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Case report

Successful use of linezolid for refractory *Mycobacterium abcessus* infection: A case report

Teppei Inoue[a,*], Akihito Tsunoda[a], Eriko Nishimoto[a], Kohei Nishida[a], Yuka Komatsubara[a], Rintaro Onoe[a], Junko Saji[b], Masamichi Mineshita[a]

[a] Division of Respiratory Disease, Department of Internal Medicine, St. Marianna University School of Medicine, 2-16-1 Sugao, Miyamae-Ku, Kawasaki-Shi, Kanagawa-Ken 216-8511, Japan
[b] Division of Respiratory Disease, Department of Internal Medicine, Kawasaki Municipal Tama Hospital, 1-30-37 Syukugawara, Tama-Ku, Kawasaki-Shi, Kanagawa-Ken 214-8525, Japan

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ABSTRACT

A 51-year-old male patient was receiving treatment for *Mycobacterium abscessus* infection for approximately 10 years. However, as his condition gradually progressed to type II respiratory insufficiency, he was referred to our hospital, which was near his home. Computed tomography on his first visit revealed an abscess in the right lower lobe. Because respiratory insufficiency was evident, he was admitted the same day. We began treatment with meropenem, amikacin, and clarithromycin, but his symptoms did not improve. In accordance with the 2007 American Thoracic Society/Infectious Diseases Society of America statement, we administered linezolid, which resulted in gradual improvement in his physical status and imaging findings.

1. Introduction

Mycobacterium abscessus infection is the most difficult non-tuberculous mycobacterial infection to treat. In the present study, we used linezolid (LZD) on a patient with refractory *M. abscessus* infection that had been diagnosed at another hospital and achieved therapeutic effect.

2. Case presentation

A 51-year-old male presented with a chief complaint of respiratory insufficiency and fever. He had a medical history of tympanitis at 12 years of age, right pneumothorax at 35 years of age, video-assisted thoracic surgery performed for recurring right pneumothorax at 46 years of age, and left pneumothorax (only drainage) at 50 years of age. He had no relevant family history. He occasionally consumed alcohol and smoked 20 cigarettes a day from 20 to 46 years of age. At 40 years of age, he was diagnosed with nontuberculous mycobacterial infection due to *M. intracellulare* at another hospital and was treated with clarithromycin (CAM) + rifampicin + ethambutol. While his symptoms temporarily improved initially, they gradually became exacerbated; during the course of treatment, only *M. abscessus* was detected in the sputum. The patient was diagnosed with microbial substitution from *M. intracellulare* to *M. abscessus* and continued to be treated with various combinations of CAM, imipenem (IPM)/cilastatin, meropenem (MEPM), faropenem (FRPM), amikacin (AMK), and sitafloxacin (STFX). However, the symptoms gradually progressed, developing into type II respiratory insufficiency. As per the patient's wish, he changed hospitals and was treated at our hospital, which is located closer to his home. An abscess was found in the right lower lobe on computed tomography (CT) images taken during the initial visit (Fig. 1a), and as respiratory insufficiency was apparent, he was admitted the same day.

Physical findings at the time of admission were as follows: height, 169 cm; weight, 38.4 kg; BMI, 13.4; body temperature, 36.7 °C; blood pressure, 110/80 mmHg; heart rate, 125 beats per min; respiration rate, 18 times per min; and percutaneous oxygen saturation level, 91% (in-door air). Moreover, chest auscultation showed rale on the right side. Laboratory findings (Table 1) were as follows: elevated leukocyte/C-reactive protein (CRP) level, negative for β-d glucan, sputum general bacteria, normal bacterial flora in the upper respiratory tract, positive for sputum Mycobacterium smear, Gaffky scale 3, and positive for *M. abscessus* in nucleic acid identification of Mycobacterium group. DNA

Abbreviations: ATS/IDSA, American Thoracic Society/Infectious Diseases Society of America; CT, Computed tomography; LZD, linezolid; CAM, clarithromycin; IPM, imipenem; MEPM, meropenem; FRPM, faropenem; AMK, amikacin; STFX, sitafloxacin; MAC, *Mycobacterium avium* complex; CRP, C-reactive protein

* Corresponding author.
E-mail addresses: t3inoue@marianna-u.ac.jp (T. Inoue), a2tsunoda@marianna-u.ac.jp (A. Tsunoda), e2koda@marianna-u.ac.jp (E. Nishimoto), k2nishida@marianna-u.ac.jp (K. Nishida), y2komatsubara@marianna-u.ac.jp (Y. Komatsubara), r2onoe@marianna-u.ac.jp (R. Onoe), j2saji@marianna-u.ac.jp (J. Saji), m-mine@marianna-u.ac.jp (M. Mineshita).

