Genetic and Phenotypic Characterization of Pyrazinamide–Resistant Mycobacterium tuberculosis complex isolates in Japan. Diagnostic Microbiology and Infectious Disease. Chika Miyagi, Nobuhisa Yamane, Bhusal Yogesh, Hiromi Ano, Tetsuya Takashima

【Abstract】

The pncA gene mutations associated with pyrazinamide (PZA) resistance in Mycobacterium tuberculosis complex were determined in 26 PZA–resistant isolates in Japan. Of the 26 PZA–resistant isolates included, twenty–ones were negative for pyrazinamidase (PZase). Of these, twenty isolates had various pncA mutations, resulted in alteration of primary amino acid sequence. However, another one PZase–negative isolate which did not have any mutation on pncA gene. The remaining five PZA–resistant isolates were positive for PZase and had identical pncA alleles with PZA–susceptible isolates. The IS6110 RFLP analysis demonstrated various distinct IS6110 types and five pairs of isolates were very close with each other (>90% identical pattern). This study demonstrates that most of the PZA resistance is due to various mutations on pncA resulting in loss of PZase activity. Further investigation, particularly into PZase–positive but PZA–resistant isolates and a PZase–negative isolate with no mutation on pncA, should be urgent.