Respiratory Medicine Case Reports 21 (2017) 71–73

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

A *M. avium* complex spondylodiscitis in a middle-aged woman with diabetes

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ARTICLE INFO

Article history:
Received 17 December 2016
Accepted 21 March 2017

Keywords:
Spondylodiscitis
M. avium complex
Bone marrow

ABSTRACT

Spondylodiscitis, the inflammation of the vertebral bodies and the intervertebral disk space, is the reason for low back pain in a minority of cases. This is caused by various pathogens. *Mycobacterium tuberculosis* is responsible for 17–39% of all the cases of spondylodiscitis. On the contrast, spondylodiscitis from *non tuberculous* mycobacteria is extremely rare in literature. We describe a 68 -year old diabetic woman which is the first case of bone marrow involvement by *M. intracellulare* (member of *M avium* complex) with spondylodiscitis.

1. Introduction

Low back pain is one of the main causes of medical consultations and the fifth most common reason of all physician visits in the USA. The lifetime prevalence of spinal pain has been estimated at as high as 54%–80% of population and its frequency raises with age. This most common form of this pain is mainly associated with mechanical and degenerational changes of various spinal structures. In a minority of cases the back pain may be a symptom of a severe disorder, the spondylodiscitis which is the inflammation of the vertebral bodies and the intervertebral disk space, caused by various pathogens. Its incidence is estimated at 0.4–2.4/100000 [1]. The most common pathogens are *Staphylococcus aureus, Escerichia coli, Proteus, Klebsiella, Pseudomonas aeruginosa, Mycobacterium tuberculosis* (which is reported to cause 17–39% of all the cases of spondylodiscitis) [2]. On the contrast, non tuberculous mycobacteria seldom cause extrapulmonary disease and particularly spondylodiscitis is extremely rare in literature.

2. Case report

A 68 -year old woman was admitted to an orthopedic department for intense backpain. One year ago she had undergone two epidural infiltrations with good results. Two months prior to admission she had experienced a recurrence of acute debilitating thoracic backpain, so she was hospitalized for further evaluation by magnetic resonance imaging (MRI) of the thoraco-lumbar spine and further investigations. Her medical history included type I diabetes mellitus for the last 42 years. The patient denied fever or weight loss over the previous months. She also denied symptoms of pulmonary disease such as cough, sputum, dyspnoea, haemoptysis or pleural pain.

On physical examination her temprerature was 36.8 °C, blood pressure 120/80 mm/Hg, heart rate 90/min. Palpation of the thoracic spine was painful. Peripheral reflexes were unaffected and there was no neurological deficit. Laboratory findings were hemoglobin 11.5, white blood cells (WBC) 4.100/mm^3 with segmented 57% neutrophils; platelets 188.000/mm [3]. Erythrocyte sedimentation rate (ESR) was 50mm/h; C-reactive protein (CRP) 0,7mg/dl, normal renal and liver function tests. She was negative for human immune deficiency viral infection (HIV).

MRI of the thoraco-lumbar spine was done. The sagittal T1-weighted post gadolinium image with fat suppression showed enhancement of the vertebral bodies (Th5-Th8) with relative preservation of the intervertebral discs. There was also some anterior subligamentous enhancement indicative of soft tissue mass. The axial T1-weighted post gadolinium image with fat suppression confirmed the presence of paraspinal enhancing soft

Abbreviations: MAC, *M avium* complex.

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http://dx.doi.org/10.1016/j.rmcr.2017.03.020

tissue mass(Fig. 1). Chest radiograph and HRCT scan showed nodules involving upper lobes, right middle lobe and the lingula(Fig. 2). Respiratory specimens obtained by bronchoscopy were negative for malignant cells. Moreover, cultures of bronchial washings for common pathogens and mycobacterium grew no organisms.

Despite apyrexia, urine and blood cultures were sent on arrival but yielded negative results, as well as serological testing for Coxiella burnetti, and Brucella spp. Computed tomography guided vertebral and disc biopsy for bacteriological and histological analysis was tried but was incomplete as the patient was uncomfortable during the process.

Bone marrow aspiration/biopsy was sent for microbiologic and histologic-pathologic examination. In the microbiological laboratory, bone marrow aspirate was firstly tested by Ziehl-Neelsen (ZN) staining and then, was inoculated onto Löwenstein-Jensen slants (LJ, bioMérieux, Marcy l'Etoile, France) andBactec/9000MB culture vials (Becton Dickinson).

After 10days of incubation BACTEC culture showed growth of an acid-fast bacterium, that was identified as *M. intracellulare* (member of *M. avium* complex)by a reverse line blot hybridization (RLBH) assay (GenoTypeMycobacteriumCM/AS; Hain Lifescience GmbH, Nehren, Germany). Histopathologic examination revealed histiocytes with no caseating necrosis.

