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Case Report Open Access

A Case of Severe *Mycobacterium kansasii* Infection Complicated with the Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)

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Abstract

We present a case of severe *Mycobacterium kansasii* infection due to the clinical and radiological progression and complicated with syndrome of inappropriate antidiuretic hormone secretion (SIADH). This 54-year-old male alcoholic and heavy smoker as predisposing factors presented severe anorexia, asthenia and cachexia. Abundant acid-fast bacilli (AFB) were observed in the patient's sputum and pleural fluid after Ziehl-Neelsen (ZN) staining. The strain was identified as *M. kansasii* by culture. A treatment with isoniazid, pyrazinamide, ethambutol, clarithromycin and moxifloxacin were then initiated. The course of the illness includes impaired consciousness, behavioural disturbances and agitation; we believe was a consequence of SIADH, because of the severe hyponatremia with low serum osmolality condition. Also, generalized or local infections are important and unregarded causes of SIADH. Multiple infectious diseases are associated with this syndrome [1]. An awareness of this pathogen with clinical, radiologic, and microbiologic parameters are all needed to establish the diagnosis of this infection and the eradication of disease requires prolonged combination drug therapy.

Keywords: *Mycobacterium kansasii*; SIADH; Diagnose and course

Introduction

M. kansasii is a slow-growing acid-fast bacillus (AFB) and belongs to the group of environmental mycobacteria, also known as atypical mycobacteria or non-tuberculosis mycobacteria (NTM). *M. kansasii* is the most common cause of pulmonary non-tuberculosis mycobacterial infection in the non-human immunodeficiency virus-infected population in many parts of the world. Of all non-tuberculosis mycobacterial diseases, the clinical course of lung disease caused by *M. kansasii* is most closely related to *M. tuberculosis* infection. Large regional differences have been detected in the incidence of *M. kansasii* infection. In Spain, *M. kansasii* is the NTM that causes pulmonary disease most frequently; in some series, *M. kansasñ* caused up to 4% of all mycobacterial infections [2-4].

Recently, we encountered a rare case of severe *M. kansasii* lung infection involving both lungs and together with pleural effusion. His clinical course was complicated with syndrome of inappropriate antidiuretic hormone secretion (SIADH). To our knowledge, this is the first case of severe *M. kansasii* infection complicated with SIADH in non HIV-infected patients.

Case report

In March 2013, a fifty-four year old male with chronic alcohol abuse and smoking was admitted to our hospital because of asthenia, anorexia, significant loss of weight (15 kg), cachexia (41 kg), cough with expectoration and mild haemoptysis intermittently for more than 4 months and progressive dyspnea that had worsened gradually with minimal activity.

Initial laboratory tests showed anaemia with a Haemoglobin level of 8.7 g/dl, leucocyte count 23,900 µl, platelet count 18,000 µl, C-reactive protein level 29,84 mg/dl, hyponatremia 123/62 mmol/L (serum/urinary sodium), plasma osmolality 254 mOsm/kg and vasopressin (ADH)<1.2 pg/ml.

Chest X-ray and CT scan showed two cavitation lesions: in the right upper lobe, branching lesions tree-in-bud appearance through hemithorax suggesting endobronchial spread along nearby airways resulting in pseudonodular consolidations. In the left lung, destructive changes with volume loss secondary to pleural effusion with a tendency to encapsulation throughout the hemithorax, high cavitations in upper lobe, bronchiectasis and consolidations in lower lobe. Numerous lymphadenopathies measuring about 1 cm in diameter were detected in the following localizations: subpleural, left paravertebral, upper left paratracheal, paraaotic, subaortic, hiliar, and subcarinal (Figures 1 and 2).

Ultrasound-guided thoracentesis was realized to remove 0.5 ml of a macroscopically pleural empyema.

