The Fell Clutch of Circumstance:
Atypical Pott Disease in a Patient on Chronic Steroids

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Introduction

Nontuberculous mycobacteria (NTM) as an etiologic agent of osteomyelitis became a focus in light of the HIV/AIDS epidemic, as severe immune compromise (IC) predisposed patients to disseminated NTM disease.

Mycobacterial vertebral osteomyelitis (VO) is a common and characteristic presentation of bony mycobacterial infection. While the majority of patients identified in medical literature with NTM VO are HIV positive, case reports of patients without clear evidence of intrinsic IC have also been noted. In this case report, we discuss a 41-year old woman who developed NTM VO, with a possible risk factor contributing to immunosuppression from repeated courses of pulse dose steroids.

Learning Objectives

- To recognize a characteristic anterior-inferior vertebral body collapse and kyphotic pattern of NTM vertebral osteomyelitis
- To acknowledge typical risk factors and to consider atypical risk factors for NTM as global prevalence increases
- To consider antimycobacterial treatment regimens for NTM osteomyelitis, challenges related to medication interactions and toxicities

Imaging Findings

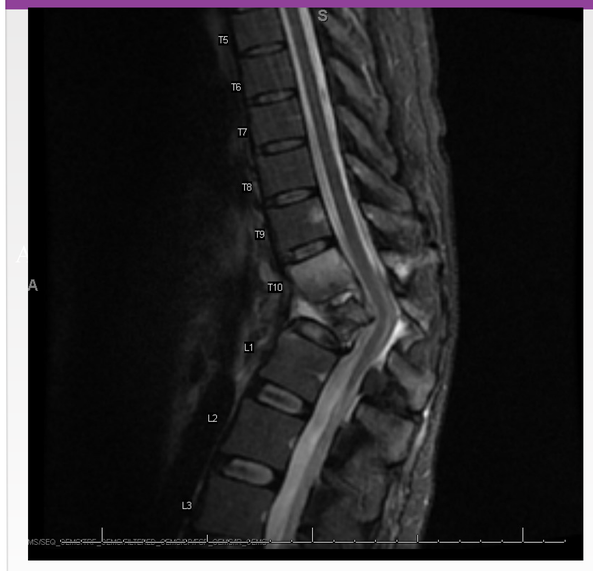

Figure 1: MRI of the thoracic and lumbar spine with T2 weighted imaging revealing almost complete collapse of the T11 and T12 vertebral bodies and with associated enhancement involving T10, T11 and T12 vertebrae, anterior prevertebral soft tissues with subligamentous spread and T8 to L1 epidural enhancement.

Case Summary

A 41-year-old woman with polycystic kidney and liver disease, and progressive chronic back pain and kyphosis presented to our hospital for acute on chronic back pain in light of outpatient CT imaging revealing novel deformities of T12/L1. Symptoms had been progressively worsening for about nine months, requiring buprenorphine for pain management, and multiple recent courses of pulse dose glucocorticoids to attempt to alleviate back pain.

On admission, she was hemodynamically stable and afebrile. She was able to ambulate independently, though noted to have significant debilitating kyphosis. Initial lab workup revealed mild stable microcytic anemia, and mild AKI with Cr to 1.8 mg/dL from baseline around 1.1-1.4 mg/dL (0.60 -1.3 mg/dL). Inflammatory markers were largely unremarkable with ESR 26, CRP 0.8. She underwent repeat CT abdomen, pelvis and thoracic spinal imaging which revealed severe pathological compression fractures of T12 and L1 vertebral bodies with gibbus deformity and near complete loss of T12 and L1 vertebral bodies heights. MRI of the thoracic and lumbar spine was performed to further characterize the fractures and evaluate the spinal cord, revealing almost complete collapse of the T11 and T12 vertebral bodies and with associated enhancement involving T10, T11 and T12 vertebrae, anterior prevertebral soft tissues with subligamentous spread and T8 to L1 epidural enhancement.

