INTRODUCTION

*Mycobacterium (M.) fortuitum* belongs to the Runyon Group IV of rapidly growing mycobacteria (RGM). The rapidly growing mycobacteria are opportunistic pathogens producing diseases in a variety of clinical conditions. The three major clinically significant species of RGM in humans are *M. fortuitum*, *M. chelonae*, and *M. abscessus*. Being ubiquitous in nature, *M. fortuitum* has been isolated from various environmental sources like water, sewage, dust, soil and nosocomial sources.1,2 *M. fortuitum* has been established to cause opportunistic disseminated infections especially in patients with weakened or impaired cellular immunity or on immunosuppressive therapy.3 It is mainly responsible for causing skin and soft tissue infections, wound infections following trauma and surgery, arthritis, keratitis, osteomyelitis, hepatitis and in some cases meningitis, mostly in immunocompromised patients.4 However, it can also cause infections in healthy individuals. It has been isolated from urine in otherwise healthy immunocompetent hosts with no anatomical and functional abnormalities.5

To the best of our knowledge, this is the first case report of bone marrow infection with *M. fortuitum* in an immunocompetent patient with only added finding of precaval lymph node enlargement on computed tomography (CT) scan.

ABSTRACT

Incidence and prevalence of *Mycobacterium fortuitum* infection vary greatly by location and death is very rare except in disseminated disease in immunocompromised individuals. We present what we believe is the first case of bone marrow infection with *Mycobacterium fortuitum* in an HIV negative patient. Bone marrow examination revealed presence of numerous acid fast bacilli which were confirmed as *Mycobacterium fortuitum* on culture and by molecular analysis. Patient was managed successfully with amikacin and ciprofloxacin.

Key words: *Mycobacterium fortuitum*. Diabetes. Bone marrow infection. Amikacin. Ciprofloxacin.

CASE REPORT

A 52-year-old male was admitted to tertiary care hospital with one month history of intermittent high grade fever mostly occurring in the evening hours. The fever was associated with generalized body aches and night sweats. He took few courses of antibiotics from a local clinic, but his fever did not settle. There was no history of cough, joint pains, rash, trauma, surgical intervention, urinary and bowel complaints. He was a known diabetic and was taking oral hypoglycemic drugs for the last seven years irregularly.

His physical examination revealed a temperature of 101°F with normal systemic examination and no evidence of rash or enlarged lymph nodes. Laboratory findings demonstrated a haemoglobin level of 11.8 g/dL, plasma glucose 164 mg/dL, HbA1C 8%, a platelet count of 262 x 10^9/L and white cell count of 9.16 x 10^9/L. C-reactive protein was 64 mg/L and erythrocyte sedimentation rate was 115 mm/1st hour. Urine examination showed sugar (++) with no hematuria, pyuria or proteinuria. Liver function and renal function tests were within normal limits. Thick and thin blood smears did not show any malarial parasite and serology for syphilis and human immunodeficiency virus was negative. Chest X-ray was normal and ultrasound abdomen done on second day showed enlarged paracaval lymph nodes. Computed tomography (CT) scan abdomen showed a precaval lymph node enlargement (Figure 1 a,b). Keeping in view the possibility of enteric fever which is endemic in our areas, he was empirically started with injection ceftriaxone 1gm I/V x twice daily. The patient did not respond so a bone marrow examination was done and the aspirate was sent for culture and hematological examination. Ziehl-Neelsen (ZN) stain of the bone marrow smear showed numerous acid fast bacilli (AFB) with a mycobacterial index of (4+) per high power field (HPF).

Bone Marrow Infection with *Mycobacterium Fortuitum* in a Diabetic Patient

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Injection of ceftriaxone was discontinued and he was started on antituberculous treatment (with 600 mg oral rifampin and 300 mg oral isoniazid once daily) pending identification and sensitivity results. Bone marrow specimen was digested and decontaminated according to standard Centers for Disease Control (CDC) methods. Sodium hydroxide and N-acetyl-L-cysteine (NaOH/NALC) method was used for processing with final concentrations of 2% for NaOH. Concentrated specimen was inoculated on Lowenstein Jensen (LJ) medium, automated MGIT 960 system, Middle Brook 7H11 thin layer agar (TLA) medium plain as well as with para-nitrobenzoic acid (PNB). Microcolonies with smooth appearance and rounded margins were seen under the microscope on third day both on plain TLA 7H11 medium as well as with PNB (Figure 2 a, b). On the sixth day, visible non-pigmented colonies were seen on LJ medium. MGIT 960 system did not yield any growth up to 6 weeks of incubation protocol. Keeping in mind the possibility of a rapid grower, the isolate was subsampled on Blood agar and MacConkey which revealed the growth of acid fast bacilli. The isolate was confirmed as *M. fortuitum* by Speed-oligo Mycobacteria PCR (Vircell, Spain).

