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Case report

A case of pulmonary infection caused by *Mycobacterium asiaticum*: Difficulties on diagnostic and therapeutic approaches

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ABSTRACT

A 56-year-old previously healthy female presented with chronic productive cough and fever. Chest X-ray revealed right middle lung opacities. Sputum acid fast bacilli smear was positive, however polymerase chain reaction was negative for *Mycobacterium tuberculosis*. Further investigations were pursued, which identified *Mycobacterium asiaticum*. Appropriate therapy with isoniazid, rifampin and clarithromycin for total 18 months (including pyrazinamide and ethambutol for first 4 months) resulted in clinical and radiographic improvement. Recognition of the possibility of this rarely described pulmonary pathogen is essential for successful treatment.

1. Introduction

Mycobacterium asiaticum (*M. asiaticum*) is a species of non-tuberculous mycobacteria (NTM) which was first described by Weiszfeiler et al., in 1971 [1]. It is a slow growing mycobacterium, closely related to *M. simiae*. Its isolate shows photochromogenic like *M. kansasii and M. marinum*, which can be differentiated by molecular methods. Although *M. asiaticum* is rarely isolated and a frequent colonizer, it is established to cause both pulmonary and extrapulmonary diseases in human [2]. Patients infected with *M. asiaticum* possibly have the same predisposing factors as those infected with other NTM species. Currently, there is no guideline for treatment of this rare pathogen. Therapeutic regimens are prescribed on case-by-case basis by expert opinions, resulting in variable outcomes. Here we report a case of *M. asiaticum* causing pulmonary disease.

2. Case presentation

In April 2007, a 56 year-old female visited our clinic with history of productive cough with whitish sputum, mild shortness of breath on exertion and low-grade fever especially in the evening for several months. She denied hemoptysis, anorexia, weight loss, other chronic respiratory symptoms and history of tuberculosis close exposure. Her previous medical illness was unremarkable. Additionally, she never smoked nor used alcohol and illicit drugs. On examination, there were no abnormalities on physical findings, including no fever, normal breath sounds and no lymphadenopathies. Chest radiography showed reticulonodular and patchy opacities at the right middle lung (RML) field and minimal bilateral apical pleural thickening (Fig. 1 left). One of the sputum specimens for acid fast bacilli (AFB) smear was positive but Polymerase Chain Reaction (PCR) for *M. tuberculosis* was negative (Seegene, Korea, Republic of) [3]. In Thailand, the negative predictive value of the PCR for *M. tuberculosis* in smear positive specimens was 97% [4]. However, concerning of her persistent symptoms and risk of spreading tuberculosis infection, we decided to start the anti-tuberculous regimen of daily isoniazid 300 mg, rifampin 450 mg, pyrazinamide 1500 mg and ethambutol 800 mg during the waiting time for a result of mycobacterium culture. The treatment was justified according to the local guideline [5].

At the 2-month follow-up visit, her symptoms were significantly improved, and chest radiography showed interval decrease in the size of the opacities. Nevertheless, the sputum culture showed non-tuberculous mycobacterial growth. The working diagnosis was changed to pulmonary NTM disease with partial response to the anti-tuberculous medication. Thus, high-performance liquid chromatography (HPLC) for specific mycobacterial identification and in vitro drug susceptibility test were subsequently performed. Besides, we sent a repeated sputum specimen for mycobacterium culture. In addition, we planned to alter the therapeutic regimen after receiving the drug susceptibility result.

Four months after the treatment, the definite species of the mycobacterium was unable to be identified due to inconclusive results of HPLC. The drug sensitivities showed susceptibility to rifampin but resistance to isoniazid, ethambutol, streptomycin, amikacin, ciprofloxacin, clarithromycin, imipenem and tetracycline. As a consequence of uncertain diagnosis and the knowledge of the discordance between in vitro drug susceptibility and therapeutic response of NTM infection, clarithromycin 1000 mg daily and levofloxacin 500 mg daily were added, and pyrazinamide was discontinued. However, 1 month later,

