Case study

A case of pulmonary infection due to *Mycobacterium paraaffinicum* from the Amazon Region

Adriana Rodrigues Barrettoa, José Tadeu Colares Monteirob, Maria Luiza Lopes, Ana Roberta Fusco da Costac,⁎

a Federal University of Para/Belem, Para, Brazil
b University Center of Para/Belem, Para, Brazil
c Bacteriology and Mycology Section, Evandro Chagas Institute, Road BR316, Km7, S/N, 67030-000 Ananindeua, Para, Brazil

ARTICLE INFO

Keywords:
*Mycobacterium paraaffinicum*
Pulmonary disease
Amazon Region

ABSTRACT

*M. paraaffinicum*, a slow-growing scotochromogenic mycobacterium that uses paraaffinic hydrocarbons other than methane, i.e. inorganic carbon sources, was originally isolated from soil samples, but only in 2010 definitely achieved the species status. We have described here the first report of pulmonary disease due to *M. paraaffinicum* in Amazon Region.

Case report

An 86-year-old female patient, weighing 28.6 kg, was admitted to the Pulmonology Service at the University Hospital in 2014. The patient presented complaints of dyspnea on minor exertion, marked emaciation, ventilatory-dependent chest pain in right hemithorax and productive cough with mucopurulent sputum. She had no fever or hemoptysis, reported a history of smoking with the daily use of tobacco pipe for 53 years and exposure to smoke from wood stoves and charcoal. The HIV test was negative. Chest images by high-resolution computed tomography (HRCT) are presented in Fig. 1. She was initially diagnosed with pulmonary tuberculosis, based on sputum smear microscopy, and treated with regimen of rifampin, isoniazid, ethambutol and pyrazinamide, however, she remained with positive AFB smears between the 5th and 6th month of treatment. Nontuberculous mycobacteria (NTM) was repeatedly isolated from her sputum samples and identified as *Mycobacterium paraaffinicum* (Fig. 2), by partial 16S rRNA and *hsp65* gene sequencing [1,2]. Patient started an oral empirical regimen including rifabutin, clarithromycin and ciprofloxacin, which was discontinued after 15 days in consequence of dyspeptic complains.

Due to persistence of respiratory symptoms, the patient received 250 mg of oral azithromycin three times per week with good tolerance and clinical improvement (reduction of cough and dyspnea) after three months of therapy, remaining persistently acid-fast bacilli (AFB) smear-positive sputum. Her sputum samples exhibited a mucoid aspect in that time. Antibacterial susceptibility testing results were not available at the time of treatment initiation. Determination of minimum inhibitory concentrations (MIC) was performed by broth microdilution method according to Clinical Laboratory and Standards Institute [3], using alternatively susceptible breakpoint for first and second line drugs recommended for *M. kansasii*. Isolates exhibited sensitivity to clarithromycin (MIC 16 μg/mL), moxifloxacin (MIC 2 μg/mL) and sulfamethoxazole-trimethoprim (MIC 2/38 μg/mL); and resistance to ciprofloxacin (MIC 16 μg/mL), rifampicin (MIC 4 μg/mL), amikacin (MIC 32 μg/mL) and ethambutol (MIC 10 μg/mL).

The patient abandoned treatment due to undesirable side effects caused by therapeutic regimen proposed and her clinical follow-up was lost. Until then we had no news of her return to the Pulmonology Service.

Discussion

*M. paraaffinicum*, a slow-growing scotochromogenic mycobacterium that uses paraaffinic hydrocarbons other than methane, i.e. inorganic carbon sources, was originally isolated from soil samples, but only in 2010 definitely achieved the species status. It exhibit resistance to ethambutol and susceptibility in vitro to amikacin, rifabutin, clarithromycin and linezolid [4,5].

There are rare reports in clinical settings on *M. paraaffinicum* infections, including a pseudo-outbreak described in a tertiary hospital,
where the species was identified in clinical specimens from 21 patients over 2.5-year period. Epidemiological and environmental analysis established an ice machine located in the hospital unit as infection source [6]. Beside this, there is the report of the first M. paraﬃnicum lung disease case in 2014, in an 85-year-old patient with the nodular bronchiectasis form. Isolates exhibited sensitivity to ciprofloxacin, clarithromycin, linezolid and doxycycline; and resistance to ethambutol, streptomycin, amikacin and imipenem. The patient was treated with azithromycin, ciprofloxacin and linezolid, which was discontinued due to nausea and vomiting symptoms [7].

Comparing results in susceptibility tests with M. paraﬃnicum reports, we have found different susceptibility proﬁles, which point to the need of performing susceptibility tests for each isolate with the objective of verifying the in vivo behavior of different drugs and thus aid in the therapeutic conduct.

In this context, NTM treatment remains a challenge and related to several matters including: (I) proﬁles on drug susceptibility in vitro testing in NTM may be both species and strain-dependents, (II) correlation between in vitro susceptibility tests and in vivo response are not always possible, (III) few drugs available for NTM treatment, (IV) regime may vary according to severity of disease or oral medication tolerability, and (V) limited number of publications with data on in vitro susceptibility or even reports of experiences of empirically established therapeutic schemes accompanied by clinical outcomes for rarely isolated or newly established species, such as M. paraﬃnicum. All those factors diﬃcult the definition of therapeutic protocols or recommendations to aid clinicians in selection of appropriate therapeutic regimen.