Antimicrobial sensitivity testing was performed on Mueller-Hinton agar by using E-test method and the organism was found sensitive to ciprofloxacin (minimum inhibitory concentration [MIC] 0.064 μg/ml), amikacin (MIC 0.75 μg/ml), clarithromycin (MIC 0.19 μg/ml) and resistant to isoniazid (MIC > 6 μg/ml) and rifampin (MIC > 32 μg/ml). The treatment was changed accordingly to intravenous amikacin (500 mg once daily) and oral ciprofloxacin (500 mg twice daily). Within three days, his fever started settling and he gained about 6.6 lbs of weight in one month. Amikacin was discontinued after one month and ciprofloxacin was continued for three months. Repeat CT scan abdomen after two months did not reveal any enlarged lymph node. However, the patient denied repeat bone marrow examination. The patient remained asymptomatic and afebrile during the follow-up.

**DISCUSSION**

Bone marrow infection with *M. fortuitum* in an immunocompetent host has not been reported till today. *M. fortuitum* can cause disease both in immunocompetent as well as in immunocompromised hosts. The disease presentation is variable and in almost all the cases, culture and biochemical tests are confirmatory for diagnosis. Multiple case reports of infection with *M. fortuitum* have been reported after surgical procedures, subcutaneous injections, pedicures, use of contaminated whirlpool footbaths, and with laparoscopic gastric banding.

*M. fortuitum* can be confused with Nocardia species on staining, thus leading to a delay in appropriate therapy and its detection can be a problem in conditions where the bacilli are scanty. In this case, however, visualization of AFB in bone marrow smear was not a problem as the smear had numerous AFB per high power field. For culture of mycobacteria, a combination of solid medium and one broth-based system such as MGIT 960 is widely accepted as gold standard. In this case, culture on MGIT 960 system was negative which may be due to the fact that this system is not suitable for culture of blood and bone marrow specimens. Initially, on positive ZN stained smear of bone marrow, conventional first line therapy for *Mycobacterium tuberculosis* was started, but after sensitivity testing, both the first line drugs that is isoniazid and rifampicin were found to be resistant. This highlights the importance of accurate identification and prompt sensitivity testing of rapidly growing mycobacteria as the first line anti-tuberculous drugs are less effective in infections with these mycobacteria. The isolates of *M. fortuitum* are generally susceptible to amikacin, and quinolones as was in this case.

This case is unique in a sense that the patient presented with fever, but had no significant findings on physical, radiological, and biochemical examination. The only positive finding before the detection of acid fast bacilli on bone marrow smear and later on identification on culture and molecular assay was enlargement of precaval lymph node on CT scan abdomen. We could not trace the primary focus of infection from where the organism disseminated to the bone marrow. The patient had no pulmonary symptoms, no history of trauma or surgery and was not immunocompromised. The only
possible answer could be that he might have had transient mycobacteremia at some stage of life with no apparent clinical signs and symptoms and the organisms got settled in the bone marrow. At that time due to good immune response, the body cleared the organisms from blood. But later on, due to weak immune response and might be due to uncontrolled diabetes, as he was not taking drugs regularly, the mycobacteria in the bone marrow got the chance to multiply and produce symptoms. However, the source of infection needs further explanation.

Primary bone marrow infection with *M. fortuitum* in a patient presenting with fever of unknown origin is a very rare presentation in an immunocompetent host. This case was presented because of its common presenting symptoms, but uncommon etiology. Although, infections with non-tuberculous mycobacteria are common in immunocompromised hosts due to the extensive use of immunosuppressive drugs and rapid spread of human immunodeficiency virus, there is also a surge in the isolation of these mycobacteria in healthy hosts in recent year. This signifies the importance of the use of recently introduced rapid diagnostic modalities such as 16S rRNA gene sequence analysis, nucleic acid amplification tests (NAAT) and use of gene probes. Nevertheless, acid fast staining, conventional culture techniques and biochemical tests are still widely used in many resource-poor countries in the diagnosis of non-tuberculous mycobacteria.

REFERENCES