

## Original Article

A STUDY OF ADVERSE DRUG REACTIONS IN THE TREATMENT OF  
PULMONARY *MYCOBACTERIUM AVIUM* COMPLEX DISEASE

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and <sup>2</sup>Masahiro ABE

**Abstract** [Objectives] Adverse drug reactions interfere with the standard treatment of pulmonary *Mycobacterium avium* complex (MAC) disease; however, few studies have investigated this issue. We studied adverse drug reactions in the treatment of pulmonary MAC disease.

[Subjects] We retrospectively examined 74 patients who underwent treatment for pulmonary MAC disease in our hospital between January 2001 and December 2009. These patients had received treatment with rifampicin, ethambutol (EB), and clarithromycin. We analyzed the adverse drug reactions seen in these patients.

[Results] Twenty-two patients developed one or more adverse drug reactions that led to treatment discontinuation or change in medication, whereas 52 patients did not experience any adverse reactions. The incidence rate of adverse reactions was 29.7%. The adverse drug reactions included visual impairment in 9 patients, liver function disorder in 2, skin eruption in 5, and fever in 5. In most of the cases, the standard treatment could not be continued.

[Discussion] Visual impairment associated with EB was

the most common adverse drug reaction, and it led to the discontinuation of EB, and thus the standard treatment. Additionally, in case of other adverse drug reactions, it was difficult to find appropriate replacements for the causative drugs. Further investigations are required to establish a standard policy for the management of adverse drug reactions that can lead to the discontinuation of chemotherapy.

**Key words** : Pulmonary *Mycobacterium avium* complex (MAC) disease, Adverse drug reaction, Ethambutol (EB), Visual impairment

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## Original Article

IDENTIFICATION OF NOVEL VARIABLE NUMBER TANDEM REPEAT (VNTR) LOCI IN *MYCOBACTERIUM AVIUM* AND DEVELOPMENT OF AN EFFECTIVE MEANS OF VNTR TYPING

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**Abstract** [Introduction] To make more effective use of variable number tandem repeat (VNTR) typing, we identified novel VNTR loci in *Mycobacterium avium* and used them for modified *M. avium* tandem repeat-VNTR (MATR-VNTR) typing.

[Method] Analysis of a DNA sample extracted from a clinical isolate (strain HN135) with the FLX system<sup>®</sup> genome sequencer (Roche Diagnostic System) led to discovery of several novel VNTR loci. The allelic diversity of the novel VNTR loci was evaluated for 71 clinical isolates and compared with the diversity of the MATR-VNTR loci. To improve efficacy of MATR-VNTR typing, we tested typing using 2 sets of loci selected from the newly identified loci and the MATR loci, i.e., one set containing 7 and another 16 loci. Hunter Gaston's discriminatory index (HGDI) was calculated for these sets.

[Results] Six VNTR loci were newly identified, of which 5 showed a high diversity. The HGDI was 0.980 for the improved new typing using a set of 7 loci, and 0.995 for another set of 16 loci, while it was 0.992 for the conventional MATR-VNTR typing.

[Discussion] VNTR typing with the set of the 7 loci enabled a rapid analysis, and another set of 16 loci enabled a precise analysis, as compared with conventional MATR-VNTR typing. A method that uses only VNTR loci with relatively high

allelic diversity is considered to be a useful tool for VNTR typing of MAC isolates.

**Key words:** *Mycobacterium avium*, Variable Number Tandem Repeat (VNTR), Molecular epidemiology, Optimization, Genome analysis

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## A CASE OF PULMONARY TUBERCULOSIS ASSOCIATED WITH ORBITAL MYOSITIS

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**Abstract** Ocular tuberculosis is rare. We report a case of orbital myositis suspected to be infected with tuberculosis. In January 2008, a 34-year-old man experienced discomfort in the right eye. In May 2008, this patient developed right exophthalmos, diplopia, and pain in the right eye, and he was diagnosed with idiopathic orbital myositis. The patient underwent 2 courses of steroid pulse therapy; after which, the dosage of steroids was reduced. The steroid treatment reduced the eye pain, but his diplopia and exophthalmos persisted. By November of the same year, his general malaise had increased, and chest X-ray radiography and computed tomography were performed on 3rd December. On the basis of the imaging results, we suspected active pulmonary tuberculosis of the right upper lobe. The smear made by using the sample obtained after bronchial brushing was negative for acid-fast bacilli, but a *Mycobacterium tuberculosis* nucleic acid amplification test of the post-bronchoscopic sputum yielded positive results. Therefore, the patient was diagnosed with pulmonary tuberculosis. After the 2HREZ/7HR regimen of treatment, the extent of the tuberculosis lesions of the lung was reduced and the exophthalmos and eye pain were alleviated. Orbital myositis is inflammation of the extraocular muscles and can be

either idiopathic, without a known etiology, or secondary to conditions such as tuberculosis, sarcoidosis, or hyperthyroidism. Our patient was not definitively diagnosed with tuberculosis of the eye. A definitive diagnosis of tuberculosis of the eye would require detection of granulomatous lesions in the eye or isolation of *Mycobacterium tuberculosis* by puncturing the eye muscles; however, our findings suggested the possibility that it was secondary to tuberculosis. We think that a careful examination of the chest should be performed for patients with ocular abnormalities.

**Key words:** Orbital myositis, Exophthalmos, Diplopia, Tuberculosis, Response to steroid therapy

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**Report and Information**

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**TUBERCULOSIS ANNUAL REPORT 2010****—(2) Tuberculosis in Foreign Nationals—**

Tuberculosis Surveillance Center (TSC), RIT, JATA

**Abstract** Surveillance data on tuberculosis (TB) in foreign nationals in Japan since 1998 have been obtained. The proportion of foreign nationals infected with TB increased from 2.1% (739 patients) in 1998 to 4.2% (952 patients) in 2010. Most importantly, the proportion of TB patients aged 20–29 years among foreign nationals reached 29% in 2010. About half of the foreign nationals with TB were from China (29%) and the Philippines (23%). In most cases, foreign nationals developed TB within 5 years of immigrating to Japan; moreover, 84% of these patients were 20–29 years old. The proportion of foreign nationals with TB among all TB cases was the highest in Hamamatsu city (9.5%), followed by Gunma prefecture, and Fukuoka city. Twenty-three percent of foreign nationals with TB were employed full-time, 22% were students, and 20% were unemployed. As the number

of immigrants to Japan increases, the proportion of foreign nationals with TB is expected to increase, particularly among young adults and in those from countries with a high burden of TB.

**Key words:** Tuberculosis, Epidemiology, Foreign nationals, Sex and age distribution, Trend, Occupation

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