Use of Molecular Identification Analysis in a Case of Intra-familial Transmission of Tuberculosis

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결핵균의 유전자 분석법으로 증명된 가족 내 결핵 전파 1예

박의주, 김양기, 캐런, 이영목, 김기업, 운수택, 박영길

결핵균은 공기를 매개로 전파되고 결핵균에 노출된 시간과 최초의 노출 정도가 전파의 위험을 증가시키는 중요한 인자로 알려져 있다. 활동성 폐결핵 환자와 함께 생활하는 가족 내에서 감염이 현저히 증가하는데 이는 결핵균에 노출되는 기회 및 시간이 증가하기 때문이다. 하지만 고식적인 접촉자 조사만으로는 흔히 결핵 발생률을 과소평가할 수 있기 때문에 접촉자 조사와 결핵균의 유전형 조사를 병행하는 것이 감염의 위험이 높은 집단을 선별해내고 발생빈도 및 전염경로를 밝히는 데 보다 효과적인 것으로 보고되고 있다. 이에 접촉자 조사와 결핵균의 유전형 조사를 통해 가족 내 결핵균 전파를 증명한 1 애를 보고하는 바이다. (Tuberc Respir Dis 2008;65:512-516)

Key Words: Mycobacterium tuberculosis, Genotype, Transmission, Family

Introduction

Tuberculosis is an infectious disease caused by Mycobacterium tuberculosis and the transmission occurs nearly always through an airborne route. The length of time exposed to air contaminated with M. tuberculosis, and the extent of intimate exposure are regarded as important factors increasing its risk of transmission of M. tuberculosis. Close contacts living environments with active pulmonary tuberculosis patient increase the time exposed to M. tuberculosis. Patients with active pulmonary tuberculosis produce and expel droplet nuclei holding tubercle bacilli into the air which remain suspended unless ventilation is performed effectively. This can greatly increase the risk of M. tuberculosis transmission during close contact. Conventional contact investigation has been used to identify contact persons with high transmission risks. Genotyping of M. tuberculosis is a very effective way to evaluate contact investigations for transmission. After the introduction of M. tuberculosis genotyping, epidemiologic studies reported that conventional contact investigations compared to genotyping underestimated transmission rates because casual transmission was hard to detect with traditional contact tracing. On the contrary, a case series showed that conventional contact investigations compared to the genotyping approach actually overestimated transmission rates because 5 of 14 isolates proved not to be acquired from the expected source. We report a case of intrafamilial transmission of M. tuberculosis was clearly identified by both conventional contact investigation and genotyping.

Case Report

A 57-year-old male presented to our emergency department complaining of dyspnea (NYHA Classification...
IV). He was a 40 pack-year ex-smoker with a past medical history significant for diabetes and myocardial infarction. The patient had been prescribed HERZ anti-tuberculous medication (Isoniazid 300 mg, Rifampicin 450 mg, Ethambutol 600 mg, and Pyrazinamide 1,000 mg once daily) for the past month after being diagnosed with pulmonary tuberculosis at a primary care clinic. On examination, he was found to have a left sided pleural empyema. Acid-fast bacilli (AFB) were found in the pleural effusion as well as sputum. Subsequent AFB cultures were positive for *M. tuberculosis* and sensitivity testing revealed sensitivity to all anti-tuberculosis medications. Contrastenhanced CT of the chest at the time of diagnosis of pulmonary tuberculosis revealed multiple, variable sized cavity lesions and multiple small nodules with branching opacities in both upper lobes.

To investigate the potential transmission of tuberculosis within his family members, the spouse and three sons of the patient were asked to visit our hospital for the detailed examinations. His spouse agreed, but the three sons declined because they recently all had unremarkable health examinations, to include a chest X-ray without sputum analysis. The wife reported no prior tuberculosis infections or pulmonary symptoms. The mean time of exposure to her husband, the "source patient", was calculated to be 9 hours daily (mealtimes, watching TV, sleeping). The spouse of "contact patient" on physical exam appeared relatively healthy except for a low body mass index of 1.64. After further evaluation, nodular opacities were shown in the right upper lobe by chest radiography (Figure 1). Chest CT demonstrated active pulmonary tuberculosis characterized by small cavities and small nodules with branching opacities. Her sputum AFB smear was negative, but eventually grew positive AFB cultures. Subsequent analysis of the AFB revealed sensitivities for all anti-tuberculosis drugs. She was also administered with HREZ therapy, which included Isoniazid 300 mg, Rifampicin 450 mg, Ethambutol 600 mg, and Pyrazinamide 1,000 mg once daily.

IS6110 Restriction Fragment Length Polymorphism (RFLP) for the isolates was performed separately for the two cases at the Korean National Tuberculosis Association to ascertain whether the husband's *M. tuberculosis* was the transmitted source. The pattern of RFLP proved

![Figure 1](image-url)