Specimens were sent and processed in our laboratory of Microbiology in the Hospital of Basurto. The samples (sputum and pleural fluid) were tested for the presence of mycobacterium species. Each smear (direct from untreated specimen and from concentrated deposit) was prepared on a glass slide in a drop of formalin taking proper precautions, dried and heat fixed and then stained with Ziehl-Neelsen (ZN) method. Then, samples were decontaminated with N-acetyl-l-cysteine–sodium hydroxide (Mycoprep; BD) and cultivated for mycobacterium; including liquid media broth systems that is the non-radiometric mycobacteria growth indicator tube (MGIT) BD BACTECTM MGITTM 960, which contains a modified Middlebrook 7H9 broth in conjunction with a fluorescence quenching–based oxygen sensor to detect mycobacterial growth. Solid media broth

include either egg based-media, such as Löwenstein-Jensen agar media such as Middlebrook 7H10 and 7H11 media. Both broths are used for the detection and enhancement of mycobacterial growth.

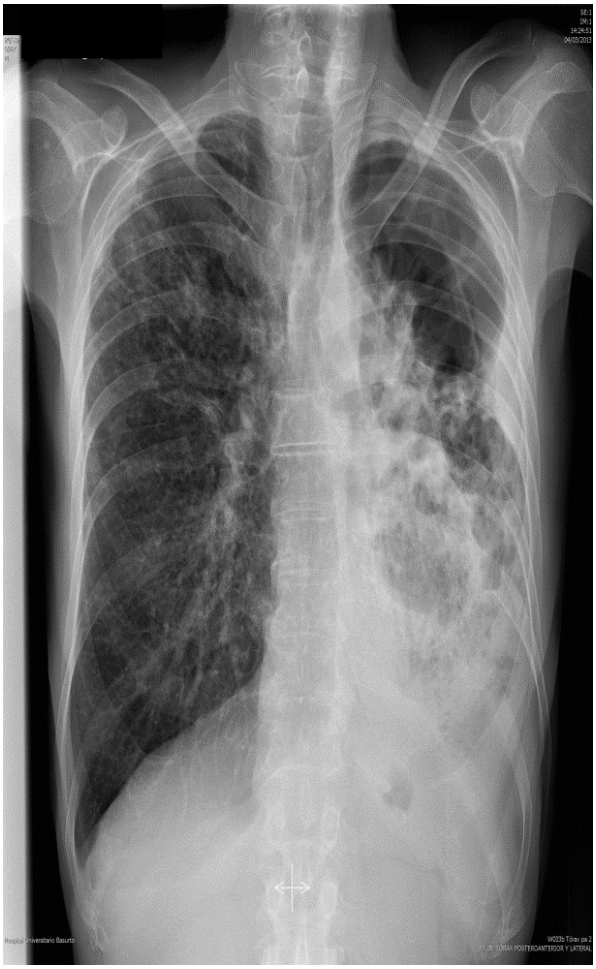

Figure 1: Posteroanterior chest X-ray.

Abundant AFB was observed in the patient's sputum and pleural fluid after ZN staining. The strain was identified as *M. kansasii* by commercially available DNA probe (Accuprobe *M. kansasii* culture identification test; Gen-Probe-BioMérieux) and INNO-LIPA MYCOBACTERIA (Innogenetics, Ghent, Belgium). Drug susceptibility testing (DST) was performed using BACTEC MGIT 960 SIREP; Becton Dickinson to first-line drugs, including streptomycin, isoniazid, rifampin, ethambutol, and pyrazinamide. *M. kansasii* organism showed resistance to isoniazid and pyrazinamide at 1 mcg/ml as expected.

Before having the diagnosis of *M. kansasii* treatment was empirical with isoniazid, rifampicin and pyrazinamide suspecting infection by *M. tuberculosis*, but in this context the patient developed jaundice (total bilirubin 6.80 mg/dl); so rifampicin was suspended and replaced by streptomycin and ethambutol. Fortunately he was recovered of cholestasis within few days. After microbiological confirmation of the isolation of *M. kansasii* in Lowenstein-ensen medium, pyrazinamide was retired adding moxifloxacin. Then after two months of treatment with streptomycin, it was changed by clarithromycin.

