Case Report

Pleural effusion caused by nontuberculous mycobacteria*

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ABSTRACT

Mycobacterium kansasii, a nontuberculous mycobacterium, can cause pulmonary disease presenting clinical and radiological similarities to tuberculosis. *M. kansasii* infection has been associated with risk factors such as bronchiectasis, chronic obstructive pulmonary disease, tuberculosis sequelae, pneumoconiosis and immunosuppression. Herein, we describe a case of pleural effusion in a 67-year-old patient with chronic obstructive pulmonary disease and a history of pulmonary tuberculosis. The histological analysis demonstrated a granulomatous chronic process and acid-fast bacilli positivity, suggesting a diagnosis of pleural tuberculosis. *M. kansasii* was detected both in pleural fluid cultures and in cultures of tissue samples. We discuss the differential etiologic diagnosis with other infectious agents of granulomatous diseases, and we address treatment options.

Keywords: *Mycobacterium kansasii*; Mycobacterium infections; Pleural effusion; Case reports

INTRODUCTION

Mycobacterium kansasii belongs to a group of microorganisms known as nontuberculous mycobacteria (NTM). It is an acid-fast bacillus recognized by its photochromogenic nature (it produces a yellow pigment upon exposure to light) and its slow growth (two to four weeks). It has been identified as the second leading cause of pulmonary NTM disease, the leading cause being the Mycobacterium avium complex.[1]

Unlike other NTM that normally inhabit the environment, M. kansasii is not found in natural waters or in the soil, although it has been isolated in reservoirs and water pipelines. It is considered the most virulent of the mycobacteria known to cause diseases, and it occasionally becomes a colonizing agent. Transmission may occur via inhalation, aspiration of gastric residue or skin infection. In the lung, this mycobacterium may trigger a disease that is clinically and radiologically similar to tuberculosis. The disease mainly occurs

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in immunosuppressed individuals such as patients submitted to transplants, patients with lymphoproliferative disorders or individuals infected with human immunodeficiency virus. In other patients, it is frequently associated with chronic obstructive pulmonary disease, pneumoconiosis, bronchiectasis, and esophageal disease accompanied by chronic aspiration of esophageal secretions, as well as with a history of tuberculosis.[2-3]

Herein, we describe the case of a patient with chronic obstructive pulmonary disease and a history of tuberculosis who presented pleural effusion caused by M. kansasii. We discuss the differential diagnosis with other infections that result in chronic granulomatous pleural processes, mainly tuberculosis.

CASE REPORT

A 67-year-old white male patient who worked as a salesperson presented with complaints of dyspnea upon exertion and chest pain for 30 days. The patient reported having experienced no hemoptysis, cough, fever, night sweats or weight loss. He had been a smoker for 48 pack-years and had stopped smoking six years prior. He reported a 33-year history of arterial hypertension, chronic obstructive pulmonary disease and tuberculosis. The physical examination revealed fever, weight loss and reduced vesicular murmur in the left hemithorax.

Blood counts, as well as assessment of liver and renal function, were normal. Chest X-rays and computed tomography scans revealed left pleural effusion accompanied by bands, bronchiectasis and calcified nodules in both upper lobes (Figure 1).

The patient was submitted to thoracentesis and pleural biopsy using a Cope needle. The analysis of the pleural fluid revealed pleural effusion, and the biochemical analysis showed an exudate, according to the criteria established by Light.[4] Laboratory tests of the pleural fluid revealed serum lactate dehydrogenase of 1882 U/L, total protein of 5.2 g/dL, glucose of 83 mg/dL and adenosine deaminase of 98.5 U/L. Cytological examination revealed 600 cells/mm3, absence of mesothelial cells, 1% macrophages and 99% leukocytes, of which 95% were neutrophils, 4% were lymphocytes, and 1% were monocytes, with no basophils or eosinophils. No neoplastic cells were found. Direst testing for acid-fast bacilli and for fungi, as well as Gram stain, was negative. The anatomopathological examination of the pleural biopsy sample revealed a granulomatous chronic process and acid-fast bacilli positivity.

