous mycobacteria (NTM) group. *M. haemophilum* typically causes cervicofacial lymphadenitis in children, cutaneous diseases, septic arthritis and osteomyelitis. However, it rarely causes isolated spinal cord disease. We report the first case, to our knowledge, of isolated intramedullary spinal lesions secondary to *M. haemophilum*. This case involved a patient with newly diagnosed human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS). He developed significant immune reconstitution inflammatory syndrome (IRIS) during his treatment. *M. haemophilum* should be on the differential for isolated intramedullary spinal lesions, particularly in immunocompromised patients. Given our patient's severe IRIS, patients with HIV and *M. haemophilum* infection should be closely monitored for IRIS and treated aggressively. In high risk circumstances such as *M. haemophilum* spinal disease in patients with HIV, clinicians should consider pre-emptive treatment for IRIS.

Introduction

M. haemophilum is an acid-fast bacillus (AFB), slow growing nontuberculous mycobacteria (NTM). It was first described in 1978 in a patient with cutaneous nodules [1]. It is frequently found in the environment, although no specific reservoir has been identified. It derives its name from its "blood loving" nature and a requirement for iron supplementation in culture media [2].

Common infections include cutaneous disease, septic arthritis, osteomyelitis, pneumonitis and cervicofacial lymphadenitis in children. It is closely related to *Mycobacterium leprae*, and can cause skin lesions similar to *Mycobacterium uclerans* and *Mycobacterium marinum*. The propensity to cause skin lesions may be related to the organism's affinity for lower temperatures [3,4]. *M. haemophilum* has been known to cause localized or disseminated diseases, predominately in immunocompromised hosts. Susceptible patients include patients with hematologic malignancies, stem cell transplant recipients, solid organ transplant patients, and patients living with HIV/AIDS [5]. There are about 250 reported cases in the literature. There is no standard regimen for *M. haemophilum* infections. Triple therapy with a macrolide, fluoroquinolone and one of the rifamycins for a prolonged course is typically used [3,4]. Our case is unique in the location of the infection and that significant IRIS developed during treatment. The purpose of this case report is twofold. First, to encourage consideration of *M. haemophilum* in the differential of isolated intramedullary spinal cord lesions. Second, to advocate for heightened awareness of IRIS in patients with HIV and *M. haemophilum* infections, with consideration of aggressive early corticosteroids and steroid sparing agents in the clinical management of these patients.

Case report

A 51 year old man presented with a six week history of right sided pain and paresthesias. He reported no significant medical history. His vital signs were normal, and his physical examination was notable for allodynia on his right trunk up to T3 and paresthesias in his right lower extremity. HIV test was positive and CD4 count was 50 cells/μL with an HIV-RNA of 58,693 copies/mL. A Magnetic Resonance Image (MRI) of the spine demonstrated multiple enhancing intramedullary lesions spanning from the cervical to the lower thoracic spine (Fig. 1A and B). An MRI of his brain was normal.

We undertook an extensive work-up to determine the cause of the spinal cord lesions. Lumbar puncture showed: protein 73 mg/dL,