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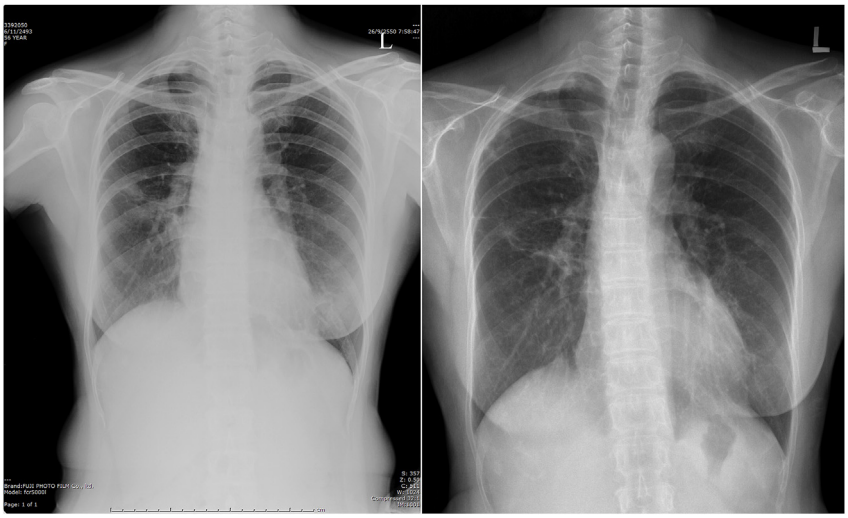

Fig. 1. Chest radiography at the time of diagnosis shows opacities at the right middle lung field. (Left figure) Chest radiography after treatment completion shows residual bronchiectasis in the right middle lung field. (Right figure).

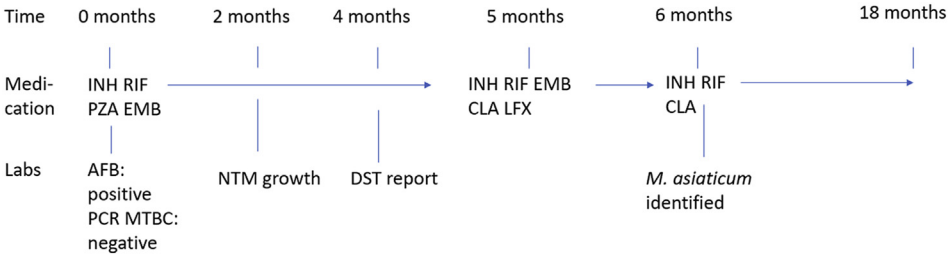

Fig. 2. The timeline of anti-mycobacterial treatment. INH: isoniazid, RIF: rifampin, PZA: pyrazinamide, EMB: ethambutol, CLA: clarithromycin, LFX: levofloxacin, AFB: acid fast bacilli, MTBC: *M. tuberculosis* complex, DST: drug sensitivity testing.

levofloxacin and ethambutol were withdrawn due to tendinitis and toxic optic neuropathy. Thus, she took only isoniazid, rifampin and clarithromycin. Subsequently, her respiratory and constitutional symptoms disappeared in the 5th month of the latest regimen, and *M. asiaticum* was certainly identified during this period. The treatment was planned for total of 18 months, which was completed eventually. The timeline of the anti-mycobacterial treatment was shown in Fig. 2. In addition, all sequential sputum cultures for mycobacterium became negative and chest radiography after treatment completion showed residual bronchiectasis in the RML field (Fig. 1 right). Interestingly, she had regular follow-up visits for 10 years without relapse of this infection.

3. Discussion

Our patient presented with chronic cough, minimal functional class change and low-grade fever with pulmonary infiltrations on chest radiography. Her sputum culture showed *M. asiaticum* growth in only one specimen. With reference to the IDSA/ATS guideline for NTM infection, this did not meet the fulfilled criteria for NTM lung disease. However, we strongly believed that *M. asiaticum* was the culprit pathogen due to the following reasons. Firstly, sputum AFB smear was positive but sputum PCR for mycobacterial tuberculosis complex was negative, compatible with NTM organisms. Secondly, no evidence suggested other diseases or pathogens. Lastly, the patient responded to anti-mycobacterial macrolide-based regimen.

According to data from published literatures, *M. asiaticum* causes infection in several organs including respiratory and musculoskeletal system [2]. This organism has a predilection for a tropical climate and is commonly found in environmental water [2]. Exposure to this natural source is the likely mode of transmission, and there is no published evidence suggesting person-to-person transmission. However, the natural history of the disease and the appropriate therapeutic regimen for *M. asiaticum* infection have not been established. Similar to predisposing factors for other NTM infections, immunocompromised status and chronic lung diseases such as bronchiectasis, COPD, etc. are frequently reported as the comorbidities of patients with the *M. asiaticum* infection. However, noticeably, our patient had no predisposing conditions and the source of infection was not identified.

