**INTRODUCTION**

*Mycobacterium flavescens* is an unusual pathogen that, to our knowledge, has not been previously reported as a cause of vertebral osteomyelitis. We wish to report a rare case of vertebral osteomyelitis caused by *Mycobacterium flavescens* in a subject with apparent normal immune function, with a brief review of previous reports of human infection caused by this atypical mycobacterium. This case demonstrates that non-tuberculous mycobacteria (NTM) vertebral osteomyelitis can occur not only in immunosuppressed patients but also in immunocompetent patients. We have also reviewed the literature on vertebral disease due to rapidly growing mycobacteria.

**CASE REPORT**

A 70-year-old man with a history of severe chronic ischemic cardiopathy and diabetes mellitus was admitted to our hospital because of a 3-month history of fever, night sweats, fatigue, weight loss, and an increasing lower back pain and left-sided chest pain. On admission his body temperature was 38 °C. Examination of the joints revealed moderate signs of inflammatory activity in the thoracic spine that was tender to palpation. Results of laboratory tests included a leukocyte count of $89 \times 10^9/l$ with neutrophils 69% and lymphocytes 32%, C-reactive protein and albumin of 120 mg/l and 28 g/l, respectively, and an ESR of 35 mm/h. Screening for HIV, syphilis and Brucella were negative. Lymphocytes subset analysis was normal. A chest radiograph showed an infiltrate in the left upper lobe, and a CT scan of the thorax showed a small pleural-based lesion of 1-cm in diameter. Bronchoscopy with bronchoalveolar lavage (BAL) and repeated CT-guided biopsies were non-diagnostic. Abdominal ultrasonography revealed no hepatosplenic lesion. Radiograph of the spine disclosed sclerosis and wedge-shaped deformities of TH 10, TH 11 and TH 12. MRI showed massive spondylodiscitis of TH10/12, with paraspinal and intraspinal abscess formation. Neurologic symptoms were absent. A purified protein derivative skin test was negative. A bone debridement and a diagnostic bone biopsy were performed. Gram staining of the purulent material from the vertebral lesion showed no microorganisms, while acid fast stain revealed acid-fast bacteria. Therapy with isoniazid, rifampin, and streptomycin was initiated for suspected vertebral tuberculous osteomyelitis (Pott’s disease). After two consecutive months of treatment, the patient continued to experience low fever, lumbar pain, night sweats, and fatigue. Mycobacterial blood and bone cultures drawn on admission proved positive for *Mycobacterium flavescens*. This organism was susceptible to streptomycin and rifampin, and it was resistant to ethambutol and isoniazid. Therapy was changed to rifampin, ciprofloxacin and ethambutol, and the patient improved rapidly. Therapy was well tolerated for 13 months and he completely recovered.

**DISCUSSION**

Mycobacterial diseases cause substantial morbidity and mortality throughout the world, and
in recent years diseases caused by emergence of rapidly growing mycobacteria have been reported from both developing and industrialized countries. Although most diseases due to pathogenic mycobacteria are caused by Mycobacterium tuberculosis, the rates of infections caused by NTM are increasingly reported in both healthy and immunocompromised patients in the last decades.

NTM are ubiquitous organisms in our environment, ranging from harmless inhabitants of aquatic reservoirs and soil to species pathogenic to man and animals; in addition, NTM may also contaminate microbiological specimens [1]. In recent years it has come to be appreciated that nosocomial transmission of these organisms is increasing [1]. More than 65 different species have been recognized, but many of the NTM are isolated as laboratory contaminants or colonizers, and infrequently as true pathogens. Indeed, only a handful of NMT are usually associated with diseases in clinical practice in humans.

It has been reported that among the most common risk factors associated with disease due to NTM are smoking, chronic lung disease, HIV infection, alcoholism, and less often immunosuppressive therapy, malignancy, connective tissue disease, previous Mycobacterium tuberculosis infection, leprosy, and diabetes [1-3]. NTM have been categorized into different groups based on characteristic colony morphology, growth rate, and pigmentation; growth rates have remained a practical means for grouping species within the laboratory [1-3]. The rapidly growing mycobacteria include eight taxonomic groups of non-pigmented and pigmented organisms, also known as Runyon group IV; these organisms exhibit growth in < 7 days under optimal conditions in agar plates. The most common disease associated with these organisms is cutaneous disease associated with a penetrating wound or foreign body, but nosocomial infections can also occur [1-3]. Rapidly growing mycobacteria may also be associated with respiratory tract colonization or infection and surgical infections, while they are only occasionally associated with infections related to hemodialysis, peritonitis in patients undergoing peritoneal dialysis, injection-associated cutaneous and joint infections, and intravascular catheter infections [1-3]. These pathogens are rarely transmitted by human-to-human contact and are resistant to common antituberculosis drugs.

The diagnosis of infection due to rapidly growing mycobacteria requires appropriate tissue specimens to be obtained. Among the rapidly growing mycobacteria found in abundance in the environment, strains associated with human disease are more frequently restricted to Mycobacterium fortuitum, Mycobacterium chelonae and Mycobacterium abscessus [1-3]. In addition, there are several saprophytic species of rapid growers documented as occasional etiological agents of disease, including Mycobacterium phlei, Mycobacterium aurum, Mycobacterium neoaurum, Mycobacterium flavescent, Mycobacterium vaccae, and the thermophilic species Mycobacterium thermoresistibile [1-3].

Extrapulmonary disease caused by NTM has a broad spectrum of clinical manifestations referable to almost any organ system, although the spine is rarely affected. NTM infections of the bones may occur following surgical procedures, trauma, penetrating injuries or following the injection of steroids. NTM osteomyelitis may be a complication of skin and soft tissue infections most frequently associated with a history of penetrating injury or surgery. Moreover, extrapulmonary tuberculosis due to NTM with involvement of the spine remains an uncommon entity. The rarity of this condition was emphasized in recent articles [4, 5].

