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CASE REPORT

Isolation of *Mycobacterium branderi*, an unusual species from an acute myelogenous leukemia patient

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ABSTRACT

We report a case of pulmonary infection caused by Mycobacterium branderi, a slow growing non-tuberculosis mycobacteria, in a patient with acute myelogenous leukemia. The pulmonary disease was treated successfully with the combination of Ciprofloxacin, Doxycycline and Clarithromycin. M. branderi may be considered as an opportunistic pathogen, especially among immunologically compromised patients.

Key words: Acute myelogenous leukemia, *Mycobacterium branderi,* PCR-restriction fragment length polymorphism

INTRODUCTION

Non-tuberculosis mycobacteria (NTM) have been recognized as human pathogens since the 1950s and more than 100 genera of NTM have been identified. They are a diverse group of environmental organisms that can be isolated from water sources, soil, animals and food.[1] Human NTM infection is assumed to result from environmental exposure and there has been no documentation of human-to-human or animal-to-human transmission.[2] Studies reported increasing incidence of NTM isolation over the last decades, probably as a result of the increasing prevalence of patients immunosuppressed by old age, human immunodeficiency virus and cancer chemotherapy and also due to improved methods of NTM detection.[3]

We report a rare case of *Mycobacterium branderi* in a patient with (acute myelogenous leukemia [AML]) who had good clinical response to both chemotherapeutic and anti-NTM drugs.

CASE REPORT

The present case report is about a 31-year old male patient who presented to our medical center with a productive cough, hemoptysis and chest pain for a month. He had a history of pulmonary tuberculosis (TB) twice over the last 10 years. In the first episode, he was treated with the World Health Organization category (CAT) I standard regimen including: Isoniazid (H), Rifampin (R), Pyrazinamide (Z) and Ethambutol (E) for 6 months (2HRZE/4HR). In the second episode, a CAT II regimen including streptomycin in the 1st 2 months (2HRZES/1HREZ/5HRE) was prescribed for 8 months.[4] His treatment was successful, however one year after completion of the second therapy, he presented with respiratory symptoms to our hospital. His vital signs were within the normal limits. On physical examination, he was pale and afebrile with generalized wheezing and bilateral bronchial rhonchi. Laboratory studies revealed the following values: Total white blood cell (WBC) count: 103,600 cells/ul with 5% neutrophils, 14% mature monocytes, 11% lymphocyte and more than 20% immature nucleated cells of myeloid lineage some with monocytoid morphology; hemoglobin 5.8 g/dl; platelets 233,000 cells/ul and erythrocyte sedimentation rate 125 mm/h. All other biochemical tests were unremarkable. Chest X-ray and spiral computed tomography scan of the thorax showed a cavitary lesion in the right upper lobe surrounding diffuse infiltrates with pleural thickening. There were also some

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areas of nodular infiltrate demonstrating a "tree-in-bud" appearance in left lung [Figure 1].

A sputum smear was positive for acid-fast bacilli, so anti-TB regimen (CAT I) was initiated, culture and drug susceptibility testing were initiated. In addition, bone marrow biopsy was performed and AML – M4 was diagnosed by histopathological examination, based on published criteria.[5] Chemotherapy agents consisting Danurubicin 70 mg/q12h plus Cytarabine 1600 mg/q12h were started. The patient was transferred to the intensive care unit due to fever and severe neutropenia (WBC 880 cells/ul) on the 6th day of chemotherapy and Meropenem 1 g/q8 h, Vancomycin 1 g/q12h and Itraconazole 100 mg/daily were initiated.