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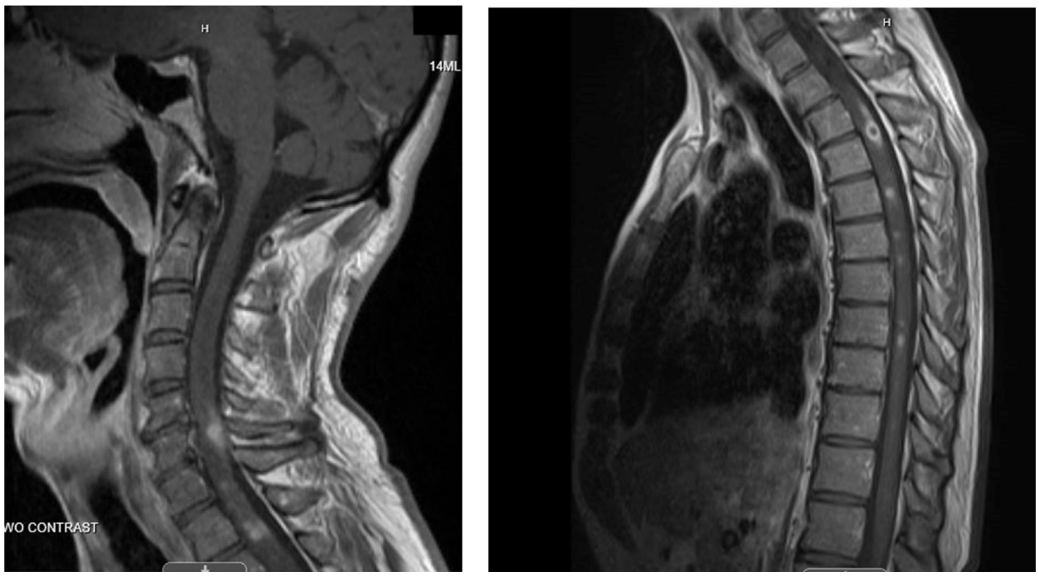

Fig. 1. A and B: MRI C and T spine with intramedullary lesions.