Interestingly, there were several learning points from our patient. Firstly, the clinical presentation of pulmonary *M. asiaticum* infection was indistinguishable from pulmonary tuberculosis, so sputum culture was essential to confirm the diagnosis. Secondly, HPLC could not identify *M. asiaticum* due to the similarity of the HPLC profiles among other related NTM species. Thirdly, *M. asiaticum* partially responded to the standard anti-tuberculous regimen. Moreover, according to the reported case of Grech et al. [2], prolonged treatment was necessitated to eradicate the organism and prevent relapse of the infection. Our patient took medications for 18 months without clinical relapse during the 10 year follow-up period. Lastly, delayed diagnosis was not uncommon due to nonspecific clinical manifestation, unrecognized pathogen and initial response to anti-tuberculous treatment.

Regarding the rare pathogen, from our knowledge, there were only 6 previously published cases of pulmonary *M. asiaticum* infection (Table 1) [6–9]. This organism commonly infected middle aged and elderly patients with male predominance. The majority of them had chronic pulmonary disease. In addition, there were limited data of therapeutic regimen and long-term clinical outcomes. One of the patients had relapse of the infection within 9 months after the completion of 2 year treatment. Therefore, more evidence is needed for understanding the natural history and therapeutic issues of this mycobacterial infection.

Table 1
Summary of previously reported cases of *Mycobacterium asiaticum*.

	Reported year/ Author	Age/Gender	Symptoms	Comorbidity	Treatment	Duration	Outcomes
1	1983 Blacklock	69/male	Productive cough	COPD	RIF EMB	2 yr.	Relapse 9 mo. after complete treatment
2	1983 Blacklock	48/male	Hemoptysis	Alcoholism	RIF EMB PZA CAP	2 mo.	Partially Improved
3	1990 Taylor	62/male	Cough, weight loss	COPD	INH RIF EMB STP	At least 3 mo.	Improved No further info after 3 mo.
4	2010 Grech	52/male	Productive cough, weight loss	COPD	INH RIF EMB (PZA for first 2 mo.)	12 mo.	Cure
5	2010 Grech	73/female	Productive cough, hemoptysis	Bronchiectasis	AZT PTO CIP MIN (RIF for first 2 yr.)	4 yr.	Cure No relapsed in 18 month follow-up
6	2016 Almukhtar	68/male	Productive cough	CA Prostate s/p RT CMT	None		NA
7	2017 Our case	56/female	Fever, productive cough	None	INH RIF CLA (PZA EMB for the first 4 mo.)	18 mo.	Cure No relapse during 10 yr. follow-up

RIF: rifampin, EMB: ethambutol, PZA: pyrazinamide, CAP: capreomycin, INH: isoniazid, STP: streptomycin, AZT: azithromycin, PTO: prothionamide, CIP: ciprofloxacin, MIN: minocycline, CLA: clarithromycin, COPD: chronic obstructive pulmonary disease, CA: cancer, RT: radiation therapy, CMT: chemotherapy, NA: not available.

4. Conclusion

In conclusion, pulmonary *M. asiaticum* infection is rare. As discussed above, it is possible that some cases have been misdiagnosed, so the prevalence of the disease might be higher than previously reported. Due to phenotypic similarity among various NTM infections, identification of definite mycobacterium species is necessary. However, the diagnosis is difficult because not all rapid mycobacterium identification modalities can identify this rare species, and the treatment is also difficult because of no standard regimen in the current guidelines.

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Availability of data and materials

Relevant data and supporting material are available from the corresponding author on reasonable request.

Authors' contributions

PA wrote the article. The final version was reviewed and approved by all authors.

Ethics approval and consent to participate

The case presentation was approved by the Institutional Review Board, Faculty of Medicine, Chulalongkorn University (IRB No. 710/60).

Consent for publication

Written, informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

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Abbreviations

RIF	rifampin
EMB	ethambutol
PZA	pyrazinamide
CAP	capreomycin
INH	isoniazid
STP	streptomycin
AZT	azithromycin
PTO	prothionamide
CIP	ciprofloxacin
MIN	minocycline
CLA	clarithromycin

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.rmcr.2018.05.014.

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