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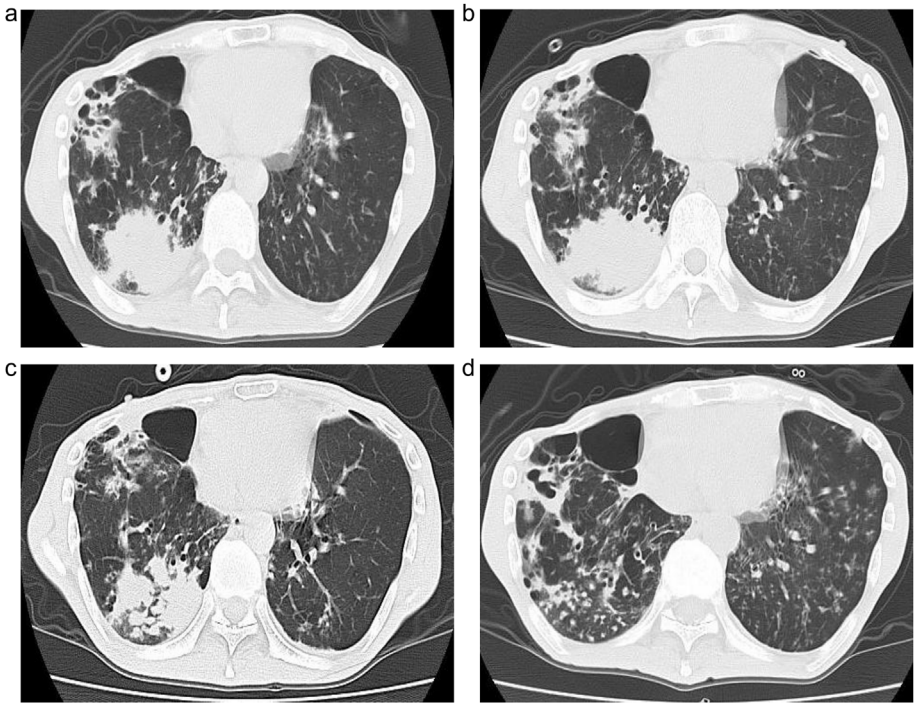

Fig. 1. a) CT images taken at the time of admission. There is an abscess in the right lower lobe. 1b) Day 18 of treatment. Despite administration of antibiotics, the abscess exacerbated. 1c) Day 35 of treatment (day 18 of LZD administration). The abscess in the right lower lobe is reduced. 1d) Day 195 of LZD administration. A notable improvement can be observed in the abscess in the right lower lobe.

Table 1
Laboratory findings at the time of admission.

Hematology		Biochemistry		Serology	
WBC	21200/μl	T-Bil	0.4 mg/dl	CRP	5.53 mg/dl
Stab	32 %	D-Bil	0.1 mg/dl	β-D-glucan	11 pg/ml
Seg	54.5 %	AST	20 IU/l		
Eosinophil	1 %	ALT	10 IU/l	Sputum	
Basophil	1 %	LDH	266 IU/l	Culture	normal flora
Lymphocyte	7.5 %	ALP	479 IU/l	AFB smear	Gaffky III
Monocyte	4 %	γ-GTP	51 IU/l	DDH	*M. abscessus*
RBC	460 × 10^4/μl	HDL-Chol	29 mg/dl		
Hb	12 g/dl	LDL-Chol	90 mg/dl		
Hct	38 %	TG	108 mg/dl		
MCV	82.5 fl	BUN	7.8 mg/dl		
MCH	26 pg	Cr	0.5 mg/dl		
MCHC	31.6 %	Na	134 mg/dl		
PLT	69.4 × 10^4/μl	Cl	96 mg/dl		
		K	4.2 mg/dl		
		GLU	164 mg/dl		

AFB, Acid-fast bacteria; DDH, DNA-DNA hybridization nucleic acid identification of Mycobacterium group; M. abscessus, Mycobacterium abscessus.

sequence analysis for *M. abscessus* was neither performed at the previous hospital nor at our hospital.