The polymerase chain reaction (PCR) of deoxyribonucleic acid collected from sputum sample of patient (based on IS6110 primer) was negative for *Mycobacterium tuberculosis* complex. The *Mycobacterium* identification was performed by PCR-restriction fragment length polymorphism (RFLP) polymorphism analysis and subsequently *M. branderi* was isolated from the sputum of the patient. A 440 bp fragment of hsp65 gene was first amplified (based on TB11, TB12 primer) and then the PCR product digested using BstEII and HaeIII restriction endonucleases.[6] The obtained digested pattern (BstEII; 235,211 bp: HaeIII; 130,106,80,41,37 bp) was compared with the standard strains published on database[7,8] [Figure 2]. To further confirm the identification of *M. branderi* pure colonies were isolated at 25°C and 45°C within 3 weeks of incubation. Differentiation of *M. branderi* from *Mycobacterium celatum* was done based on phenotypic characteristic of colonies and pigment production. The colonies of *M. branderi* had not produced pigment.

The susceptibility testing observed for the clinical isolate included resistance to Isoniazid and Rifampin.

The anti-TB drugs were stopped and treatment was modified to Clarithromycin 500 mg/q12 h, Ciprofloxacin 500 mg/q12h and Doxycycline 100 mg/q12 h. This combination regimen was well tolerated and the patient's symptoms resolved. After 1 month of treatment, sputum smear and culture conversion was reported.

Following discharge from hospital, mycobacterial treatment was continued for 12 months and our patient remained smear negative and free of pulmonary symptoms in follow-up appointments.

DISCUSSION

NTM are distributed world-wide and are considered important in some special clinical settings, where they may cause pulmonary involvement, skin or soft-tissue infections, lymphadenitis and disseminated infections in the immune compromised.[9,10] In the lung, manifestations vary from asymptomatic carriage to extensive involvement with cavitary lesions, which may lead to death.[11]

The role of M. branderi as a human pathogen is not well-explained. This strain was first reported in 1992 as a member of the Helsinki group, including *M. branderi* and *M. celatum*.[12] In general, they are non-pigmented mycobacteria and grow at 25°C to 45°C, reaching full colony size after 2-3 weeks. They produce arylsulfatase, nicotinamidase and pyrazinamidase and are negative for tween 80 hydrolysis, catalase, urease, tellurite and nitrate reductase activities and niacin. There are several methods used for the diagnosis and differentiation of *M. branderi* from similar

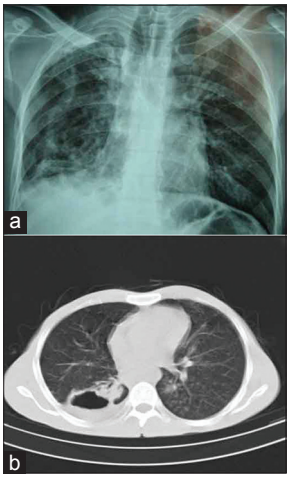

Figure 1: Radiographic images of the patient's chest on admission. Chest radiograph (a) and chest computed tomography (b)

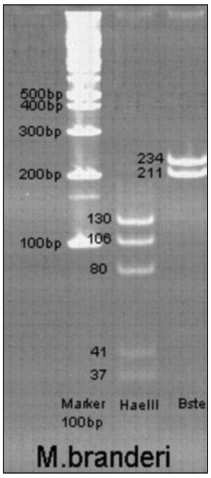

Figure 2: The restriction fragment length polymorphism pattern of hsp65 amplicon fom *Mycobacterium branderi*. Lane (1) 100 bp deoxyribonucleic acid size marker, lane (2) fragment digested with HaeIII, lane (3) fragment digested with BstEII

species. They include biochemical and lipid characteristics and 16S ribosomal sequencing and PCR-RFLP.[12,13]

M. branderi has been isolated rarely from pulmonary and wound lesions in immune-competent patients.[13-15] However, our case is notable as it is the first report of this species to occur in an immunocompromised patient with AML.

