INTRODUCTION

Nontuberculous mycobacterial (NTM) osteomyelitis is rare and few cases have been reported in the literature. Although a case of NTM osteomyelitis has been reported in an immunocompetent child, in general people who develop these infections are likely to harbor immunodeficiencies such as HIV/AIDS. The following is a representative case of NTM osteomyelitis caused by mycobacterium avium complex (MAC) in a patient with HIV/AIDS, which reflects the important aspects of the multidisciplinary approach required to care for these complex patients.

CASE REPORT

The patient is a 51-year-old woman who was born in Mozambique and has lived in Zimbabwe, Portugal and Ohio, who presented with worsening left leg pain to an outside hospital 4 weeks after hitting her leg against a car doorframe sustaining a minor abrasion. The pain progressed to a point beyond which she could no longer tolerate and she sought medical attention. Her past medical history was significant for pneumonia, tenia corporis, recurrent vaginal yeast infections and genital herpes. She denied intravenous drug use and did report that her husband had been unfaithful. On initial examination at the outside hospital, she was found to have an erythematous, warm, swollen and tender left leg with no disruption of the skin. X-rays showed cortical thickening of the left distal tibial diaphysis associated with a radiolucent defect. Bone scan showed focal periosteal reaction and adjacent soft tissue uptake. Computed tomography revealed left tibial and subcutaneous calcifications consistent with post-traumatic osteomyelitis. Routine admission laboratory analysis revealed neutropenia. She was subsequently tested for HIV and found to have HIV-1 infection with a CD4 cell count was 20/mm³ and a viral load of 51,371 copies/ml. Because her underlying diagnosis was unknown, she had not been on any antiretroviral therapy or opportunistic infection (OI) prophylaxis prior to presentation. She was empirically started on intravenous vancomycin and cefazolin. Five days after the initiation of antibiotics, she underwent bone biopsy. Both bone and blood cultures at that time were negative for any bacteria. Mycobacterial culture data from the outside hospital was not available. Bone pathology revealed osteonecrosis without mention of granulomas. She was started on a combination pill containing efavirenz, emtricitabline and tenofovir. A PICC line was placed and she developed a subclavian vein thrombosis. She was started on enoxaparin bridge to warfarin with a plan of continuing systemic anticoagulation for 4 months. The patient was discharged to a state-run institution for continuing care needs and rehabilitation after a sixteen day hospital course on vancomycin and cephalexin, coumadin, combination antiretroviral therapy and prophylactic trimethoprim/sulfamethoxazole with azithromycin. Vancomycin was stopped after 6 weeks and oral cephalexin was continued.

FIGURES 1 & 2: Orthogonal radiographs of the left tibia demonstrate dystrophic calcification in the anterior soft tissues with endosteal sclerosis and a vague lucency of the anterior cortex of the distal tibial diaphysis which imply persistent infection and necrotic bone.
Two months after her initial presentation and within 2 weeks of stopping the vancomycin, the patient presented to our hospital with recurrent erythema, swelling, warmth and tenderness of her left leg. Additionally, she also had a left gluteal carbuncle and right groin cellulitis. The patient had no fevers or chills prior to presentation. The patient’s white count was 2.8 x 10^9/L and her ESR was 48 mm/hr and her CRP was 17 mg/L. Her most recent CD4 cell count was 34/ mm^3 prior to admission. X-rays showed endosteal sclerosis and lucency of the anterior cortex of the distal tibial diaphysis and soft tissue changes consistent with prior biopsy (Figures 1 & 2).

She was taken to the operating room and underwent thorough irrigation and debridement with sequestrectomy. A subatmospheric pressure dressing was applied. She also underwent incision and drainage of the left gluteus. Specimens were sent to microbiology for aerobic, anaerobic, fungal and mycobacterial analysis. Specimens were also sent to pathology. Biopsies from both sites showed granulomas (Figure 3 & 4) and were positive for acid-fast bacilli, which were determined to be Mycobacterium Avium Intracellulare Complex (MAC) sensitive to clarithromycin (Figure 5). The left gluteal abscess was also positive for 2 strains of sensitive coagulase-negative staphylococcus. Postoperative blood and sputum cultures were negative for bacteria, fungi and mycobacteria. A subsequent chest, abdomen, and pelvic CT showed no evidence disseminated mycobacterial involvement. Postoperative x-rays were obtained for a baseline for follow up care (Figures 6 & 7). The patient’s
symptoms resolved and she was discharged 10 days after presentation on her unchanged HIV antiviral and prophylactic regimen, and rifabutin, isoniazid, pyrazinamide, ethambutol, and clarithromycin which were changed to rifabutin, clarithromycin and ethambutol based on final speciation.