The patient was treated with azithromycin, rifampicin, ethambutol and streptomycin for the first two months and started feeling better three months later.

3. Discussion

M avium complex or MAC includes at least two mycobacterial species, *M. avium* and *M. intracellulare*. These two species cannot be differentiated on the basis of traditional physical and biochemical tests. There are specific DNA probes for identification of and differentiation between *M. avium* and *M. intracellulare*.

MAC organisms are commonly in many environmental sites, including water and soil, and in animals. MAC has been found to colonize natural water sources, indoor water systems, pools and hot tubs. It is generally believed that environmental sources, especially natural waters, are the reservoir for most human infections caused by MAC. Aerosols of fresh-and salt water may contain MAC, and these have also been proposed as vehicles leading to transmission of MAC respiratory disease [3]. The most frequent clinical expression is the disseminated disease in subjects with compromised cellular immunity and the respiratory disease.

Disseminated MAC occurs largely in patients with AIDS. This manifestation of MAC disease was extremely rare before 1980 but rose to an estimated 37000 cases in the United States in 1997. The incidence of disseminated has declined markedly since that time. Children with AIDS have rates of disseminated MAC similar to adults. Untreated disseminated MAC is a life-threatening illness. In the pre-antiretroviral era, of 191 patients with AIDS diagnosed with disseminated MAC, only 13% survived 1 year without treatment. Deaths in this group were attributable to both MAC and other complications of HIV [4].

The most common MAC respiratory presentation is apical fibrocavitary lung disease, sometimes with large cavities, in males in their late 40s and early 50s who have a history of cigarette smoking and frequently, excessive alcohol use. MAC lung disease also presents with nodular and interstitial nodular infiltrates involving the upper lobes, middle lobe or lingula, predominantly in postmenopausal, nonsmoking, white females. This form of disease, termed “nodular bronchiectasis ” or “nodular bronchiectatic disease” tends to have a slower progression than cavitary disease, such that long term follow up (months to years) may be necessary to demonstrate clinical or radiographic progression [5].

MAC lymphadenitis is underestimated in the United States because in many cases of lymphadenitis the specimens are not cultured or cultures fail to grow an organism [6]. MAC cervical adenitis is almost exclusively a disease of children, with most cases occurring in those under the age of 3 years. MAC lymphadenitis is also seen in HIV-infected persons, particularly as a manifestation of the immune reconstitution syndrome; cervical, mediastinal, or the

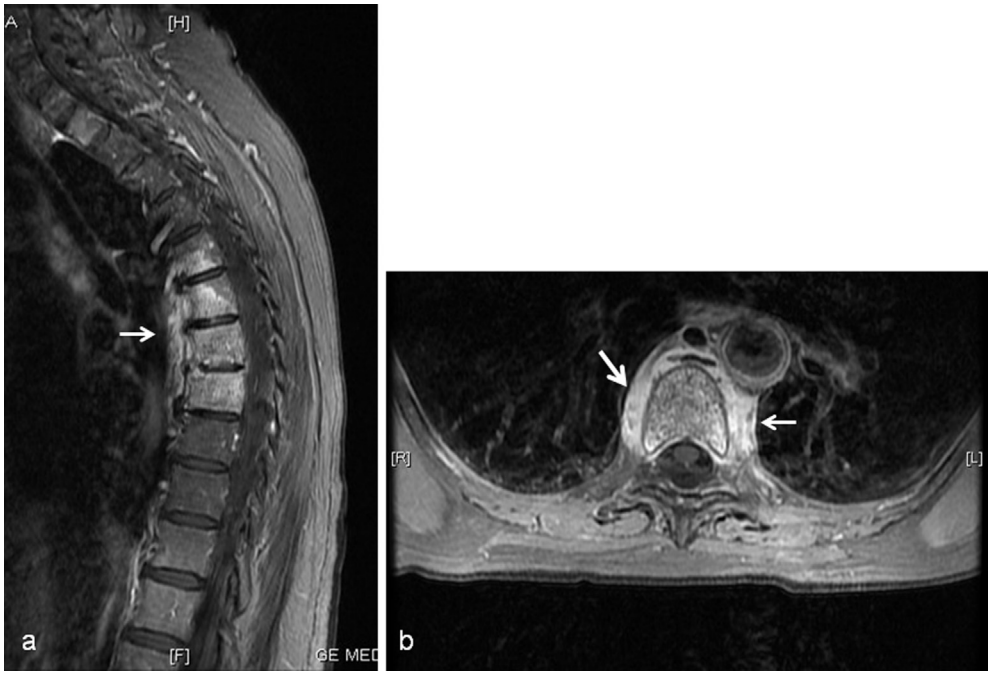

Fig. 1. MRI scan of the patient with thoracic spinal involvement. (a) Sagittal T1-weighted post gadolinium image with fat suppression shows enhancement of the vertebral bodies (Th5-Th8) with relative preservation of the intervertebral discs. There is also some anterior subligamentous enhancement indicative of soft tissue mass. (b) Axial T1-weighted post gadolinium image with fat suppression confirms the presence of paraspinal enhancing soft tissue mass.

