International Journal of Infectious Diseases 67 (2018) 65–69

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

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

Clinical characteristics of pulmonary *Mycobacterium lentiflavum* disease in adult patients

Kazuma Yagi[a], Kozo Morimoto[b], Makoto Ishii[a,*], Ho Namkoong[a], Satoshi Okamori[a], Takanori Asakura[a], Shoji Suzuki[a], Takahiro Asami[a], Yoshifumi Uwamino[c], Yohei Funatsu[a], Hiroshi Fujiwara[c], Hirofumi Kamata[a], Tomoyasu Nishimura[d], Tomoko Betsuyaku[a], Atsuyuki Kurashima[b], Naoki Hasegawa[c]

[a] *Division of Pulmonary Medicine, Department of Medicine, Keio University School of Medicine, Shinjuku-ku, Tokyo, Japan*
[b] *Respiratory Disease Center, Fukujuji Hospital, Japan Anti-Tuberculosis Association, Kiyose, Tokyo, Japan*
[c] *Center for Infectious Diseases and Infection Control, Keio University School of Medicine, Shinjuku-ku, Tokyo, Japan*
[d] *Keio University Health Center, Minato-ku, Tokyo, Japan*

ARTICLE INFO

Article history:
Received 26 October 2017
Received in revised form 21 November 2017
Accepted 1 December 2017
Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Pulmonary *Mycobacterium lentiflavum* disease
Non-tuberculous mycobacteria
Case series
Literature review

ABSTRACT

Background: Mycobacterium lentiflavum is a slow-growing non-tuberculous Mycobacterium that is often associated with an immunocompromised state and cervical lymphadenitis in young children. However, little is known about the clinical importance of pulmonary infection with *M. lentiflavum* in adults.
Methods: The medical records of all adults who met the diagnostic criteria of pulmonary *M. lentiflavum* disease at Keio University Hospital and Fukujuji Hospital from 2001 to 2015 were reviewed. In addition, the PubMed database was searched to identify further reported cases in non-HIV adults.
Results: Five cases of pulmonary *M. lentiflavum* disease were identified in the medical records search and 11 additional cases were identified in the literature review. Eleven of the total 16 cases were female, and 15 of 16 cases showed a nodular/bronchiectatic pattern on chest computed tomography imaging. No cases showed an aggressive clinical course of pulmonary *M. lentiflavum* disease, although one patient died of an exacerbation of underlying vasculitis and bacterial pneumonia.
Conclusions: The clinical characteristics of pulmonary *M. lentiflavum* disease in adult patients were identified. This disease mainly affects females, displays a nodular/bronchiectatic pattern on chest computed tomography imaging, and does not demonstrate an aggressive clinical course. Further larger studies are needed to reveal detailed clinical features.

Introduction

Emerging evidence suggests that the incidence of pulmonary diseases caused by non-tuberculous mycobacteria (NTM) has been increasing gradually (Galarraga et al., 2002; Namkoong et al., 2016; Satta et al., 2014). *Mycobacterium lentiflavum* is a slow-growing Runyon II NTM that was first identified in a cluster of 22 isolates in 1996 (Springer et al., 1996). As with other NTM, *M. lentiflavum* has been isolated from water and soil samples; most isolates have represented fortuitous isolations (Marshall et al., 2011; Springer et al., 1996; Tortoli et al., 1997).

Although it has rarely shown pathogenicity in humans, some recent reports have suggested the clinical importance of *M. lentiflavum* in young children with cervical lymphadenitis and in immunocompromised patients (Haase et al., 2017; Montejo et al., 2006; Niobe et al., 2001; Safdar and Han, 2005; Tortoli et al., 2006). Other infected sites, including pulmonary infection, are less frequent (Ibanez et al., 2002; Lee et al., 2015; Molteni et al., 2005; Niobe et al., 2001; Shamaei et al., 2010; Shin et al., 2007; Springer et al., 1996; Tortoli et al., 2002; Tortoli et al., 2006). Although *M. lentiflavum* is the third most common Mycobacterium isolated in cystic fibrosis patients (Phelippeau et al., 2015), little has been reported regarding the clinical importance of pulmonary *M. lentiflavum* infection in adult patients (Hiraki et al., 2012; Jeong et al., 2013; Lee et al., 2015; Marshall et al., 2011; Molteni et al., 2005; Shamaei et al., 2010; Shin et al., 2007; Tortoli et al., 1997). The clinical features and outcomes of five cases of pulmonary

* Corresponding author at: Division of Pulmonary Medicine, Department of Medicine, Keio University School of Medicine, 35 Shinanomachi Shinjuku-ku, Tokyo 160-8582, Japan.
E-mail address: ishii@keio.jp (M. Ishii).

https://doi.org/10.1016/j.ijid.2017.12.001

Table 1
Characteristics of patients with pulmonary *Mycobacterium lentiflavum* disease at the two study institutions (Keio University Hospital and Fukujuji Hospital).

Characteristics of patients ($N = 5$)	
Age, years, median (range)	68 (58–83)
Female sex, *n* (%)	4 (80.0)
Smoking history, *n* (%)	2 (40.0)
Underlying disease, *n* (%)	
Old pulmonary TB	1 (20.0)
Bronchial asthma	1 (20.0)
ANCA-associated vasculitis	1 (20.0)
Chronic obstructive pulmonary disease	0 (0)
Radiological findings, NB, *n* (%)	5 (100.0)
Cavitary lesion, *n* (%)	1 (20.0)

ANCA, anti-neutrophil cytoplasmic antibody; NB, nodular/bronchiectatic pattern; TB, tuberculosis.