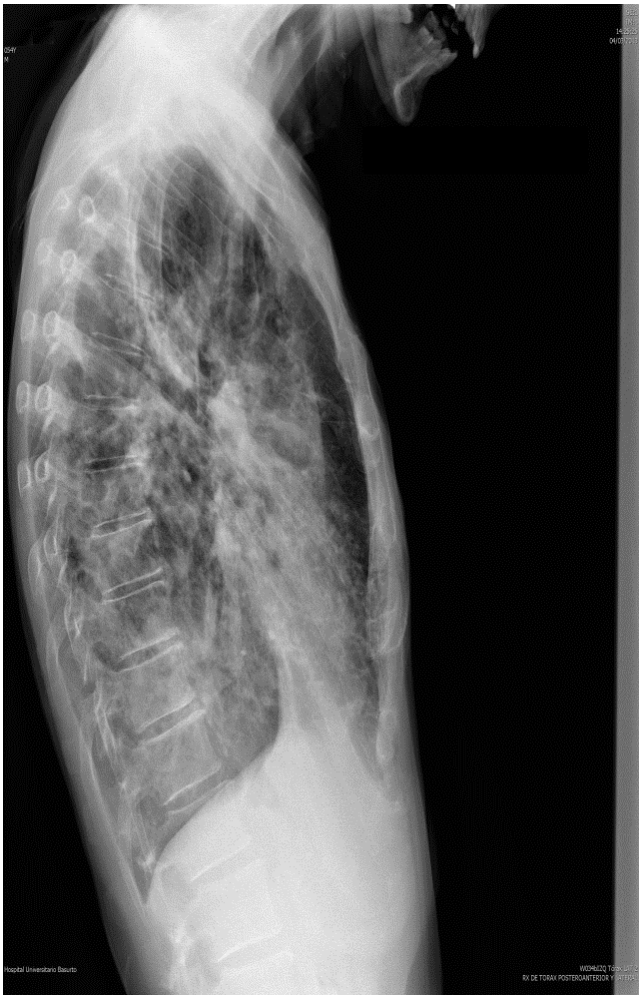

Figure 2: Lateral chest X-ray.

After having three negative cultures (results after 3 months and a half of treatment) moxifloxacin was suspended continuing with clarithromycin, isoniazid and ethambutol. This treatment was continued for 12 months.

During the course of the disease, the patient develops severe hyponatremia (117 mmol/L), with impaired consciousness, behavioural disturbances and agitation. But cerebral organic pathology was ruled out (by cerebral CT). Therefore, we believed that this hyponatremia was a consequence of SIADH and established upon the exclusion of other hyponatremia etiology, as a complication of *M. kansasii* pulmonary infection. Over time, the patient improved clinically his respiratory symptoms. Currently weighs 58 kg. Radiological monitoring showed residual lesions some of them with a small air-fluid level (Figure 3).

Discussion

Between 1993-1998 years, there had been an increase in the number of patients with disease caused by *M. kansasii* in the province of Bizkaia, (Basque Country, Spain) 407 cases in 1995, 512 in 1996, 428 in 1997 and 363 in 1998 . The disease was more frequent in male patients,

individuals who were HIV negative, and in urban areas. Nowadays, although *M. kansasii* is the second mycobacteria isolated in Bizkaia after *M. tuberculosis*, the number of isolations has decreased very significantly [2-4].

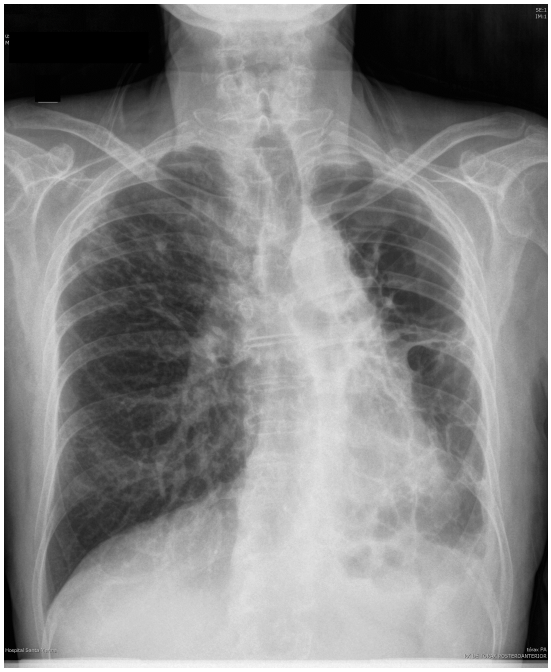

Figure 3: Post Treatment chest X-ray.