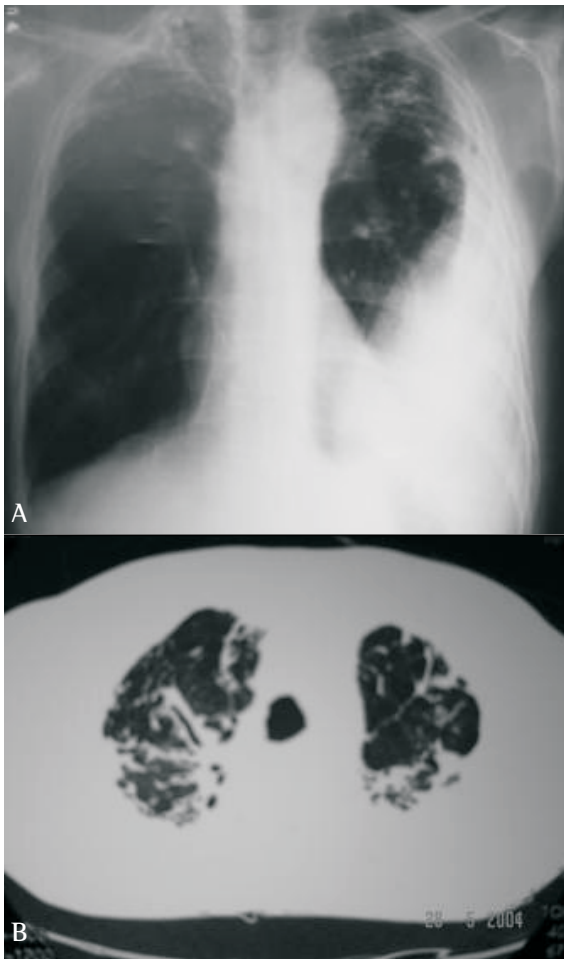

Figure 1 - a) Chest X-ray revealing left-sided pleural effusion accompanied by bands in both upper lobes of the lungs b) Computed tomography scan of the chest revealing bronchiectasis and nodules.

The clinical history, imaging characteristics, biochemical/cytological examination of the pleural fluid and the anatomopathological examination of the pleura suggested a diagnosis of pleural tuberculosis and concomitant bacterial infection. The patient was initially treated for tuberculosis with Regimen 1 (rifampin, isoniazid, and pyrazinamide), and chest-tube drainage was performed. However, since the pleural index remained elevated (> 300 mL/day) and neutrophilic for over fifteen days, we decided to perform a tube thoracostomy using a

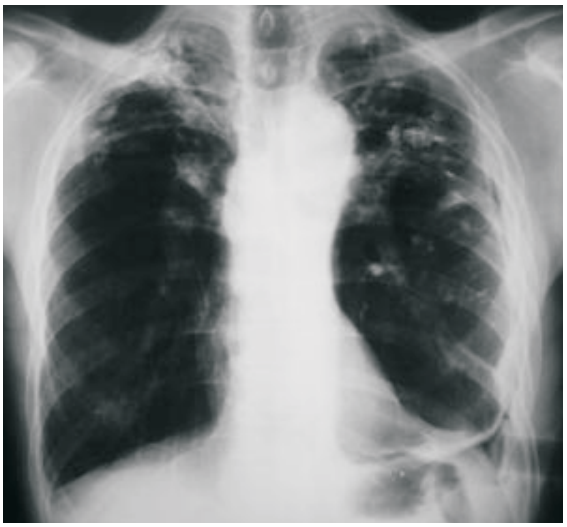

Figure 2 - Chest X-ray revealing pulmonary expansion after drainage and tube thoracostomy with the prosthesis inserted into the left costophrenic angle.

Filomeno prosthesis (Figure 2).[5]

At 60 days after the puncture and pleural biopsy, M. kansasii was identified in several pleural fluid culture samples and in the pleural biopsy sample.

Based on the results of these cultures, the chemotherapy regimen was altered to rifampin isoniazid, ethambutol and clarithromycin. After two months of treatment, the results of pleural fluid cultures were negative, there was clinical improvement, and the pleural effusion was under control. The patient presented a favorable evolution with slight pleural thickening and without functional repercussions. The chest tube was left in place for a year, and the chemotherapy treatment was continued for eighteen months

DISCUSSION

Among the pleural infections that result in granulomatous chronic inflammatory processes, the one caused by M. tuberculosis is the most frequent. This sort of inflammatory process can also be observed in rheumatoid arthritis and in sarcoidosis, as well as in infections caused by NTM or fungi (Candida sp, Aspergillus sp, Cryptococcus neoformans, Coccidioides immitis, Histoplasma capsulatum, Sporothrix schenckii) and bacteria (Actinomyces israeli and Nocardia sp).[6]