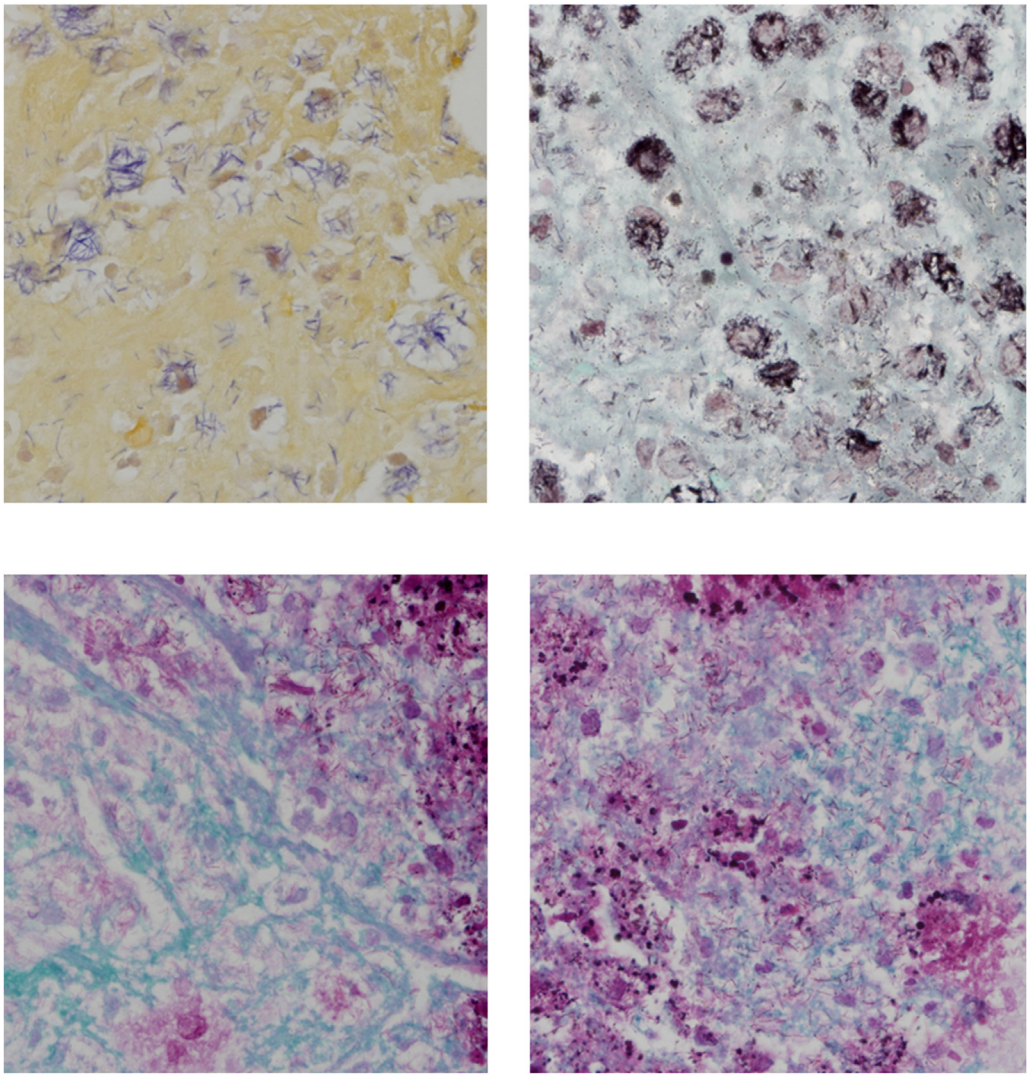

Fig. 2. GMS and Fite stain of biopsy specimens showing long gram positive bacilli.

glucose 42 mg/dL, 80 WBC's/uL with 98 % lymphocytes. Analysis of his cerebrospinal fluid (CSF) including cryptococcal antigen and cytology were all negative. Although serum toxoplasmosis IgG was negative, he was started on empiric toxoplasmosis treatment as that was the most likely infection in the setting of a negative work up. Two weeks later he was started on ART for HIV with co-formulated tenofovir alafenamide, emtricitabine and dolutegravir and achieved viral suppression within five weeks. Despite these interventions, he had progressive neurological symptoms and therefore underwent a spinal cord lesion biopsy. Histopathological examination showed innumerable long gram-positive bacilli (Fig. 2) with necrotizing granulomatous inflammation. Since cultures did not yield any organisms, the biopsy specimen was submitted for 16S rRNA sequencing revealing the presence of *M. haemophilum*.

The patient was started on moxifoxacin 400 mg daily, azithromycin 500 mg daily, rifampin 600 mg daily, doxycycline 100 mg BID, and amikacin 850 mg IV (M/W/F). His ART was adjusted to tenofovir disoproxil fumerate/emtricitabine with twice daily dolutegravir. He had initial improvement but after 3 weeks developed worsening of his neurologic symptoms. MRI of his spinal cord showed diffuse swelling. The clinical worsening and spinal cord edema were thought to be secondary to immune reconstitution inflammatory syndrome (IRIS) and he was started on high dose dexamethasone. Since *M. haemophilum* is a phylogenetically-related organism to *M. leprae*, clofazimine and thalidomide were added sequentially with the goal of acting as immunomodulatory agents. The patient's course was complicated by bilateral LE DVTs, minimal rise in CD4 count despite suppressive HIV therapy, and progressive neurological deficits leading to tetraplegia. He decided to pursue comfort care with hospice and died after seven months of treatment.

Discussion

Intramedullary spinal lesions present an exceptionally difficult diagnostic entity, as biopsy is high risk and the infectious diseases differential alone is broad (Table 1). We report the first case, to our knowledge, of isolated intramedullary spinal lesions secondary to *M. haemophilum*. There have been four other cases of central nervous system (CNS) disease reported, including a spindle cell pseudotumor of the brainstem, infection of the optic apparatus and hypothalamus, lesions of the brainstem, basal ganglia, and thalamus, and an intraventricular mass [5–7].

M. haemophilum requires iron supplemented media and prefers lower temperature (28°–30 °C) for culture, which can make it difficult to recover in culture [2]. Therefore, *M. haemophilum* should be considered in AFB smear positive cases with no growth on typical AFB media [3,4]. Diagnosis typically requires biopsy, which shows characteristic short, often curved bacilli and case-ating granulomas. Culture with specialized media and PCR are often needed to identify the organism [3].