3. Patient progress

From the time of admission, treatment was initiated with MEPM (3 g/day), AMK (600 mg/day), and CAM (800 mg/day). Until day 6 of the treatment, the CRP level remained at approximately 10 mg/dl, without showing any decrease. When the effect of the nonsteroidal antipyretic analgesic ceased, the patient developed a fever of +38 °C; thus, STFX (200 mg/day) was administered on day 6. Subsequently, the CRP level gradually improved, but it ceased to decrease at approximately 5 mg/dl, and the fever remained. In the CT image taken on day 18, it was evident that the infiltrative shadow on the lower right lobe had worsened (Fig. 1b). Because of resistance to each drug, his symptoms worsened and became life-threatening. This was presumed to be because of poor response to therapy. Thus, he and his family were explained of the situation, and LZD was then additionally administered intravenously at 600 mg/day on day 18 to continue the treatment. Once LZD administration began, the CRP level gradually decreased, and CT imaging findings showed an improving trend. On day 35 (day 18 of the LZD administration), the fever alleviated without NSAIDs, with the CRP level decreasing to 2 mg/dl. Because his imaging findings also showed improvement (Fig. 1c), intravenous administration of LZD was changed to oral administration on day 36, and MEPM and AMK were discontinued and oral administration of 900 mg/day of FRPM was added. The patient's clinical course was observed for a week, and as no exacerbation of inflammatory response or imaging findings was observed and the fever came down to +37 °C, he was discharged on day 41. Sterilization was continued after discharge, and although the inflammatory response and sputum Mycobacterium smear did not become negative, continuous oral medical treatment led to notable improvement in CT images (Fig. 1d). Since discharge, the treatment effects have been maintained for over 6 months, with the patient exhibiting good overall physical condition. However, the patient's pulmonary hypertension (right ventricular systolic pressure, 54 mmHg) and heart

failure progressed over time. His activities of daily living dramatically decreased on day 250, and he was almost completely confined to bed. He subsequently died on day 268. In the CT image taken just before death, the infiltrative shadow on the lower right lobe had not worsened; therefore, the cause of death was heart failure due to secondary pulmonary hypertension associated with chronic respiratory failure.

4. Discussion

M. avium complex (MAC syndrome) is the most common cause of nontuberculous mycobacterial infection, followed by *M. kansasii,* which accounts for the majority of such infections. In Japan, rapidly growing mycobacteria, including *M. abscessus,* are reported to be the third most common cause of nontuberculous mycobacterial infection [1]. *M. abscessus* is found in tap water and soil and is known to cause infections associated with wounds. There is no human-to-human infection, and pulmonary infection is relatively rare. However, in the recent years, cases of pulmonary infection have increased [2,3]. In addition, it has been reported that *M. abscessus* infection develops following MAC syndrome, and treatment-resistant cases of nontuberculous mycobacterial infection need a sputum acid-fast bacterial test keeping the microbial substitution phenomenon in mind [3–5]. Pulmonary infection due to *M. abscessus* is the most difficult of the nontuberculous mycobacterial infections to treat, and there is no established treatment regimen in the 2007 American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) statement. However, a multidrug combination therapy of macrolide-type antibiotic with AMK, cefotaxime, or IPM is expected to suppress the progression of symptoms, and LZD has also been described as a potentially effective drug [3]. The normal amount of LZD administered is 1200 mg, but by reducing the dose to 600 mg while maintaining the antibacterial activity, side effects such as peripheral neuropathy, anemia, gastrointestinal symptoms, and thrombocytopenia can be reduced [6]. Alternatively, by using it with vitamin B6, LZD-related cytopenia can be reduced [7]. The present patient received treatment with various antibiotics for 10 years as prescribed by his previous doctor, and after being admitted at our hospital, treatment was continued with MEPM (3 g/day), AMK (600 mg/day), STFX (200 mg/day), and CAM (800 mg/day) for 2 weeks. However, as exacerbation of symptoms was confirmed in imaging, it was determined that there was a possibility of drug resistance. With the progression of the illness, the patient experienced decreasing physical strength and poor nutritional status. Thus, based on previous reports of LZD, we added vitamin B6 and began treatment at 600 mg/day and confirmed improvement in symptoms. After more than 6 months of observation, no LZD-related side effects were observed other than mild dysgeusia. According to the ATS/IDSA guideline, periodic administration of multidrug therapy, including macrolide agents administered over several months, may help control symptoms and progression of *M. abscessus* lung infection [3]. In this patient, we administered treatment with the goal of improving the symptoms. This patient subsequently died because of secondary heart failure. However, as LZD administration temporarily improved the patient's systemic state and imaging findings, it can be considered that LZD contributed to improving the patient's condition.

We administered LZD to successfully treat a very rare case of pulmonary infection due to *M. abscessus* that had become resistant to a combination of various drugs. It appears that in such patients, LZD can be an effective treatment option. The limitation of this study was that the sensitivity of the drugs was judged by clinical response because performing sensitivity test for each drug is difficult in daily clinical practice.

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