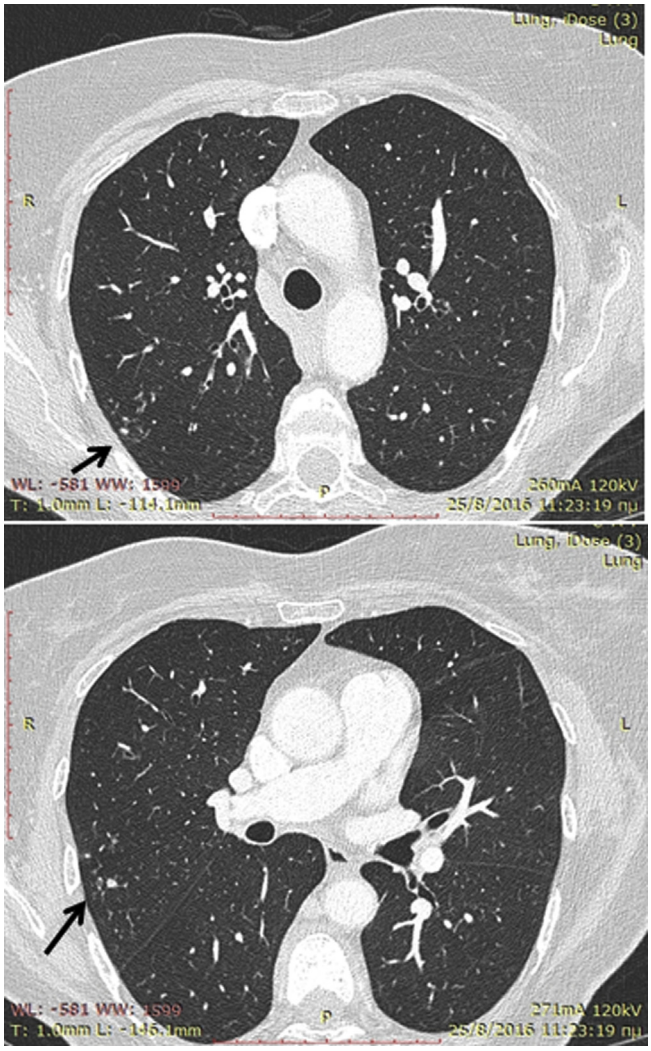

Fig. 2. CT findings of the patient with some nodules, most prominent at the posterior segment of the right upper lobe.

intraabdominal nodes may be involved [7,8].

In patients with atypical presentation, organ-specific symptoms occur at sites of the involvement. For adult patients with extrapulmonary, localized MAC disease involves skin, soft tissue, tendons, joints and occasionally bones. The diagnosis of MAC is confirmed by cultures.

Drug therapy for MAC lung disease involves multiple drugs; therefore the risk of adverse drug reactions and/or toxicities is relatively high. In addition, the optimal therapeutic regimen has yet to be established. For these reasons, the treatment of MAC disease may be accomplished by physicians experienced in the treatment of mycobacterial diseases. The cornerstones of MAC therapy are the macrolides, clarithromycin and azithromycin and ethambutol. These agents are then combined with companion drugs, usually a rifamycin and, possibly, an injectable aminoglycoside [9]. Multiple combinations of these drugs are possible, frequently dictated by the tolerance of the patient.

The recommended drug regimen for infections other than lung disease is the same as for MAC pulmonary disease including clarithromycin or azithromycin, ethambutol and rifampicin with or without streptomycin. The optimal duration of treatment is unknown but 6–12 months of chemotherapy is usually recommended [9].

Our case is intriguing for various reasons. The patient had no respiratory symptoms, bronchial washings of bronchoscopy were negative for MAC and the only predisposing immunocompromising factor was diabetes. In our knowledge this is the first case of bone marrow involvement by *M. intracellulare* (member of *M. avium* complex) with spondylodiscitis in a middle aged patient. Probably, it is essential to consider that M. *intracellulare* and other mycobacteria can infect almost any tissue or organ of the body in patients with diabetes mellitus. Bone marrow aspiration and/or biopsy including culture for non tuberculous mycobacteria may be considered for differential diagnosis in patients with spondylodiscitis.

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