As her three month follow-up appointment, she was ambulatory with a cane and able to bear weight. X-rays at that time demonstrated a stable post surgical defect without evidence of new disease (Figures 8 & 9). A MRI of the left tibia four months after her debridement showed no evidence of ongoing osteomyelitis (Figures 10 & 11). Nine months after discharge, the patient developed sudden bilateral decrease in visual acuity which was believed to be secondary to optic neuropathy from ethambutol. She had an initial evaluation including formal visual field testing with ophthalmology and shortly thereafter returned home to Zimbabwe. In doing so, she was subsequently lost to follow-up.

**DISCUSSION**

According to a 2008 Centers for Disease Control synopsis, at the end of 2003 an estimated 1,039,000 to 1,185,000 people within the United States were living with HIV/AIDS and an additional 56,300 contracted the disease in 2006. While the incidence of opportunistic infections within the HIV population has declined since the introduction of highly active antiretroviral therapy (HAART), there is still a substantial risk of OI in those patients with low CD4 cell counts.

Nontuberculous mycobacterium osteomyelitis is a rare OI which has been reported in the HIV population. While 1% of HIV patients in the US corresponds to approximately 10,000 people, there have been less than 50 cases of atypical mycobacterium osteomyelitis reported in patients with HIV. Of the cases reported, mycobacterium haemophilum and mycobacterium kansasi were the most common causative agents respectively; mycobacterium. avium complex (MAC) infection was responsible for the third largest portion of NTM osteomyelitis. Although disseminated mycobacterium avium Complex (DMAC) in patients with CD4 cell counts < 50/mm3 is relatively common, localized infection is rare. DMAC was reported to be present in 16% of the HIV population before 1996; the current rate is < 1% per year because of HAART and MAC prophylaxis.

While NTM osteomyelitis is rare, there are specific risk factors which predispose people to these infections. Trauma, surgery, compromised immune status and disseminated disease all increase the risk of developing osteomyelitis with NTM. Whereas penetrating trauma is the most common etiologic mechanism for NTM osteomyelitis, there are reports of blunt trauma precipitating NTM osteomyelitis. One possible explanation is the locus minoris resistentiae theory, which postulates that macrophages containing dormant mycobacteria migrate to the site of injury and release the bacteria into traumatized bone which is more susceptible to infection. Of note, the patient presented in this report experienced trauma to the site of infection; however there was reportedly no break in the skin. Another point to consider in our case is the possibility that the localized infection was in part due to immune reconstitution inflammatory syndrome (IRIS). IRIS is a pathological inflammatory response seen in HIV patients that have an underlying OI when they begin HAART. The syndrome is in part due to the renewed effectiveness of the immune system against the underlying OI after receiving HAART, resulting in inflammation and localized findings. IRIS is seen in 15-25% of HIV patients within 3 months of HAART initiation.

NTM is a rare cause of osteomyelitis in patients with HIV infection. Some general features of these infections include a CD4 cell count <100/mm3, the involvement of several joints or skeletal sites, coexistent septic arthritis, and cutaneous lesions. Our patient did not have coexistent septic arthritis but did have two cutaneous lesions, one of which was confirmed to be due to MAC infection. These mycobacteria and endemic and a common history involves trauma or a puncture site. The definitive diagnosis of NTM osteomyelitis is dependent upon a bone biopsy with cultures and staining for mycobacteria. Blood cultures are often negative. Once diagnosed, a combination of surgical and antimicrobial therapy is required to completely eradicate the infection. Since effected bone in NTM osteomyelitis is poorly perfused and true sequestrum may exist, surgical debridement plays an important role. Any associated hardware should also be removed and sinus tracts should be excised. Standard treatment for MAI osteomyelitis involves a three-drug combination of clarithromycin (or another macrolide), rifabutin, and ethambutol for a 6 month course. It is important to actively monitor for signs of recurrent infection or
toxicities of the antibiotics. Of note, ethambutol-induced optic neuropathy and visual loss is estimated to occur in approximately 1% of patients and ophthalmology follow up should be arranged.\textsuperscript{3,4} If visual changes do occur, the ethambutol should be stopped immediately.

In summary, NTM osteomyelitis is a rare entity and is most likely to be found in patients who are immunocompromised, e.g., HIV/AIDS. Since the advent of HAART, it is rare to see DMAC but when patients present with advanced HIV/AIDS without previous treatment, it should be considered a diagnostic possibility. When treating patients with HIV and suspected osteomyelitis, the surgeon and the care team must maintain a high degree of suspicion and take careful mycobacterial cultures. These cases require a multidisciplinary approach to treatment including orthopaedic surgery, pathology, infectious diseases, primary care and ophthalmology.

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References