There are no standardized clinical guidelines to treat *M. haemophilum*. As in other mycobacterial infections, dual or triple therapy is advised. Therefore, a combination of a macrolide, a fluoroquinolone, and one of the rifamycins for a duration of 12–24 months is a common treatment [3,4]. Treatment is often empiric, as in our patient. Our patient developed IRIS in the course of his treatment. The data for IRIS with *M. haemophilum* is limited, however Woodworth et. al also described a case of IRIS during *M. haemophilum* treatment in a patient with HIV. The patient initially improved but eight weeks after starting treatment he developed worsening symptoms consistent with IRIS. The patient was treated with prednisone for 3 months with symptom improvement. [8] Although the incidence of IRIS with *M. haemophilum* is not known, one case series notes the incidence of IRIS in general NTM infections was 3.5 % among patients initiating HIV therapy with a baseline CD4 count <100 cells/μL [9]. This case adds to the literature and experience with *M. haemophilum* and IRIS. Interestingly, similar paradoxical reactions are seen with treatment of *M. leprae* even in immunocompetent patients [10].

Overall, *M. haemophilum* is a rare infection and there needs to be a strong clinical suspicion for diagnosis. This infection should be considered in immunocompromised hosts, when specimens are AFB smear positive, but cultures do not recover an organism.

Table 1
Infectious Diseases differential of isolated intramedullary spinal cord lesions: Rare entities [11–17].

Disease	Associations and Patient Characteristics	Potential CNS MRI characteristics*
Tuberculosis	Subacute presentation with systemic symptoms, may see muscle weakness, paraparesis or quadriparesis. Typically occur secondary to pulmonary infection, but may exist without pulmonary involvement.	Ring enhancing lesion on T1 images
Non-Tuberculosis Mycobacterium	May see spinal involvement	Intramedullary ring enchancing lesions
Toxoplasmosis	Acute onset weakness in immunocompromised patients, especially HIV. Typically, also have brain involvement.	Multiple ring enchancing lesions
Neurocystercicosis	May be asymptomatic or have weakness. CNS lesions are more common, with spinal involvement rare (estimated 2–5 % of cases)	Cysts, scolex is diagnostic
HIV myelopathy	Advanced HIV patients, vacuoles are formed in nerve fibers	Atrophy with single or diffuse lesions
Bacterial abscess	<100 cases have been reported in the literature. IVDU is risk factor.	Focal ring-enhancing lesion or lesions with central hyperintense area on DWI
Medullary schistosomiasis	From endemic region, acute subacute myelopathy	Conus medullaris expansion, other sites of involvement are rare. Can see linear and nodular enhancement pattern
Viral myelitis	HIV, HSV, enterovirus, HTLV-1, CMV	Single or multiple lesions, with or without postcontrast enhancement
Histoplasmosis	CNS involvement rare, usually accompanied by disseminated disease	Enlargement of the conus terminalis, low-intensity signal on T1-weighted images, high-intensity signal on T2-weighted images
Blastomycosis	Few reports of CNS disease in literature, but can present as isolated intramedullary lesion	Unknown
Coccioides	Few reports of CNS disease in literature, usually part of disseminated disease	Leptomeningeal enhancement with intramedullary extension
Cryptococcus	Progressive bilateral lower limb weakness, cryptococcoma lesion can mimic tumor in immunocompetent or immunocompromised patient	Localized solid, tumor like mass. Lesions are isointense or slightly hyperintense on T1-weighted, hyper to hypointense on T2-weighted MR images with surrounding edema

* MRI characteristics are based on limited case report information.

The differential for isolated intramedullary spinal lesions is broad but should include *M. haemophilum*. MRI characteristics can help narrow the differential. Additionally, patients with and without HIV should be closely monitored for IRIS. Given this case, clinicians may consider pre-emptive treatment with corticosteroids when NTM treatment is initiated; however more experience is needed to determine the optimal management of IRIS in this setting.

Authors contributions

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

All authors have no declaration of interest to disclose.

All authors have approved the manuscript. We confirm that our article has not been published elsewhere and is not under consideration by another journal.

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CRediT authorship contribution statement

Shelley Kon: Writing - original draft, Writing - review & editing. **Carlos Franco-Paredes:** Writing - review & editing. **Kellie L. Hawkins:** Conceptualization, Supervision, Writing - review & editing.

Declaration of Competing Interest

None.

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