M. lentiflavum disease encountered at two institutions during the years 2001–2015 are reported here. A review of previously reported cases of pulmonary *M. lentiflavum* disease occurring in adult patients without HIV is also provided.

Methods

The medical records of all adult patients who met the diagnostic criteria of pulmonary *M. lentiflavum* disease at two institutions (Keio University Hospital and Fukujuji Hospital) from 2001 to 2015 were reviewed retrospectively. The diagnostic criteria were based on the American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) statements (Griffith et al., 2007). *M. lentiflavum* was identified by PCR amplification of the 16S ribosomal RNA gene and the beta subunit of the RNA polymerase gene fragment (*rpoB*) at the Research Institute of Tuberculosis/Japan Anti-Tuberculosis Association (Han et al., 2002; Jeong et al., 2013; Niobe et al., 2001). The following information was collected for these cases: patient characteristics, smoking history, underlying pulmonary and other diseases, immune status, sputum acid-fast smear and culture findings, radiological findings, antimicrobial therapy, and clinical course. The ethics review boards of Keio University Hospital and Fukujuji Hospital approved the study protocol. Written informed consent was obtained from each patient for publication of this study.

In addition, a literature review was performed. Articles reporting pulmonary *M. lentiflavum* disease in non-HIV adults, written in English or Japanese, were identified in the PubMed database using the keywords "*Mycobacterium lentiflavum*". All reports were assessed to confirm whether each case met the diagnostic criteria based on the ATS/IDSA statements and had adequate information available for inclusion in this study. The following data were collected from these reports: patient age; sex; underlying pulmonary and other diseases; radiological findings; treatment history; and clinical course.

The radiological pattern seen on chest computed tomography (CT) imaging was classified as one of the following four forms: nodular/bronchiectatic (NB), fibrocavitary (FC), NB + FC, or unclassified (Asakura et al., 2017).

Results

Case series

Five cases of pulmonary *M. lentiflavum* disease were identified in the medical records of the two institutions. Tables 1 and 2 show the background data and clinical characteristics of these five cases. The median age at diagnosis was 68 years (range 58–83 years). Four patients (80.0%) were female and two of the five (40.0%) patients had a smoking history. One patient (case 4) was treated with prednisolone (4 mg/day) for anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis. All of the patients were negative for HIV. Two of the five patients had an underlying pulmonary disease, such as bronchial asthma (case 4) and old pulmonary tuberculosis (case 2). Only one patient (case 2) was smear-positive at diagnosis. All cases showed the NB pattern on chest CT imaging (Figure 1), and only one patient (case 2) had a cavitary lesion.

Only one patient (case 2) received antimycobacterial combination therapy for pulmonary *M. lentiflavum* disease. The therapeutic regimen included clarithromycin (CLA), rifampicin (RIF), and ethambutol (EMB), which was also used to treat pulmonary *M. avium* complex (MAC) disease as the standard multidrug regimen. He was treated with streptomycin (STR) in addition to combination therapy including CLA, RIF, and EMB for the first 2 months, because there was a cavitary lesion in the left upper lobe on the chest CT. He received the indicated combination therapy for 12 months. Case 2 showed sputum conversion at 8 months after the initiation of the combination therapy.

Case 5 received erythromycin (ERY) monotherapy due to its beneficial immunomodulatory effects on NTM without inducing cross-resistance to CLA (Komiya et al., 2014). After treatment, the patient's symptoms, radiological findings, and clinical course did not worsen.

Case 4 died from an exacerbation of ANCA-associated vasculitis and pneumonia due to *Pseudomonas aeruginosa* 4 months after the diagnosis of pulmonary *M. lentiflavum* disease.

Literature review

Eleven previously reported cases of pulmonary *M. lentiflavum* disease in non-HIV adult patients were identified in the literature review. These cases are shown in Table 3 (Hiraki et al., 2012; Jeong

Table 2
Clinical characteristics of the five cases.

Case	Age (years)	Sex	Smoking history (pack-years)	Underlying diseases		Sputum smear	Radiological findings	Treatment	Observation period (months)	Clinical course
				Pulmonary	Other					
1	66	F	40	–	–	Neg	NB	–	30	No change
2	83	M	30	Old PTB	BPH	Pos	NB	CLA + RIF + EMB + STR	68	Improved
3	68	F	0	–	HT, DL	Neg	NB	–	18	No change
4	79	F	0	BA	AAV, chronic sinusitis	Neg	NB	–	4	No change[a]
5	58	F	0	–	Palmoplantar pustulosis	Neg	NB	ERY	14	No change

AAV, anti-neutrophil cytoplasmic antibody-associated vasculitis; BA, bronchial asthma; BPH, benign prostatic hyperplasia; CLA, clarithromycin; DL, dyslipidemia; EMB, ethambutol; ERY, erythromycin; F, female; HT, hypertension; M, male; NB, nodular/bronchiectatic pattern; PTB, pulmonary tuberculosis; RIF, rifampicin; STR, streptomycin.
[a] This patient died from an exacerbation of ANCA-associated vasculitis and pneumonia due to *Pseudomonas aeruginosa*.