When pleural infectious granulomatous processes are identified, tuberculosis is the first diagnosis suggested in 95% of cases. Since the smear microscopy of the pleural fluid is positive in less than 10% of cases, and culture of the pleural fluid/biopsy sample also presents low sensitivity (ranging from 11% to 70%),[1,7] a diagnosis of tuberculosis is suggested based on the clinical history, biochemical aspects, adenosine deaminase and cytological aspects of the pleural fluid, with or without pleural histology of the chronic granulomatous process. When the etiology is not confirmed by culture, diagnostic confirmation is based on the parameter of clinical improvement after specific treatment. Other agents, although rare, should be investigated in patients who present risk factors such as comorbidities, immunodeficiency or advanced age.[1,3,6]

In developed countries, the incidence of NTM infection has increased, mainly as a consequence of human immunodeficiency virus infection, other causes of immunosuppression, chronic obstructive pulmonary disease and, perhaps, improvement in the diagnostic techniques/clinical recognition of the disease.[1] In a study carried out in California (USA), 270 cases of M. kansasii were identified, and 69% of the patients tested positive for human immunodeficiency virus.[2] It is interesting to observe that, among the patients who tested negative for the human immunodeficiency virus, the identification of the mycobacteria was frequently correlated with the mean average of 60 years of age and with chronic diseases.

In the Brazilian literature, it has been speculated that pulmonary disease caused by M. kansasii or other NTM is underestimated, and that many cases are being treated as tuberculosis. This hypothesis is based on the fact that identification of the mycobacteria is not routine, and that the treatment regimen used for the treatment of tuberculosis contains drugs that are partially efficacious for the treatment of NTM.[8-9] In a study carried out at the Adolfo Lutz Institute of São Paulo from 1995 to 1999, 10% of the 9381 mycobacteria identified were NTM. M. kansasii was the second most frequent (3.2%), the first being the M. avium complex.[10]

The concept that NTM can colonize the lungs without triggering a disease is controversial, especially when the agent is the M. kansasii, M. gordonae or M. avium complex. In order to classify

such colonization as a disease according to the criteria established by the American Thoracic Society,(3) there must be pulmonary lesions and NTM identified in multiple cultures of at least three sputum samples, or the histological analysis should demonstrate a granulomatous chronic process and positive tissue culture. In sterile material, the culture and identification of NTM in only one sample of pleural or cerebrospinal fluid will suffice for diagnostic purposes.

Clinically, pulmonary infection by M. kansasii mimics tuberculosis, manifesting insidious onset of productive cough, night sweats, weight loss and hemoptysis. The chest X-ray alterations are also similar to those seen in tuberculosis, being described as cavitations (in posterior segments of the upper lobes), nodules and (occasionally) pleural effusion.[11-12]

In the present study, pleural tuberculosis was the first diagnosis suggested due to the pulmonary alterations seen in the imaging (bronchiectasis and nodules, which are suggestive of tuberculosis), the chronic granulomatous process seen in the anatomopathological exam of the pleura and the acid-fast bacilli positivity. The fact that biochemical and cytological analysis of the pleural fluid demonstrated an exudate with high lactate dehydrogenase and persistent predominance of neutrophils also suggested concomitant bacterial or fungal infection. In pleural tuberculosis, predominance of neutrophils may occur at the onset of the inflammatory process. However, after a few days, the T-activated lymphocytes predominate in the pleural fluid. The persistence of neutrophil fluid in pleural tuberculosis may signal concomitant bacterial infection.[6]

According to the guidelines of the American College of Chest Physicians,[13] pleural drainage is necessary in cases of empyema and in cases of moderate to sever parapneumonic effusion which are Gram positive, present positive culture or present a pH lower than 7.2. However, when effusion recurs, pleural drainage should also be considered due to the risk of loculations or clinical worsening. Tube thoracostomy is indicated when the prolonged drainage is required, when standard drainage is not efficacious, or when the patient is extremely debilitated.