The natural reservoirs of non-primary pathogenic mycobacteria include aquatic and terrestrial environments. Predisposing factors have been identified. These include (i) reduced immune competence as a result of human immunodeficiency virus (HIV) infection, cancer, chemotherapy, or immunosuppression associated with transplantation; (ii) pre-existing lung disease, including chronic obstructive pulmonary disease (COPD), pneumoconiosis and silicosis, and prior tuberculosis; (iii) altered chest architecture; (iv) alcoholism, (v) smoking (vi) mutations in either the cystic fibrosis trans membrane conductance regulator or the a-1-antitrypsin gene and (vii) elderly slender individuals may cause disease. Biofilm formation, amoeba-associated lifestyle, and resistance to chlorine are been recognized, as important factors that contribute to the survival, colonization and persistence of environmental mycobacteria in water distribution systems [5,6].

In agreement with previously established predisposing factors, our patient's risk factors were alcoholism and tabaquism without pre-existing lung disease. We do not know about if he had exposure to tap water.

In most cases, *M. kansasii* causes lung disease that is clinically indistinguishable from tuberculosis. Symptoms may be less severe and more chronic than M. tuberculosis infection. In healthy host, the most common symptoms of pulmonary *M. kansasii* infection include cough (91%), sputum production (85%), weight loss (53%), breathlessness (51%), chest pain (34%), hemoptysis (32%), and fever or sweats (17%) [7]. Cough, sweating, and fever were more common in patients with pulmonary tuberculosis, and chest pain was more common in patients with lung infection. In our patient it should be emphasized that anorexia, asthenia and cachexia are the mainly symptoms. Lung affectation was so important that dyspnea was severe. He did not complain about chest pain, symptom more common in patients with *M. kansasii* related by authors as distinctive feature of *M. tuberculosis* infected patients.

The radiographic features of pulmonary infections caused by *M. kansasii* have been reviewed by several authors. *M. kansasii* pulmonary infection has been described as a right-sided, apical or subapical, thin-walled cavitary infiltrate, and frequently unilateral infection. Pleural effusions and air space shadowing involving multiple bronchopulmonary segments were less common in *M. kansasii* infection than *M. tuberculosis* infection [8-9]. On the other hand, our patient's radiological features were the greater involvement of the lower lobe, empyema and multiple bilateral lymphadenopathies. These radiographic findings made *M. kansasii* infection very unlikely in the first instance, although gram-positive moderately long-to-long rods were seen in the stain and identified as bacillis gram-positive, that guided us to a presumptive identification of *M. kansasii* infection.

SIADH is the most common cause of euvolemic hyponatremia. It can be caused by many clinical conditions, including malignancy, pulmonary disorders, central nervous system disorders, infections, and drugs. We reviewed the literature written in English and available in abstract or full text form, that reported SIADH with pulmonary tuberculosis infection. There were reports that have associated SIADH with severe types of tuberculosis such as military tuberculosis, tuberculosis meningitis, and pulmonary tuberculosis with massive bacterial excretion and hyponatremia secondary to lung disease caused by *M. kansasii* is not exceptional, like it seems to be the full development of the syndrome with neurological symptoms, as it happened in this patient.

The 2007 ATS/IDSA guidelines for non-tuberculosis mycobacterial (NTM) infections recommended rifampin plus ethambutol plus isoniazid for treatment of *M. kansasii* infection with the treatment duration until sputum culture results is negative for 12 months. Alternative regimens include clarithromycin or azithromycin, moxifloxacin, sulfamethoxazole, or streptomycin. More recently in vitro data for *M. kansasii* suggest increasing resistance to fluoroquinolones, including ciprofloxacin and moxifloxacin (30% and 40% resistance, respectively). However, clarithromycin remains active against *M. kansasii*, with 100% of isolates displaying susceptibility in vitro. Because of cholestasis caused by rifampicin the classical regimens of *M. kansasii* treatment was changed and two antibiotics more, clarithromycin and moxifloxacin were added for the severe infection. Close clinical follow-up was carried out until full recovery.

In conclusion our case emphasizes that although there is no defining criteria for severe infection by *M. kansasii*, we considered it as severe as, *M. tuberculosis*, because of the rapid clinical, radiological and bacteriologic progression in lungs and pleura; sometimes in non-HIV patients, and complicated with SIADH. Special attention to stain morphology for presumptive identification and cultivation for definitive identification must be made to initiate appropriate treatment promptly.

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