Additional workup for secondary causes of atypical vertebral fractures included evaluation for endovascular nidus of infection, which included negative blood cultures and transthoracic echocardiogram. There was no evidence of multiple myeloma with a serum protein electrophoresis and immunofixation revealing only mildly elevated IgG to 2.03 g/dL (0.70-1.60 g/dL) and without monoclonal proteins. HIV testing was negative. Labs revealed a Vitamin D deficiency with 25-OH Vitamin D levels <5 ng/mL (25-100 ng/mL) though notably 1,25 OH2 Vitamin D were not tested. ACE levels were elevated to to 93 U/L (9-67 U/L). She was found to have a borderline reactive Quantiferon Gold (TB2 minus nil 0.35 IU/mL, <0.34 IU/mL). She was placed in isolation precautions and three induced sputum samples were collected to evaluate for tuberculosis.

She was recommended to undergo a CT guided vertebral biopsy prior to orthopedic surgery to guide management. Given chronicity of vertebral deformity and patient's functional status, surgical planning and CT guided biopsy were deferred to the outpatient setting, with rehabilitation, smoking cessation and management of her chronic diseases as identified goals prior to a T10-12 corpectomy and T7-L3 PSF.

One week following her discharge from the hospital, induced sputum samples grew *Mycobacterium avium*. She was referred to the infectious disease outpatient clinic, where she was initiated on rifabutin, ethambutol, and azithromycin for one year of treatment. Surgical planning remains ongoing while seeking to optimize risk factors and maintain physical functioning.

Clinical Considerations

Risk Factors

- HIV/AIDS
- Hematologic Malignancy
- IL-12/INF-gamma Axis Defects
- TNF-alpha Inhibitor Exposure
- Corticosteroid Exposure
- Advanced Age
- Higher Cumulative Disadvantage Scores

Treatment Considerations

- Antimicrobial Susceptibility/ Synergy
- Slowed Microbial Growth Kinetics In Bony Tissue
- Antimicrobial Penetration in Bone
- Medication Interactions
- Treatment Toxicities
- Ultimate Surgical Management

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Discussion

It is presumed that the pathogenesis of mycobacterial vertebral osteomyelitis (MVO) is similar between TB and NTM organisms, which are thought to be seeded hematogenously via the paravertebral venous route, leading to characteristic destruction in the anterior-inferior vertebral body, with progression to involve the anterior spinal ligament and periosteum to adjacent vertebrae. CT and MR Imaging thus typically reveal involvement of one or more contiguous vertebral bodies resulting in significant kyphosis, disc destruction and soft-tissue inflammation that may extend extradurally or cause abscesses in surrounding soft tissue. MVO is characterized by a slower progression of bone destruction relative to typical pyogenic osteomyelitis, and given this natural history as well as the fastidious growth of mycobacteria in the laboratory setting, time to diagnosis from initial development of symptoms is estimated at about ten months for TB MVO.

While bone biopsy and culture remain the gold standard for diagnosis of osteomyelitis, the pathognomonic imaging findings and evidence of active mycobacterial disease were considered confirmatory in this patient. Bone biopsy is recommended to guide management as cases of co-infection with pyogenic bacteria that may not be susceptible to typical antimycobacterial antibiotics have been reported.

At this time, there are no clear international guidelines regarding the treatment of extrapulmonary NTM infections. Given the rarity of NTM osteomyelitis, decisions regarding first line therapy and duration of treatment are largely extrapolated from treatment of TB MVO and NTM pulmonary disease. This is a challenge in determining best treatment protocols as the most recent guidelines for management of NTM infections date to 2007, with increasing resistance to antimycobacterial agents reported in intervening years. Additionally, when extrapolating data from pulmonary infections, mycobacteria in the bone are noted to have slowed growth kinetics and metabolism, which is presumed to render these infections less quickly responsive to antibiotic therapy. Antimicrobial combination therapy for NTM is typically dependent on severity of illness, and must consider possible resistance patterns including those that may not be reliably predicted by *in vitro* testing, as well as bony penetration . Extrapolation from treatment of macrolide susceptible *Mycobacterium avium* was used to develop an initial treatment strategy for our patient, with initiation of a regimen including a macrolide, ansamycin and ethambutol. Susceptibility testing was performed on MAC isolates to ensure the prescribed regimen would be efficacious against her disease.

Conclusion

Rates of NTM infections are rising globally. While pulmonary disease is the most common manifestation of NTM infection, disseminated disease is increasingly being recognized, including in patients who lack traditional risk factors for disseminated disease. NTM osteomyelitis should be considered among patients with atypical anterior vertebral factures, and treatment should be initiated upon identification of organism susceptibility.