Through an extensive literature search by means of MEDLINE consultation, we have identified only 20 cases of atypical mycobacteria vertebral osteomyelitis reported in the current English literature from 1955 to 2001 [4-7]. The study population consisted of 10 men and 10 women with a mean age of 47 years (range 16-79). Of these cases, 5 were due to Mycobacterium xenopi, 4 were due to Mycobacterium avium-intracellulare, 4 were due to Mycobacterium fortuitum, 3 were due to Mycobacterium abscessus, and the remaining episodes were due to Mycobacterium simiae, Mycobacterium kansasi, Mycobacterium bovis BCG and an atypical, non-classified, mycobacterium.

Vertebral infection caused by NTM involves the anterior inferior portion of the vertebral body, is adjacent to an intervertebral disk, and spreads under the anterior longitudinal ligament to involve the adjacent vertebrae, as described for vertebral osteomyelitis due to Mycobacterium tuberculosis.

The most common clinical predisposing events preceding the diagnosis of vertebral os-
With chronic granulomatous disease [8-10]. This was the first report of Mycobacterium flavescens disseminated infection. M. flavescens was also cultured from the CSF of 4 patients with atypical clinical and CSF profiles [11]. In a trial performed to test the efficacy of BCG vaccination in the prevention of tuberculosis in the Chingleput district of Madras state, South India, NTM were obtained from 8.6% of 16,907 sputum specimens; the species isolated most frequently were Mycobacterium avium, Mycobacterium terrae and Mycobacterium scrofulaceum, while those species accounting for 8-5% of all NTM were Mycobacterium fortuitum, Mycobacterium chelonae, Mycobacterium gordonae, Mycobacterium vaccae and Mycobacterium flavescens [12]. The detection of M. flavescens from a variety of clinical specimens obtained from patients with HIV infection has also been described in a few reports [13-15].

The results of a retrospective survey concerning atypical cutaneous mycobacterioses contracted from aquariums, swimming pools and as a result of mesotherapy, showed that the pathogens most commonly identified among the 92 cases observed included Mycobacterium marinum, Mycobacterium chelonae and Mycobacterium avium-intracellulare, while Mycobacterium flavescens was rarely identified [9]. M. flavescens has been isolated from tuberculosis lesion found in buffaloes examined during routine post-mortem inspection at 2 export abattoirs in Australia [16]. Moreover, M. flavescens and other NTM were isolated from raw milk in several studies [17, 18]. In a study investigating the prevalence of environmental mycobacteria in drinking water supply systems in a demarcated region in Czech republic Mycobacterium gordonae and Mycobacterium flavescens were the most common cultured and identified species [19].

Biofilms are an important habitat and site for proliferation of aquatic mycobacteria, including M. flavescens. Biofilms may account for the problem of controlling mycobacterial contamination of water distribution systems by means of chemical disinfection [20]. M. flavescens has also been identified in biofilm samples from the waterlines of dental units [21]. Mycobacterial proliferation in biofilms forming within dental units may explain the extent of NTM contamination of dental spray and cooling water.
In summary, our study has stressed the importance of recent reports that have described the occurrence of vertebral osteomyelitis due to non-tuberculous mycobacteria, recognized with an increasing incidence among immunocompetent hosts.

Management of vertebral osteomyelitis due to NTM infection often requires both surgical débridement and drug therapy. The best treatment for infections due to rapidly growing mycobacteria is controversial; however, patients may respond well to an appropriate treatment, in cases of non-visceral associated disease due to NTM. Designing the ideal therapeutic regimen for rapidly growing NTM infections is complicated by their frequent resistance to common antituberculous drugs. Thus, therapy with more than one drug should be employed to increase efficacy and avoid the development of resistance; the best regimen used is influenced by the results of susceptibility studies on the species identified and the underlying medical conditions of the patient being treated.

Chemotherapeutic regimens for joint and bone disease must be prolonged with the use of multiple drugs with a regular monitoring of potential side effects.

SUMMARY

The aim of this paper is to describe a rare case of vertebral osteomyelitis caused by Mycobacterium flavescens in an immunocompetent patient. Mycobacterium flavescens is a rapidly growing, pigmented, non-tuberculous mycobacterium, usually described as non-pathogenic for humans but occasionally reported as the cause of serious infectious complications recognized in clinical practice. This study stressed the importance of recent reports that describe the occurrence of vertebral osteomyelitis due to non-tuberculous mycobacteria that have also been recognized with an increasing incidence among immunocompetent hosts. A brief review of the current literature on human disease caused by Mycobacterium flavescens is also reported.

RIASSUNTO

L’obiettivo dell’articolo è quello di descrivere un raro caso di osteomielite vertebrale causato da Mycobacterium flavescens in un paziente immunocompetente. Mycobacterium flavescens è un micobatterio non-tubercolare, incluso nel gruppo dei micobatteri a crescita rapida, pigmentato, usualmente non patogeno per l’uomo ma occasionalmente responsabile di infezioni gravi diagnosticate nella pratica clinica. Lo studio riportato ha stressato l’importanza delle recenti descrizioni di casi di osteomielite da micobatteri non-tubercolari descritti in maniera crescente anche in ospiti immunocompetenti. L’analisi si completa di una breve rassegna sui casi di complicanze infettive da Mycobacterium flavescens riportate in letteratura.

REFERENCES

[7] Kulasegaram R., Richardson D., Macarae B., de Ruiter A. Mycobacterium xenopi osteomyelitis in a pa-