Similarly to Chan et al. [7], our case also occurred in an elderly female patient, but with chronic cavitary form, who was not able to tolerate to treatment due to gastric symptoms. We prescribed azithromycin as an immunomodulatory agent, despite the risk of developing monotherapy-related resistance in the treatment of NTM [8–10]. In addition, azithromycin administration could bring some beneﬁts to the patient’s qualities of life, since studies have shown that prolonged use of macrolides is associated with a reduction of the number of infectious exacerbations in patients with non-fibrocystic bronchiectasis [11–14]. Currently, macrolides are indicated to patients with three or more infectious exacerbations per year, colonization by Pseudomonas aeruginosa and in those with less frequent exacerbations and signiﬁcant impairment of the quality of life [15].

Conclusion

Although it was initially described only in pseudo outbreak M. paraﬃnicum is capable of causing symptomatic lung disease and should be considered as NTM species with pathogenic potential.

Disclosure statement

The authors declare that they have no competing interests.

Acknowledgements

We would like to thank all the other staﬀ from Instituto Evandro Chagas and Hospital Universitário João de Barros Barreto who have contributed to this research. This work was supported by Instituto Evandro Chagas/Ananindeua/Brazil.
Fig. 2. Relationships between sequences from some reference strains of slowly growing mycobacteria and IEC-2816 strain inferred from the partial 16S rDNA gene. The phylogenetic tree was constructed using the Neighbor-Joining method and Kimura-2-parameter distance correction model. The numbers at the nodes indicate bootstrap values obtained in 1000 repetitions (expressed in percentages). M. abscessus was used as outgroup. The 16S rDNA gene sequence was deposited in GenBank under accession number KY992517.

References

[1] Lane DJ. 16S/23S rRNA sequencing. In: Stackebrandt E, Goodfellow M, editors. Nucleic Acid Techniques in Bacterial Systematics. 1st ed. Chichester, NY: John Wiley & Sons; 1991. p. 115–75.
[2] Kim H, Kim SH, Shim TS, Kim MN, Bai GH, Park YG, et al. Differentiation of Mycobacterium species by analysis of the heat-shock protein 65 gene (hsp65). Int J Syst Evol Microbiol 2005;55(July (Pt 4)):1649–56.
[3] CLSI. Susceptibility Testing of Mycobacteria, Nocardiae and Other Aerobic Actinomycetes; Approved Standard-Second Edition. CLSI document M24-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2011.
[4] Chase HH, Davis JB, Raymond RL. Mycobacterium paraaffnicum n. sp., a bacterium isolated from soil. Appl Microbiol 1956;4(November (6)):310–5.
[5] Toney N, Adekambi T, Toney S, Yakrus M, Butler WR. Revival and emended description of ‘Mycobacterium paraaffnicum’ Davis, Chase and Raymond 1956 as Mycobacterium paraaffnicum sp. nov., a bacterium isolated from soil. Appl Microbiol 1956;4(November (6)):310–5.
[6] Wang SH, Mangino JE, Stevenson K, Yakrus MA, Cooksey R, Butler WR, et al. Characterization of Mycobacterium paraffinicum associated with a pseudo-outbreak. J Clin Microbiol 2008(May (5)):1850–3. http://dx.doi.org/10.1128/JCM. 02079-07. Epub 2008 Mar 26.
[7] Chan AW, Kabbani S, Staton G, Kraft CS. Mycobacterium paraffinicum causing symptomatic pulmonary infection. J Clin Microbiol 2014;52(April (4)):1281–3. http://dx.doi.org/10.1128/JCM. 03107-13. Epub 2014 Jan 22.
[8] Serisier DJ. Risks of population antimicrobial resistance associated with chronic macrolide use for inflammatory airway diseases. Lancet Respir Med 2013;1(May (3)):262–74. http://dx.doi.org/10.1016/S2213-2600(13)70038-9. Epub 2013 Mar 29.
[9] Parnham MJ, Erakovic Haber V, Giamarellos-Bourboulis EJ, Perletti G, Verleden GM, Vos R. Azithromycin: mechanisms of action and their relevance for clinical applications. Pharmacol Ther 2014;143(August (2)):225–45. http://dx.doi.org/10.1016/j.pharmthera.2014.03.003. Epub 2014 Mar 11.
[10] Philley JV, Griffith DE. Treatment of slowly growing mycobacteria. Clin Chest Med 2015;36(March (1)):79–90. http://dx.doi.org/10.1016/j.ccm.2014.10.005. Epub 2014 Nov 6.
[11] Wong C, Jayaram I, Karalus N, Eaton T, Tong C, Hockey H, et al. Azithromycin for prevention of exacerbations in non-cystic fibrosis bronchiectasis (EMBRACE): a randomised, double-blind, placebo-controlled trial. Lancet 2012;378(August (9842)):660–7. http://dx.doi.org/10.1016/S0140-6736(12)60953-2. 386.
[12] Altenburg J, de Graaff CS, Stienstra Y, Sloos JH, van Haren EH, Koppers RJ, et al. Effect of azithromycin maintenance treatment on infectious exacerbations among patients with non-cystic fibrosis bronchiectasis: the BAT randomized controlled trial. JAMA 2013;309(March (12)):1251–9. http://dx.doi.org/10.1001/jama.2013. 1937. 309.
[13] Serisier DJ, Martin ML, McGuckin MA, Lourie R, Chen AC, Brain B, et al. Effect of long-term, low-dose erythromycin on pulmonary exacerbations among patients with non-cystic fibrosis bronchiectasis: the BLESS randomized controlled trial. JAMA 2013;309(March (12)):1260–7. http://dx.doi.org/10.1001/jama.2013.2290. 309.
[14] McMullan BJ, Mostaghim M. Prescribing azithromycin. Aust Prescr 2015;38(June (3)):87–9. Epub 2015 Jun 1. Review.
[15] Chalmers JD, Martin MB, Blasi F. Management of bronchiectasis in adults. Eur Respir J 2015;45(May (5)):1446–52. http://dx.doi.org/10.1183/09031936.00191114. Epub 2015 Mar 18. Review.