Previous studies on the susceptibility patterns of *M. branderi* have shown resistance to Amikacin, Rifampin, Pyrazinamide and Cycloserine and sensitivity to Clarithromycin, Ciprofloxacin, Ethambutol, Ethionamide and Streptomycin.[12,14] One earlier report described successful treatment of a soft-tissue infection was treated with Clarithromycin, Trimethoprim/sulfamethoxazole (Co-trimoxazole) and Ciprofloxacin.[15] In our case, the pulmonary infection resolved following treatment with the combination of Ciprofloxacin, Doxycycline and Clarithromycin, which was continued for one year. It has not recurred during 1 year of follow-up.

CONCLUSION

In the field of Mycobacteriology, improvements in molecular methods have provided more accurate species identification. A therapeutic regimen of Clarithromycin, Doxycycline and Ciprofloxacin was effective and sufficient to treat the pulmonary infection caused by *M. branderi.*

REFERENCES

1. Khan K, Wang J, Marras TK. Nontuberculous mycobacterial sensitization in the United States: National trends over three decades. Am J Respir Crit Care Med 2007;176:306-13.
2. Tanaka E, Kimoto T, Matsumoto H, Tsuyuguchi K, Suzuki K, Nagai S, *et al*. Familial pulmonary *Mycobacterium avium* complex disease. Am J Respir Crit Care Med 2000;161:1643-7.
3. McCallum AD, Watkin SW, Faccenda JF. Non-tuberculous mycobacterial infections in the Scottish Borders: Identification, management and treatment outcomes: A retrospective review. J R Coll Physicians Edinb 2011;41:294-303.
4. Atif M, Sulaiman SA, Shafie AA, Ali I, Hassali MA, Saleem F. WHO guidelines for treatment of tuberculosis: The missing links. Int J Clin Pharm 2012;34:506-9.
5. Creutzig U, van den Heuvel-Eibrink MM, Gibson B, Dworzak MN, Adachi S, de Bont E, *et al*. Diagnosis and management of acute myeloid leukemia in children and adolescents: Recommendations from an international expert panel. Blood 2012;120:3187-205.
6. Telenti A, Marchesi F, Balz M, Bally F, Böttger EC, Bodmer T. Rapid identification of mycobacteria to the species level by polymerase chain reaction and restriction enzyme analysis. J Clin Microbiol 1993;31:175-8.
7. Identification of mycobacteria. Available from: http://www.app.chuv.ch/prasite/index.html. [Last updated on 2007 Sep 15; Last accessed on 2013 Oct 27].
8. Brunello F, Ligozzi M, Cristelli E, Bonora S, Tortoli E, Fontana R. Identification of 54 mycobacterial species by PCR-restriction fragment length polymorphism analysis of the hsp65 gene. J Clin Microbiol 2001;39:2799-806.
9. Marras TK, Daley CL. Epidemiology of human pulmonary infection with nontuberculous mycobacteria. Clin Chest Med 2002;23:553-67.
10. 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:S1-25.
11. Al Jarad N, Demertzis P, Jones DJ, Barnes NC, Rudd RM, Gaya H, *et al*. Comparison of characteristics of patients and treatment outcome for pulmonary non-tuberculous mycobacterial infection and pulmonary tuberculosis. Thorax1996;51:137-9.
12. Brander E, Jantzen E, Huttunen R, Julkunen A, Katila ML. Characterization of a distinct group of slowly growing mycobacteria by biochemical tests and lipid analyses. J Clin Microbiol 1992;30:1972-5.
13. Koukila-Kähkölä P, Springer B, Böttger EC, Paulin L, Jantzen E, Katila ML. *Mycobacterium branderi* sp. nov., a new potential human pathogen. Int J Syst Bacteriol 1995;45:549-53.
14. Sugawara I, Kazumi Y, Otomo K, Ooki K, Mitarai S, Mori K. *Mycobacterium branderi* isolated from pus of a right pulmonary cavitary lesion. Jpn J Infect Dis 2005;58:187-8.
15. Wolfe J, Turenne C, Alfa M, Harding G, Thibert L, Kabani A. *Mycobacterium branderi* from both a hand infection and a case of pulmonary disease. J Clin Microbiol 2000;38:3896-9.

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