Pleural effusion in which M. kansasii is identified in the pleural fluid and in the pleural biopsy sample has rarely been reported in the literature. A case of pleural effusion and pneumothorax caused by M. kansasii in an immunocompetent patient, evolving to loculations in the pleural fluid and therefore requiring decortication, has been described.[14] A case has also been reported in which a patient presented pulmonary infection by M. kansasii and concomitant pleural effusion.[15]

The treatment recommended for the M. kansasii should combine at least three drugs: isoniazid, rifampin and ethambutol. In cases of intolerance, resistance or contraindication to the use of rifampin and isoniazid, clarithromycin may be included. Aminoglycosides are indicated in cases of disseminated mycobacterium infections and cavitations. Quinolones can also be used.[1,3,16]

In conclusion, even though pleural effusion caused by NTM is rare, it should be considered in patients presenting pleural effusion that is difficult to resolve, principally if accompanied by immunosuppression, tuberculosis sequelae, chronic obstructive pulmonary disease or other comorbidities. Despite the difficulties associated with detection of the agents involved, cultures to identify mycobacteria in the pleural fluid should be routinely requested.

REFERENCES

1. Caminero JA. Enfermedades producidas por micobacterias ambientales. In: Caminero JA, editor. Guia de la tuberculosis para médicos especialistas. Paris: UICTER, 2003.p.370-89.
2. Bloch KC, Zwerling L, Pletcher MJ, Hahn JA, Gerberding JL, Ostroff SM, et al. Incidence and clinical implications of isolation of Mycobacterium kansasii: results of a 5-year, population-based study. Ann Intern Med. 1998;129(9):698-704.
3. Diagnosis and treatment of disease caused by nontuberculous mycobacteria. This official statement of the American Thoracic Society was approved by the Board of Directors, March 1997. Medical Section of the American Lung Association. Am J Respir Crit Care Med. 1997;156(2 Pt 2):S1-25. Review.
4. Light RW. Useful tests on the pleural fluid in the management of patients with pleural effusions. Curr Opin Pulm Med. 1999;5(4):245-9. Review.
5. Filomeno LT, de Campos JM, de Almeida AW, Werebe Ede C, Jatene FB, Leirner AA. A dedicated prosthesis for open thoracostomy. Ann Thorac Surg. 1997;63(5):1494-6.
6. Vargas FS, Teixeira LR. In: Vargas FS, Teixeira LR, Marchi E. Derrame pleural. São Paulo: Roca; 2004 .p.291-303
7. Valdes L, Alvarez D, San Jose E, Penela P, Valle JM, Garcia-Pazos JM, et al. Tuberculous pleurisy: a study of 254 patients. Arch Intern Med.1998; 158(18): 2017-21.
8. Matos ED, Santana MA, de Santana MC, Mamede P, de Lira

Bezerra B, Panao Ed, et al. Nontuberculosis mycobacteria at a multiresistant tuberculosis reference center in Bahia: clinical epidemiological aspects. Braz J Infect Dis. 2004;8(4):296-304.
9. Morrone N, Cruvinel MC, Morrone Junior N , Freire JAS, Oliveira LML, Gonçalves C. Pneumopatia causada por Mycobacterium kansasii. J Pneumol. 2003;29(6): 341-9.
10. Chimara E, Giampaglia CMS, Martins MC, Telles MAS, Ueki SYM, Ferrazoli L. Molecular characterization of Mycobacterium kansasii isolates in the State of São Paulo between 1995-1998. Mem Inst Oswaldo Cruz. 2004;99(7):739-43.
11. Koh WJ, Kwon OJ, Lee KS. Nontuberculous mycobacterial pulmonary diseases in immunocompetent patients. Korean J Radiol. 2002;3(3):145-57. Review.
12. Evans SA, Colville A, Evans AJ, Crisp AJ, Johnston ID. Pulmonary Mycobacterium kansasii infection: comparison of the clinical features, treatment and outcome with pulmonary tuberculosis. Thorax. 1996;51(12):1248-52.
13. Colice GL, Curtis A, Deslauriers J, Heffner J, Light R, Littenberg B, et al. Medical and surgical treatment of parapneumonic effusions: a evidence-based guideline. Chest. 2000;118(4):1158-71. Review.
14. Olafsson EJ, Naum CC, Sarosi GA, Mastronarde JG. Bilateral pleural effusions and right pneumothorax in a 25-year -old man. Chest. 2004; 126(3): 986-92.
15. Kamiya H, Toyota E, Kobayashi N, Kudo K. A case of pulmonary Mycobacterium kansasii infection complicated with pleural effusion. Kekkaku. 2004;79(6):397-400. Japanese
16. Alcaide F, Calatayud L, Santin M, Martin R. Comparative in vitro activities of linezolid, telithromycin, clarithromycin, levofloxacin, moxifloxacin, and four conventional antimycobacterial drugs against Mycobacterium kansasii. Antimicrob Agents Chemother. 2004;48(12):4562-5.